SEP Assessment report

Research Institute for Medical Innovation (RIMI)

Part B:

Evaluation of research programs

April 2026

Based on the Strategy Evaluation Protocol 2021-2027

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Introduction program evaluation

The Radboud University Executive Board asked an evaluation committee of external peers to perform a two-level evaluation of its Radboudumc Research Institute for Medical Innovation (RIMI) both at the institute level (Part A) and at the research program level (Part B). This two-level evaluation was carried out as part of the six-yearly evaluation of the RIMI institute. The RIMI institute has 47 research programs. The research of the Radboud Institute for Molecular Life Sciences (RIMLS) of the Faculty of Science is evaluated as a 48th research program. The evaluation committee reviewed and assessed each research program separately, reported in this document. The results of the RIMI institute evaluation (part A) are compiled in an overall assessment report.

This introductory chapter describes the procedure and scope of the program evaluations. Subsequently, each program is assessed in a separate chapter.

Assessment criteria and scope

The institute and research programs were evaluated according to the Strategy Evaluation Protocol 2021-2027 (SEP), the protocol for research evaluations in the Netherlands. The main goal of the SEP is to maintain and improve the quality and societal relevance of research as well as to facilitate continuous dialogue about research quality, societal relevance and viability in the context of research quality assurance. This goal is accomplished by assessing a research unit (in this case a research program) considering its own aims and strategy.

Mandatory assessment criteria

The evaluation committee assessed each program assessment according to a list of questions derived from the main assessment criteria of SEP. The assessment included a backward-looking and a forward-looking component. The committee judged the performance of each research program based on the list of SEP questions and reports its conclusions as well as recommendations here. The main assessment criteria are:

Research Quality

The quality of the research programs over the past seven years (2018-2024) was evaluated within its international and national context. The assessment committee aligned its judgment with the program's stated aims and strategy. Central to this evaluation was the contribution the research makes to the body of scientific knowledge. The committee specifically assessed the quality and scientific relevance of the research output, alongside the program's academic reputation and leadership in its field. The assessment of the criterion research quality (and the other evaluation criteria and aspects) was based on a narrative argument supported by evidence of the program's scientific achievements within the relevant research field (national and international).

Societal Relevance

The assessment of a program's societal relevance covered its impact, public engagement, and the uptake of research. This was evaluated across economic, social, cultural, educational, and other relevant terms. It is important to recognize that societal impact often takes time to become visible. Therefore, impact evident within the past six years may be the result of research conducted much earlier. The assessment committee judged the societal relevance by looking at a program's accomplishments relative to its stated goals and strategy. Where appropriate, the committee also considered the connection between teaching and research (teaching-research nexus).

Viability

The assessment also included the scientific and societal relevance of the program's upcoming six-year goals. The assessment committee evaluated the strategy, leadership, and management to ensure

these are optimal for goal attainment. The committee also assessed the adequacy of plans and resources for implementation. Finally, the committee offers reflections on the program's viability considering broader developments and its institutional context.

Additional questions

In addition to the criteria specified in the SEP, the Radboud University Executive Board requested from the evaluation committee to:

- Propose, based on particularly good research quality, social relevance and viability, up to six research programs as so-called **top programs**. These top programs will receive special attention and support over the next six years and will be used to (co-) profile research at Radboudumc. The criteria for the selection of top research programs are listed in Appendix III.
- Assess the added value of the scientific integration of research of Radboud Institute for Molecular Life Sciences of the Faculty Science (RIMLS FNWI) with RIMI, and propose, based on this added value, measures how the impact of integration can be improved.

Appendix IV lists the indicators for both the evaluation of the institute (part A) and the research programs (part B) and the link between these indicators and the different evaluation criteria and aspects.

The composition of the (sub)committee

The entire evaluation committee consisted of 21 members (19 senior and mid-career researchers, one PhD candidate and one patient representative). Eleven members participated in the assessment of the research programs only, and 10 members in the assessment of both the research programs and the entire RIMI Institute.

Each program was assigned to several committee members with an affinity for the topics in that research program. In Appendix II the composition of the subcommittees members for each program evaluation is shown.

The committee proceeded according to the SEP 2021-2027. The secretary instructed the committee chair on his role in the evaluation. In its first meeting on 18 June 2025 the entire evaluation committee was briefed by the secretary on research evaluations according to the SEP 2021-2027, and by the RIMI Research Director on the Dutch research landscape and position of the RIMI institute therein.

Prior to the site visit, committee members wrote preliminary assessment reports of both the research programs and the RIMI institute based on the written information and video recordings that were provided before the site visit. During various preparatory meetings of the ten committee members who evaluated the RIMI institute, the members discussed the preliminary assessments of the RIMI institute and identified questions to be raised during the site visit. They also agreed upon procedural matters and aspects of the evaluation.

The site visit took place from 10 November to 14 November 2025 (see the schedule in Appendix I). The first three days of the site visit focused mainly on the 48 research programs (Part B). The last two days of the site visit were devoted to the institute evaluation (Part A). After the interviews were conducted, the committee discussed its preliminary findings. This was done to allow the chair to present the preliminary findings and to provide a solid base with argumentation to draft a first version of this assessment report with the help of the secretaries. The final evaluation is based on both the documentation provided by RIMI and the information gathered during the interviews with representatives of the institute during the site visit.

The draft report by the committee was presented to RIMI for factual corrections and comments. In close consultation with the chair and other committee members, these comments were reviewed to draft the final report. The final report was sent to Radboudumc on April 1st 2026

1 Sustainable health systems

The sustainability of healthcare systems is under pressure, facing financial, labor, societal, and ecological constraints. A broad spectrum of detrimental factors can be identified, including workforce shortage, loss of solidarity, failing prevention, an increase in older patients with comorbidities, and ecological changes.

1.1 Mission, vision and strategy

Different factors interact and play a role at different levels of policy and decision-making. The program's goal is therefore to connect macrolevel strategies (benefit package designs, preparedness and readiness plans for shockwaves, and models of governance that stimulate sustainability), with meso-level improvements (promising models of care and reimbursement, networks, lifestyle medicine), and micro-level (new technologies, professional practices, shared-decision making, reducing waste, and lean practices in handling pharmaceuticals).

The program's main aim is to design, implement, and evaluate policies at the micro and meso-level, and use and scale this knowledge to contribute to sustainable health systems at the macro-level. In coming years, the program will focus on care for older individuals, labor market and personnel sustainability, health financing, and prevention.

Sub-aims of the program include the creation of a shared framework to study sustainability in healthcare systems to answer questions on four themes, which include measuring the impact of transformative changes on sustainability, further developing and operationalizing health technology assessment (HTA) lifecycle approaches including early HTA and disinvestment in low-value care, and allowing better choices on all levels of the healthcare system. This involves creating a knowledge hub on sustainable and proper use of care. The program integrates health care with disciplines such as health economics, policy, law, implementation sciences, applied ethics, and environmental science.

1.2 Research quality

The program contributes to a sustainable health system through an improved understanding of the interaction between decisions and constraint at the local and the national level. The program mainly seems to focus on the regional and national context. There are some international collaborations on projects and publications, but it is unclear whether there are any long-term, strategic collaborations with international partners.

The work is robust and follows examples conducted in other countries, for example NICE HTA and the evaluation of digital technologies and the Choosing Wisely initiative in Canada to reduce waste on low value interventions. Although carried out well with demonstrable impact, they are less robust in terms of constituting new ideas or novel research.

The aim of the program is to design, implement, and evaluate policies at the micro and meso-level, and use and scale this knowledge to contribute to sustainable health systems at the macro level. These would benefit from clear definitions, rather than being a mix of aims (contribute to sustainable health systems) and strategy (design, implement and evaluate policies).

The quality of the research is reflected in scientific publications, competitive grant acquisition, and PhD theses. The program has ample experience in research on the affordability and sustainability of the Dutch healthcare system, on how policy affects healthcare purchasers, healthcare providers, and patients, and on the effect and impact on healthcare expenditure, accessibility and personnel deployment. The program has had an eight-year financial agreement with the Dutch Ministry of Health

to align policy questions with scientific research. It is unclear whether this agreement will be renewed or not. A close collaboration with decision makers is a strength of the program.

1.3 Societal relevance

The societal relevance of the program is a strength. The program's research aims to inform policies that ensure equitable access to healthcare services while maintaining solidarity within the system. This is a highly relevant topic as healthcare costs continue to rise. By focusing on key themes such as accessibility, quality, healthcare costs, ecological burden, solidarity, and the role of healthcare policies, the program contributes to shaping sustainable healthcare. The program actively contributes to societal debate and policy development through participation in influential committees of ZonMW, the Dutch Health Council, and the Ministry of Health. These contributions ensure that research findings are translated into actions.
Regarding the research-teaching nexus: the program strives to embed the program's research in the bachelor and master programs of biomedical sciences and medicine.

1.4 Viability

The group started about 8 months ago with a new group leader. The program is viable, given the focus on a highly urgent topic. The program wants to extend its current research projects by focusing on care for older people, the healthcare labor market, and health financing. The program aims to initiate new collaborations and research grant applications on prevention. Collaboration with external partners is important to optimize finances of the group. This area remains important and relevant to society, especially with the speed of development of new medical technologies and the potential of AI to change many aspects of healthcare. A future focus on AI, how it is being used and implemented in the health system would be valuable, especially in relation to the impact on workforce.
If the resources available remain the same, then they should be sufficient for the next 6 years, with appropriate prioritization.

1.5 Future outlook

The program is in development with a new research leader/spokesperson. The group is diverse in expertise and interests. Maybe the program is, therefore, vulnerable due to scattered expertise and teams that are too small; a task for the near future is to discuss focus for the coming years. At present, the focus of the program is mainly local and national. In the future, a stronger international network and more visibility are necessary.

There are some potential risks and weaknesses. First, the shift of focus in the coming years may depend on the expertise of the current staff and be vulnerable in the future. Second, the faculty seems top-heavy with many professors and few additional senior researchers. Finally, the new focus may become too fragmented.

1.6 Conclusion

The program is of high quality, with substantial societal relevance, and viability, although there are concerns about the latter. The program mainly seems to be active in the regional and national context and will benefit from a stronger international outlook. A clearer description of the strategy can sharpen the focus. The societal relevance of the program is a strength; research findings are translated into actionable policies, and the program actively contributes to societal debate and policy development. The program is relatively new and appears viable, but the position of young researchers within the group needs to be strengthened to give the program a long-term perspective.

1.7 Recommendations

- Strengthen the cohesion in the group, especially the involvement of PhD candidates seems to be low. Young researchers do not seem to be established within this program.
- The program may benefit from a sharper focus and a clearer description of the strategy. On the website of the Radboudumc the aim is described as “make health care systems sustainable, from a financial, work force, societal, and environmental perspective.” This may be the description of the aim also for this program.
- The program’s summary suggests that most of the products relevant for societal relevance are scientific publications. The program may benefit from expanding the scope to other products to ensure translation into an actual real-world impact.
- The collaboration with clinical departments may be strengthened; for clinical departments the focus of this research program is not a high priority.

2 Stimulating appropriate care and reducing low-value care

In the coming decade, the demand for healthcare will grow much faster than the available workforce. Increasingly, we realize that healthcare is not always (cost-)effective, that it can create an unnecessary workload for healthcare professionals, that it can have a significant impact on the environment, and that it can even harm patients. To ensure a sustainable healthcare system, it is crucial that appropriate care becomes the standard in the Dutch healthcare system.

2.1 Mission, vision and strategy

Appropriate care is ideally provided according to a shared decision-making process regarding diagnostics and treatment and must have proven added value for patients in terms of effectiveness. This means that reducing care without added value, so-called low-value care, is essential for the sustainability of the healthcare system. The program addresses the following research questions from different perspectives, involving multiple research groups: how can low-value care be identified and reduced, how can high-value care be implemented, how can shared decision-making (SDM) to promote appropriate care be improved, and how can the workload for healthcare professionals be reduced and the environmental impact in terms of waste production and CO_2 emissions be minimized? The program's shared ambition is to become the leading national center for implementing high-value care and de-implementing low-value care. The program contributes to health science research at Radboudumc, with the goal of improving the health of Dutch citizens. To achieve this, the program develops and tests various outcome measures, guidelines, and protocols that can be applied both nationally and internationally. By addressing the above-mentioned questions, the program will positively impact the Dutch healthcare sector by improving patient outcomes, reducing the workload for healthcare professionals, and minimizing CO_2 emissions.

2.2 Research quality

The program builds on more than fifteen years of work on improving appropriate care and reducing low-value care. The group combines research, implementation, and evaluation. According to the group's own description, it positions itself as a pioneer in the field of implementation science. The group highlights its contributions to the theme through publications in high-quality international journals, the development of frameworks, typologies, and practical tools. It collaborates with international partners (e.g., Aarhus University, the Karolinska Institute, Choosing Wisely Canada) Nationally, the research group is aligned with Radboudumc's strategic theme of appropriate care, its strong links to Dutch initiatives, and its influence on Dutch health policy (e.g., guidelines). The program focuses on shared decision-making, sustainability, and workforce challenges, presenting a broad multidisciplinary agenda.

This practical and national orientation is visible in day-to-day research activities. Most members of the program work in clinical practice, bringing clinical experience into the research cycle and ensuring that clinical knowledge gaps translate into research and implementation efforts. This close clinical integration enables a feedback loop but also contributes to a predominantly practice-oriented output, and the theoretical and methodological development of implementation science receives less emphasis. There is some overlap with other programs and therefore a need for stronger positioning and collaboration.

There are substantial scientific contributions of high quality, supported by relevant and important competitive grants, PhD completions, and alignment with international research agendas. Within the Netherlands, the group has established itself as a recognized authority on this subject, securing large grants and shaping national policy discussions. However, while conceptual innovation is present, much of the work remains applied, which may limit visibility in broader international theoretical debates.

Furthermore, the program is mainly working on clinical (acute) care, whereas other sectors (e.g., long-term care, mental health, social care) are less represented, whereas in some clinical domains the number of studies exceeds the number of resulting publications, raising questions about the coverage of clinical domains and research depth.

In summary, this program exhibits an excellent scientific quality through a research portfolio with strong national influence, deep practical embedding, and significant implementation achievements, yet with room to strengthen theoretical contributions, enhance international visibility, and sharpen strategic focus.

2.3 Societal relevance

The program addresses key questions in Dutch healthcare, such as overtreatment, workforce strain, and sustainability, and highlights its societal impact. This work has informed national guidelines and policies, reduced unnecessary interventions, and improved patient outcomes. The development of tools such as do-not-do lists has received media attention, and collaborations with professional associations, insurers, patient groups, and industry partners show by uptake into practice. The program is integrated into national initiatives such as 'Zorgevaluatie & Gepast Gebruik' and the 'ZonMW Kaderprogramma Passende Zorg', and has concrete impacts such as 'bending the curve' in clinical practice. The international influence is growing, with projects adopted in Denmark and collaborations at the European level. The impact is primarily achieved through practical tools and implementation strategies rather than conceptual frameworks.

2.4 Viability

The program is well aligned with national priorities such as IZA (Integraal Zorgakkoord) and ZE&GG (Zorgevaluatie en Gepast Gebruik), and with a multidisciplinary team of thirteen senior researchers, and a track record in attracting competitive funding from ZonMw, NWO and others, viability is good.

The relevance of the topic offers growth potential. The absence of a formal research group board, limited meeting structures, and overlapping research scopes signal a need for stronger organizational cohesion and improved collaboration. With the upcoming retirement of key RGLs succession will need attention.

2.5 Future outlook and challenges

Looking ahead, the research group is well positioned to expand its national leadership, supported by policy alignment, substantial upcoming funding opportunities, and a growing network. However, several aspects require attention: reliance on project-based funding, limited organizational cohesion, and overlap with other research groups or lack of collaboration with other research groups may hinder long-term viability. Sustaining international visibility, engaging additional clinical domains, and strengthening theoretical contributions remain important ambitions. Time constraints, funding pressures, and forthcoming leadership transitions further underscore the need for strategic prioritization, deeper collaboration, and structured governance and team cohesion to secure continued growth and impact.

There are some potential risks and weaknesses. First, there is a lack of theoretical and conceptual contributions, which may limit international visibility. Second, the cohesion within the program is suboptimal and can be improved. Finally, the longer term planning of staff positions is lacking.

2.6 Conclusion

The research group demonstrates excellent scientific quality, and societal impact, and a good base for viability. It has established itself nationally as a leading authority in appropriate care, supported by high-quality research, substantial grant success, and clinical embeddedness. Its practical focus has generated improvements in healthcare delivery and policy. At the same time, the research group would benefit from strengthening its theoretical contributions, broadening its international visibility, and expanding beyond predominantly clinical domains. The group is well positioned for continued growth and influence, but ensuring organizational cohesion, securing funds, strategic focus, and sustainable leadership will be essential to evolve.

2.7 Recommendations

- Consider strengthening the theoretical and methodological foundation through investing in conceptual and methodological contributions
- Implement a structured internal organization, including regular joint activities to improve team cohesion and shared identity.
- Sharpen the strategic positioning, by more clearly articulating and communicating the unique contributions, and by strengthening collaboration and alignment with other programs to reduce overlap.
- Consider, within the possibilities of manpower, to broaden the research focus beyond acute care, ensuring wider applicability within and outside the clinical domain.

3 Value-based networked healthcare

This research program incorporates the patient's context in communication and care in order to improve person-centered healthcare. The program anticipates improving value of care and improving health – using Huber's Positive Health concept – for people with complex health needs, as well as improved interprofessional collaboration and job satisfaction.

3.1 Mission, vision and strategy

The program specifically addresses societal problems and is aligned with objectives for societal relevance described in the Dutch Ministerial reports on person-centered, integrated and appropriate care at the right place. The focus is on continuity of care and on optimizing self-management, empowerment, and resilience of people with complex health needs and their caregivers, with support from health professionals. The program contributes to health science research at Radboudumc for improving health of citizens in the region Nijmegen / Oost Nederland. Research is performed from a patient, caregiver, professional, organizational, and societal perspective.

The specific goals are operationalizing, validating and evaluating patients' and caregivers' values and value-based networked care in people with complex health needs and their caregivers in their personal context (including social and cultural diversity). Further goals include improving personalized healthcare through shared decision-making and prediction models, patient participation at the collective level for quality improvement, applying and extending state-of-the-art research designs and methodologies for evaluating value-based networked care for people with complex health needs. Finally, the goals include developing, evaluating, implementing and sustaining person-centered care pathways for people with complex health needs, based on patients' and caregivers' resilience and values, including attention to interprofessional collaboration and job satisfaction.

3.2 Research quality

The quality of research is high, and the program has been successful in initiating and participating in large national and EU grants. For example, three Horizon Europe consortium grants for consortia have been awarded. The program members have scientific impact as shown by their involvement in decision making procedures, the impact of their COVID-19 expert center, and the high citation scores of some of their publications.
The high research quality is further reflected by leading positions in large consortia, and by program members setting research agendas and influencing decision-making. Furthermore, program members chair and participate in many clinical guidelines, showing a strong reputation in the clinical field.

The research excels in applied relevance and policy alignment. However, a more explicit articulation of theoretical or methodological contributions to the conceptual underpinnings of value-based and integrated care could strengthen its profile within the academic discourse.
The program has a strong regional and national focus with high impact as shown in the influence on local and national decision-making, and roles in national clinical guidelines. The grants received by the EU consortia show expansion of activities outside the Netherlands. The international strategy of the program could be more explicitly articulated. While the unit's participation in several large EU-funded consortia and publications in leading international journals show a growing international footprint, it remains somewhat implicit how these collaborations contribute to a coherent international research agenda or theoretical positioning.

The program has a methodological approach that they apply to a variety of clinical topics (e.g., COVID-19, Parkinson, allied healthcare, geriatric medicine). This seems a well-considered and successful strategy, but does introduce overlap with other programs.

3.3 Societal relevance

The research projects have high impact, for example the EDOMAH program for people with dementia and their caregivers. A strength of the program is the strong involvement in national clinical guidelines development. Researchers have impacted international policymaking at numerous occasions and events, including the WHO Global Oral Health Conference 2024 (Bangkok), United Nations High-Level Meetings on UHC and NCDs (New York), the Lancet Commission on Oral Health, and the Lancet Commission on the European Health Union. Public engagement is evident through close collaboration with patients, caregivers, and professional organizations, and by translating research findings into practice and education. The standard approach for patient participation is excellent.

All outputs of this program should, by definition of value-based healthcare, have a positive impact on society. In this context, focusing on the methods for assessing the value of healthcare will have wide application and hence impact on society. As potential costs of healthcare continue to rise, this work will become essential.

3.4 Viability

Viability of the program is good. Its focus on value-based, person-centered, and networked care directly addresses key national and international healthcare challenges and hence shows clear scientific and societal relevance for the coming years. The program has established a core group and steering committee and organizes regular strategic and scientific meetings. They also organize research through national and international consortia.

Program's core group monitors opportunities for funding in collaboration with the research group leaders and senior researchers, which implies that the program uses a strategic approach to ensure optimal acquisition in the future.

The program is, however, supported by a relatively small number of researchers, and therefore links nationally and internationally will be important for the sustainability of this program. The aim of applying for a European grant is relevant, as success in this area would cement their role in this field. The key balance to get right will be a blend of work on overarching methods that have broad applicability, balanced against applied research in specific clinical areas that demonstrate the effect in practice.

3.5 Future outlook

The group's regional embeddedness is a unique strength for conducting real-world implementation research; however, ensuring that regional data and experiences are used to address international theoretical and methodological questions will be critical for long-term academic distinction. There are some risks and weaknesses which include maintaining the balance between applied and conceptual work, and a lack of clear strategy for international research.

3.6 Conclusion

The program demonstrates good research quality and good societal relevance and is viable. The program has a strong regional and national focus with high impact as shown in influencing local and national decision-making, chairing and participating in national clinical guidelines. The international strategy of the program could be strengthened. The research projects have high impact and are highly relevant to society.

3.7 Recommendations

- Consider changing the title of the program; 'value-based networked healthcare' does not seem to be a clear or understandable concept.
- The group's work is clearly recognized in the European community of practice, but the unit could articulate clearer priorities for its international partnerships and demonstrate how its regional research serves as a model for system transformation beyond the Netherlands.
- Strengthen the cohesion in the program; individual researchers are good, but the combination does not seem to lead to synergy.
- Increase focus and develop a strategy for choosing topics; the program is a merger of three smaller groups with a diverse set of topics; the program would benefit from more focus.

4 Contextual, personalized communication and care

Contextualizing healthcare is a process of incorporating information about a patient's life circumstances, behaviors, and other systemic factors into care. Research on contextualized care is urgent, as the current medical practices often focus on medical guidelines and AI-guided medical care, which threatens the importance of the individual person within their own context.

4.1 Mission, vision and strategy

The program's common aim is to incorporate patient context in communication and care to improve person-centered healthcare. The program strives to achieve this through integrating it structurally into communication between the healthcare professional and the patient and their family, the care plans, and the information exchange and transfer between healthcare professionals. The specific program mission is to enhance contextualized communication as a prerequisite to deliver meaningful person-centered care.

The program focuses on the following goals: increasing qualitative and quantitative insights in the current contextualization of communication, its integration in health care planning, documentation and information transfer, by accounting for sex, gender, culture and other factors related to health inequity such as social exclusion, poverty, inadequate housing, a lower social economic status, limited intellectual capacities, or a limited level of health literacy, developing new and actualizing existing knowledge and theory around contextualized communication and care processes, developing, actualizing and implementing methods to code, understand, quantify, and document personalized contextualized communication and care, developing and implementing interventions for all those involved to increase personalized contextual communication and care, and evaluating its impact on patients and relatives, healthcare professionals, health outcomes, and costs.

4.2 Research quality

The program is at an early developmental stage, having existed for just over a year. During this period, the group has brought together several projects and researchers that align with a shared thematic focus on communication, personalized and contextualized care in clinical practice. Three PhD projects illustrate the scientific orientation of the group: a project on moral distress in emergency departments, a project on automated medical reporting, and a project that focuses on positive health for people with intellectual disabilities. While these projects individually demonstrate relevant scientific potential, the program is still in its foundational phase. Coordination between themes is being developed, and the transition from thematic ideas to structured research programs is ongoing. Team-building meetings and collaborative discussions have been used to shape the scientific agenda and clarify shared priorities.

The program's self-assessment report demonstrates that, despite its recent establishment, the broader research program in which the researchers operate has built a good scientific foundation in the past in the field of contextual, personalized communication and care. Their overarching mission to understand, theorize, measure, intervene, and evaluate is coherent and strategically aligned with international priorities.

The scientific quality described in their report reflects meaningful contributions in shared decision-making and contextualized communication, the effectiveness of specific interventions in palliative and primary care settings, and practical tools such as the teach-back method have been evaluated with measurable effects. Large-scale population studies have contributed to understanding sex-specific health differences. Research on ethical and existential dimensions of care, such as studies on advance care planning, further illustrates the breadth of the program.

Taken together, this depicts a program that is very young but scientifically anchored in a wider, productive, and (inter)nationally connected research environment. Their envisioned trajectory is to deepen theoretical foundations, strengthen national collaboration, and consolidate thematic focus. This offers a credible path toward maturing into a more developed and impactful research program.

4.3 Societal relevance

The program demonstrates good societal impact. Its research tackles hurdles of affordability, equity, and quality in healthcare. They report outreach and knowledge translation activities, including the training of more than 1,000 healthcare professionals, contributions to national policy debates such as 'completed life', involvement in guideline committees, and active public engagement through media, podcasts, blogs, and parliamentary hearings. Their explicit attention to minority groups reflects an effort to address inequities in care.

While these examples illustrate meaningful individual impact, the societal effects at the level of the newly formed program remain limited due to its very recent establishment. The researchers' personal networks do not yet translate into collective program visibility, and structural collaborations with external partners such as universities, healthcare institutions, and patient organizations. Patient involvement has not yet been formalized, as evidenced by the absence of a Patient Board, which they envision forming. Furthermore, systematic long-term evaluation of impact is not yet in place, although early efforts include translation of findings into education, workplace coaching, and continuous feedback for practitioners.

4.4 Viability

The program has a credible and satisfactory basis for future viability. The group has a relevant mission, solid institutional embedding at Radboudumc, and the advantage of researchers who work as both clinicians and scientists. There are examples of successful past acquisition of competitive national and international grants and leadership roles in professional organizations as indicators of viability. At the same time, external partnerships and collaboration with other research groups remain limited and that the small core team may face capacity problems as the program grows.

With only one year of operation, structures, collaborations, and research lines are still maturing. Internal cohesion is developing through regular meetings and institutional support.

4.5 Future outlook and challenges

The program's future outlook involves maturing its early-stage research lines into a coherent program, strengthening thematic coordination, and expanding collaboration beyond individual networks. From the committee's perspective, and in line with the group's own SWOT analysis, the group's next steps require consolidation. They need to raise the visibility of their research lines as the program is new and as a group, they are not fully a collective entity yet. Strengthening collaboration with research groups, formalizing patient involvement, and developing clear methods to evaluate their interventions will be helpful. For societal impact, embedding impact evaluation in projects, and enhancing collaboration with healthcare providers, patient groups, and policymakers will increase the reach and demonstrate benefits of the research.

There are also risks and weaknesses. The continuity of the program could be a challenge due to its size and limited structural funding, the specificity of the topic and the upcoming retirement of a founding leader. Furthermore, the work may also risk being seen as peripheral to clinical research.

4.6 Conclusion

Although still in its infancy, the research group stands on a solid scientific foundation built within a broader, well-established past. Its thematic focus aligns with national and international priorities and shows clear potential for impact. Current projects demonstrate relevance, and the team's clinical ties and motivation support future growth. However, the program must mature structurally: strengthening external collaborations, formalizing patient involvement, enhancing visibility, and ensuring sustainable staffing and funding. With strategic consolidation and clearer focus, the group is well positioned to evolve into a contributor to research and practice.

4.7 Recommendations

- To strengthen the research program's scientific program, by shaping the current projects into a clear and cohesive research agenda. This requires a better definition of concrete research lines. A useful guiding principle is to choose lines that allow sufficient focus and depth to deliver high-quality scientific output.
- To increase the program's visibility and position through joint publications, a shared communication strategy, and clearer representation as a unified program in national and international networks, but also within the departments of Radboudumc and research groups of RIMI.
- To enhance societal impact through active patient and public engagement, including establishing a Patient Board, embedding patient perspectives in all research activities, and evaluating the societal impact of their work.
- To continue translating research into practice, particularly through education and workplace coaching, but ensure this is grounded in strong scientific outputs rather than service provision alone.

5 Psychology, Behavior and Health

Behavior change is not only necessary in prevention of disorders, but also in adherence to treatment and aftercare. For example, it is important to study how we can get patients to improve their lifestyle. This research program addresses behavior change and psychology related to health.

5.1 Mission, vision and strategy

The mission of the program is to improve the impact of health psychology and behavioral medicine research on health and healthcare through the injection of core psychological and behavioral change principles.

The program's associated goals are collating expert insights about psychological and behavioral methodologies across Radboudumc psychological and behavioral scientists, enhancing internal collaboration and external awareness of central mechanisms and approaches in health psychology and behavioral medicine, and co-creating and evaluating suitable interventions to contribute to well-being of people living with mental health or somatic conditions.

The program focuses on methodological rigor, scientific rigor and clinical relevance. To make impact with methodological and scientific rigor, the program aims to use high quality research methodologies for societal and scientific challenges in medicine with a psychological or behavioral component, integrate these methodologies (and related expertise) in high specialist clinical care to advance clinical care and scientific output across various mental health and somatic conditions, contribute to unraveling the 'black box' of psychological and behavioral change mechanisms in health and disease, innovate health and healthcare through implementation of psychological and behavioral change scientific outcomes, integrate basic mechanisms of psychology and behavior in health problems in research designs across Radboudumc research programs, and increase uptake of psychological and behavioral change outcomes in research in the medical setting.

In addition, regarding clinical relevance, the program aims to reduce psychological distress and enhance self-management and well-being in people with somatic conditions. Furthermore, the program addresses secondary prevention of mental health problems and disorders, and broader awareness of psychological and behavioral principles in health and among healthcare professionals. Lastly, the program focuses on reduced health inequalities based on psychosocial barriers.

5.2 Research quality

This rather new (three-year-old) research program, partly based on already existing collaborations, is positioned at the intersection of psychology and medicine and aims to improve the impact of health psychology and behavioral medicine research on health and healthcare through the integration of core psychological and behavioral change principles. It focuses on methodological rigor, scientific innovation, and clinical relevance, with a strong emphasis on interdisciplinary collaboration and translational research. The multidisciplinary approach is reflected in the composition of its team of key researchers with amongst others RGLs from Medical Psychology, Psychiatry, IQ Health and Primary Care. The program demonstrates in general a good research quality using various state-of-the-art methodologies and numerous peer-reviewed, usually open access publications, successful grant acquisition, and impactful key articles. Over 60 PhD theses, most resulting from transdisciplinary collaboration, have been defended. Prime examples of scientific output include eHealth tools developed in collaboration with industry partners and a position paper on a behavioral change implementation framework. The program maintains strong connections with its close academic partners (Radboud University and the Open University) and has a strong national impact focus. Researchers have received prestigious awards and grants, and member researchers are in editorial boards of leading journals and involved in formal collaborations with academic and industry partners. The program's impact pathway is well aligned with its goals and seems viable, Overall, the program's current research quality is good, with a clear potential for further improvement as it might benefit

from a better balance between breadth and focus, the implementation of its impact pathway, and expanding its participation in international networks.

5.3 Societal relevance

The program is designed for broad impact by integrating behavioral and psychological principles into routine clinical practice, affecting the entire patient journey. The strategy for societal impact is built on three approaches: infrastructure activities as a horizontal layer enabling co-creation and implementation and supported by Health Innovation labs and national expertise centers, a pillar focusing on elucidating transdiagnostic behavioral mechanisms and developing evidence-based self and shared interventions tailored to specific conditions and finally a more horizontal well-developed dissemination and implementation program. There are ample examples of evidence-based interventions that have been developed, relevant collaborations with patient organizations and others. The strategy for societal relevance was further illustrated during the meeting with the committee. The societal relevance of the program is very good.

5.4 Viability

The now three-year-old program clearly and effectively unites leading researchers with expertise in behavioral change and mental health from various departments (Medical Psychology, Psychiatry, IQ Health, Primary Care). In addition, and essential to its goals and strategies, it covers the full spectrum of care, from hospital to primary and specialized mental health care, and maintains strategic partnerships with care facilities, academic partners, and public organizations. It's so called 'octopus approach' has allowed effective dissemination as well as continuous updating and integrating developments in the field.

The program leaders plan to invest in career path landscaping, in enriching the program with neuromodulation and biomarker approaches available within the RIMI, and aim for large scale consortium grants for which the transmural, translational and transdiagnostic character of the program is indeed a good match given the current funding landscape. Sustainability, however, in terms of organization and prospects for more broader collaboration outside the RIMI seems to depend on funding from the Radboudumc fund. The viability, despite uncertainties surrounding a relatively new program, is no cause for concern.

5.5 Future outlook

The future outlook concerns the program's goals and strategies, with translational, transdiagnostic, transmural and lifespan approaches. There are perceived limitations in funding and in outreach and implementation strategies. The opportunities are significant, with growing international attention for the program's topic, also from funding agencies, which would allow for stronger participation in international networks. There is also the potential for enhancing societal impact by expanding to new fields such as primary care. Currently, the program is still mainly nationally positioned, and a tension exists between breadth and focus.

There are some risks and weaknesses including finding the right balance between focus and breadth, a lack of post-docs' career development paths and dependence on too few collaborations.

5.6 Conclusion

This three-year-old program is partly a continuation of a previous program and allows collaboration of researchers with expertise in behavioral change and mental health from various departments. In addition, and essential to its goals and strategies, it covers the full spectrum of care and has established relevant strategic partnerships. Its so-called 'octopus approach' has allowed effective dissemination as well as continuous updating and integrating developments in the field. Research quality is good, and societal relevance and viability are also strong, with clear potential for further

growth and impact through international networking and large-scale consortium grants. As for every young and diverse group, the balance between breadth and focus still must be found.

5.7 Recommendations

- Being recently founded, the program should give priority to growing cohesion and develop a strategy by defining core research themes that align with strategic goals and funding opportunities.
- Participation in national and international research networks and consortia will enhance visibility and impact, as well as competitiveness for large-scale grants.
- The program should explore synergies with other RIMI programs and institutional resources to strengthen translational research.

6 Quality of Life of Vulnerable Patients

Vulnerable patients are present in all stages of life. Future health and health care faces progressive aging, increasing numbers of vulnerable patients and rising numbers of people with intractable diseases. This research program addresses this as it focuses on assuring quality of life during life care and therapies.

6.1 Mission, vision and strategy

The mission of the program is to have a significant impact on the health and healthcare of vulnerable patients. The program's main goal is to augment quality of life of vulnerable patients across all age groups and conditions, for all those in primary care, ambulatory and clinical situations. The program aims to achieve this by exploring patient vulnerabilities in all dimensions and by developing and implementing sustainable, innovative strategies, including integrated care research programs.

Nine impactful sub-aims have been identified that will operationalize the mission of the program, encompassing a broad spectrum from personalized health care diagnosis and intervention, exploring the underlying mechanisms driving the complexity of vulnerability to integration of interdisciplinary care programs.

6.2 Research quality

The research program is a well-organized program with over twenty years of experience and a matrix structure that supports multidisciplinary collaboration. Its focus is to identify mechanisms of vulnerability, to understand working mechanisms across the care continuum, and to develop strategies to prevent complications and mitigate risks. Their research spans preoperative care, acute and chronic pain, and palliative care, all embedded in a living-lab strategy that integrates cure and care. A central element of the scientific approach is a multidimensional view of vulnerability (biological, psychological, social, and spiritual) which they regard as equally important. At the same time, the team indicates that the social dimension, particularly socioeconomic and psychological factors, require further development. The key concepts "vulnerability" and "quality of life" would benefit from clearer definition, as their multidimensional meaning is not explicitly delineated or clear.

The program has built an ongoing perioperative data register, which enables systematic identification of risk patterns and strengthens both research and clinical decision-making. It uses a department-financed research support facility, which by its proximity and dedicated resources allows the program to maintain a consistent quality cycle and timely and direct feedback. The research group has a good track record in securing competitive funding, including European and KWF grants, and high-quality publications. The assessment also shows substantial output and influence on guidelines and reimbursement strategies.

However, the breadth of thematic lines, and many aims suggests a need for sharper scientific focus to avoid fragmentation. Also, while nationally strong and influential, the group's international visibility is comparatively modest. They participate in Horizon projects and collaborate with global partners, but the group expressed a clear ambition to strengthen their international profile, including by attracting more international PhD candidates.

Overall, the combined insights indicate a research group of very good scientific quality, marked by productivity, methodological strength, and scientific embeddedness.

6.3 Societal relevance

The program's excellent societal relevance lies in the strong integration of research, clinical care, and education. In their report they highlight that more than 64% of Radboudumc patients interact with their researchers, positioning the group as a real-world living lab. According to the report,

collaborations with Radboudumc centers and alignment with institutional themes facilitate translation of findings into clinical pathways for vulnerable patients. The program also has societal impact through contributions to national and international care frameworks (e.g. The National Program of Palliative Care), guideline development, and innovations in acute and perioperative care.

The team is aligned with national inspectorate indicators and guideline development, as well as therapies reimbursed by insurers. They have intensive outreach efforts, structured patient engagement, nursing-student-led value assessments, education, and the centrality of their living-lab strategy. The program clearly sees societal impact as a defining feature that aligns their ambitions with Radboudumc's focus on prevention and value-based care.

6.4 Viability

The group's mission aligns well with scientifically and societally urgent topics. The group demonstrates good viability, characterized by a strategic vision for the future, international ambitions, and a stable track record of competitive grant acquisition. The long-standing history of the group, combined with a robust organizational structure (matrix organization) and the presence of an in-house research support facility, provides a good foundation for viability.

Early career researcher recruitment is supported by collaboration with the Radboud University international institute, although the group notes difficulties in attracting and engaging enough young researchers. Despite this, PhD candidates actively request placement in the group which reflects its excellent reputation. The program's ability to develop methods that can be implemented in both education and clinical practice further enhances its viability and relevance.

A limiting factor is the restricted scope for valorization activities at the patient's bedside. Nevertheless, the group's broad expertise across the full clinical trajectory allows them to deliver short-term and implementable benefits.

6.5 Future outlook and challenges

Looking ahead, the group is well positioned to address their mission and to build on its integration of (pre-operative) care, palliative medicine, pain management, and living-lab approaches. However, sharpening its strategic focus and increasing international visibility will be helpful for future viability. Sustaining competitive funding and improving career opportunities for early-career researchers remain significant challenges. Strengthening the social and psychological dimensions of the research program, and more clearly delineating the concepts of vulnerability and quality of life, will be important for conceptual clarity and impact. Ensuring inclusivity within living-lab participation, particularly for socioeconomically and culturally diverse groups, is also important.

There are some weaknesses and risks, which mainly concern the breadth of thematic lines, and many aims, which lead to fragmentation. Furthermore, the program's international visibility is modest.

6.6 Conclusion

The research program is scientifically and societally strong with solid viability. Its integrated living-lab approach, multidisciplinary matrix structure, and funding record, position it well to address the quality of life of vulnerable patients. The program's national impact is significant, particularly in guideline development and translational care pathways. To further enhance its standing, a sharper scientific focus, stronger conceptual articulation of vulnerability and quality of life, and greater international visibility are needed. Continued investment in early-career researcher development, inclusivity in participation, and strengthening social and psychological dimensions of the research will be needed for sustaining long-term impact.

6.7 Recommendations

- To clarify the definition of vulnerability and quality of life. While the multidimensional model is well recognized internally, external evaluators noted the need for a more explicit definition and delineation to avoid risk of fragmentation of research themes.
- To reconsider the title of the research group. The current title does not adequately represent the breadth and content of the research. A revised name could strengthen visibility and alignment with the current scientific and societal focus.
- To expand collaboration with Psychology and related disciplines. Given the wide approach to vulnerability and patient experience, collaboration, particularly with psychology, would be beneficial.
- To continue building international orientation. The group's desire to become more internationally active aligns with its strengths and could support further grant success and knowledge exchange.

7 Supportive cancer care research

Supportive cancer care is defined as the prevention and management of the adverse effects of cancer and its treatment. This research program focuses on developing, evaluating and implementing optimal supportive care for patients with cancer.

7.1 Mission, vision and strategy

The mission of this program is to perform high quality research in all aspects of supportive cancer care, including symptom management, optimizing physical, emotional, role, social and cognitive functioning and health-related quality of life of patients with cancer, and to help maintain patients' autonomy during all phases of their disease, to support evidence-based care. The overarching goal is to determine which supportive care interventions are most effective for which outcome (e.g., symptoms or toxicity, functioning, health-related quality of life), for whom, when, and how. This knowledge is essential to provide the best personalized evidence-based supportive cancer care. To do so in a cost-effective manner, the program focuses on monodisciplinary care when possible, and multidisciplinary supportive care, when necessary, supported by constructive team science or combined interprofessional research forces.

Specific program objectives are to identify high-risk population subgroups, to identify the best supportive cancer care strategies, to evaluate the effectiveness of supportive cancer care, to understand mechanisms of action underlying effects of supportive cancer care, to improve implementation through understanding of barriers and facilitators, and of process measures and shared decision-making models, and also to improve education for patients, professionals and students.

The program is committed to reducing the symptom burden for patients, improving cancer treatment tolerance, and enhancing societal participation and health-related quality of life. At the organizational level, the program aims to improve quality of care, integrate supportive and palliative care in cancer care pathways, and create international recognition.

7.2 Research quality

This is an important research program in an area that traditionally receives less attention than the active treatment modalities for cancer. The main aim of the program is to unravel which supportive care interventions are most effective for which outcome. It covers all aspects of supportive cancer care, including symptom management, and optimizing function and health-related quality of life. The scientific quality is evident from publications in high impact journals and impact citation scores, grants, national and international awards, and invitations to organize major conferences.

The strategy has a focus on monodisciplinary care when possible, and multidisciplinary supportive care when necessary. The program stimulates team science and interprofessional collaboration. There is a wide range of program objectives, and it is not clear which of these would be considered the principal objective. Although strength lies in combining monodisciplinary and multidisciplinary approaches within team science, together with the broad scope (from mechanisms to implementation) this width may introduce a risk of dispersion of efforts, and lack of deepening of certain main goals or themes within these goals (e.g., psychosocial versus clinical foci).
The research output covers all the program objectives, which is excellent, but raises the question whether it is feasible to integrate the different aspects of research and translate it into the patient pathway. The focus on monodisciplinary care is helpful to understand the mechanism of action; however, this may not be the best option for the patient. Multidisciplinary approaches could help

elucidate the best outcomes for patients. It is unclear how cost-effectiveness is considered in the research, which is of obvious importance.

7.3 Societal relevance

The increasing incidence of cancer makes this program directly relevant to society in general. The focus on mechanism of action and effectiveness potentially helps accessibility by ensuring effective treatments are available to patients. The team is helping to create rapid access to new research findings by working with guidelines, educational initiatives and through technology such as digital apps. The impact of the research will be at the patient level via reduced symptom burden, better cancer treatment tolerance, enhanced (societal) participation and health-related quality of life, and potentially improved survival. At the organizational level, the impact is visible via high quality of care, integration of supportive and palliative care in cancer care pathways, and international recognitions.

Radboudumc has received accreditation from the European Society of Medical Oncology (ESMO) as a Designated center of Integrated Oncology and Palliative Care. Scientific and societal outreach is strong and diverse through, for example, books, professional education organizing and participating in conferences, apps, platforms, decision support tools, and blended psychological support interventions. The program has collaborations with other hospitals and first-line practices (e.g., physical therapists), locally, nationally and internationally, which is highlighted via visiting (associate) professorship appointments, and active participation in international societies such as IPOS. The group's work contributes meaningfully to European and worldwide discussions on personalized supportive oncology. The impact pathway shows that education is strongly embedded in the strategy of the group, ensuring an uptake of knowledge from research in BSc and MSc programs.

A strength of the program is the close collaboration with patient representatives in setting research priorities, and in designing, conducting and disseminating research. Strengthening collaborations with health technology developers, insurers and public health policymakers can further sustainable uptake and system-level integration. A reflective point is that while the impact is broad and demonstrably practice-oriented, systematic evaluation of long-term societal outcomes, such as cost-effectiveness, equity, and sustainability, could further substantiate and quantify societal impact. The same holds for patient-centered impact, i.e. whether there is sufficient attention to the long-term effects of cancer and its impact on aspects such as work, family, and daily activities.

7.4 Viability

This is a relatively small group with five RGLs. The ongoing research funding and programs of work make it highly likely that this is a viable work stream in the future, urged on by the increasing incidence of cancer. It is also an emotive topic with supporters who encourage ongoing research. Products that are reported as examples of viability include guidelines and decision support tools. The group might benefit from a more diverse set of products.

The program highly values student mentoring (BSc, MSc, and PhDs) and actively involves them in various committees. Students are invited to the program's monthly meetings to foster their scientific growth and leadership skills. This is a commendable initiative that also positively affects continuity in research and leadership.

Radboudumc is not visible on the website as active member of the MASCC consortium. The program would benefit from a more prominent role in MASCC to increase visibility and expand international collaboration. The only risks to longer term viability might come from competition for funding from those interested in active treatment rather than supportive care, or from genomics research that provides a new mechanism for tailoring supportive treatments.

7.5 Future outlook

This is a research program that tackles a highly relevant aspect of health care, has good scientific quality and evident societal relevance. The program actively works on increasing cohesion, and includes all levels of researchers, including students, in its activities. The group is quite small, and the research agenda broad. There is strong patient involvement. The program has a solid foundation, and can expand collaboration, possibly by focusing on a more interdisciplinary approach, in the future.

There are some potential risks and weaknesses. Although the strength lies in combining monodisciplinary and multidisciplinary approaches within team science, this and the broad scope (from mechanisms to implementation) may lead to efforts becoming thinly spread, thereby losing in depth focus on some research themes. Furthermore, the program has visibility than could be attained.

7.6 Conclusion

The research quality is good, and evidenced by publications, personal and project grants, and number of citations. Funding levels also seem strong, with several large personal and institution grants. The impact is visible via high quality of care, integration of supportive and palliative care in cancer care pathways, and international recognition. The societal relevance is also high, and diverse with guideline development, decision support tools and strong stakeholder involvement. Education is strongly embedded in the strategy of the group.

7.7 Recommendations

- Consider strengthening the collaboration with other cancer groups.
- Develop a strategy for growth, and to increase visibility.
- Reconsider the strong focus on a monodisciplinary approach. The motivation that not all patients need multidisciplinary care is even true for monodisciplinary care, but both seem to be relevant in this program.

8 Hereditary cancer

Unlike most cancers that develop seemingly by chance, hereditary cancers are caused by specific genetic changes passed down through families. If these mutations are identified early, we can act before cancer develops or detect malignancy in an early stage when it is still highly treatable.

8.1 Mission, vision and strategy

The mission of the program is to optimize care for individuals with a (rare) genetic tumor risk syndrome (GENTURIS) and their relatives. The program aims to improve aspects of the entire care pathway, from recognition, diagnosis, and treatment as well as the prevention of hereditary cancer.

The program has set the following goals: to improve the recognition of hereditary cancer, the knowledge of the phenotype of cancer predisposition syndromes and novel genetic factors needs to be extended. To achieve this, both phenotypic and genetic DNA information from blood and tumors is essential. To improve the diagnostics of hereditary cancer and meet patient needs, strategies to give patients access to genetic testing and the optimal genetic diagnostic test strategies need to be evaluated and optimized.

To achieve these goals, the program uses the following strategies: 1) to improve the treatment of hereditary cancer, the effect of current treatment strategies that mostly follow the guidelines of a given tumor type needs to be evaluated. As for rare patient groups, more tailored treatment strategies are necessary and warrant exploration. The increasing knowledge on the mechanisms underlying the most frequent cancer predisposition syndromes provides ample opportunities to achieve this goal, and 2) to improve cancer prevention in those individuals with a genetic predisposition to develop cancer, access to current multidisciplinary surveillance programs, risk reducing interventions, and novel preventive measures such as vaccination need to be optimized and the efficacy of these measures needs to be evaluated. By optimizing the recognition, diagnosis, treatment and preventive measures of hereditary cancer, the program has a direct impact on the lives of individuals with a genetic tumor risk syndrome and their family members.

8.2 Research quality

Every academic medical center needs a strong genetic department, such as the one presented in the Hereditary Cancer program. The goal of the program is to move from recognition of hereditary cancer to diagnosis to treatment (when possible) and prevention. The genetic analyses (or sometimes transcriptome or microbiome analyses) of patients have many consequences across different programs such as defining potential mutated peptides in Lynch syndrome patients for immunotherapy, for vaccine development and for surgery and others. This is a strong team with many publications in high quality journals. This is also recognized by the various KWF grants awarded to the program. The work is state-of-the-art including the use of AI in sequence analyses of patients. The program is involved in a clinical trial as to the use of sunitinib in anti-tumor efficacy of metastatic phaeochromocytomas and paraganglioma. Also, the move towards more individual assessment of genetic predisposition for cancer is timely. Overall, this program is strong and timely.

8.3 Societal relevance

Genetic counseling for tumors can save lives. The program has shown its importance in the field and has discovered various genetic mutations resulting in cancer. The individualized peptide vaccination approach is an important step to individualized immunotherapy. Whether this involves T-cell receptor transfer or mRNA/peptide vaccination is another question. The program is involved in many networks to improve counseling of patients at risk of cancer, and this is obviously a subject that requires careful discussions with patients (e.g., does a patient want to know that he/she is at risk of getting cancer in the future, etc.). It is excellent that the program members engage with patients, patient

representatives, and patient organizations, but also with a range of professionals involved in the care of those individuals with hereditary cancer. Societal impact is achieved through patient days, participation in research boards, public symposia, teaching in various curricula (BSc and MSc level), and organizing courses for (clinical) professionals that are used to inform and educate professionals and public alike.

8.4 Viability

The program is based on research performed by nine RGLs, three researchers in a Talent Track, and several clinicians and laboratory specialists. A genetic screening program is central in any academic hospital, which ensures the program's viability in the long term. Also, the steps made to keep the program timely comply with this. The research is well funded by KWF project and by collaborations through different EU programs. The program aims to continue investing in new groups through 'we will continue to work on attracting early-stage career researchers through Marie Skłodowska-Curie fellowships, VENI, ERC and others. An important asset for the program is the availability of patient materials: various sources of patient materials are available through Radboudumc biobanks and registers with appropriate consent in place. This may be expanded through (international) collaborations. This is an important asset offering multiple opportunities, if the program can use these materials and data in an innovative way. The development of AI tools but also the steps toward translation in immunotherapy may provide such innovation. The program is already involved in many national and international networks.

8.5 Future outlook

This is a strong program that is also recognized nationally and internationally. It remains difficult, time-consuming and costly to identify patients with hitherto unknown mutations, and this is obviously also done at other locations. To remain relevant and especially to keep access to well-defined patient groups is essential. The program also aims to work on individualized diagnosis as well as the coupling to peptide prediction for vaccination or other forms of immunotherapy will provide an excellent unique research line for the future.

There are some potential risks and weaknesses, which include access to data and materials, which is of crucial importance. Furthermore, as many technicians work on soft money, their future financial situation is also unclear unless the next generation talent can find support for these technicians.

8.6 Conclusion

A hereditary cancer program is essential in a center like Radboudumc. Importantly, access to well defined patient groups of a reasonable size is critical. A better patient accrual system may then be crucial. The program is also embedded in the Pathology department of Radboudumc, which is a logical choice as most tissues are handled at that location as are issues related to diagnosis and more. The program builds on the genetic mutations identified in tumors to support the prediction of peptides to be used for DC-peptide vaccination studies (and possibly other routes of activating the immune system such as TCR transfer and mRNA-based vaccinations). This program runs with other RIMI programs such as tumor immunology.

For these hereditary cancers, early diagnosis can improve treatment decisions and illustrate the translational power of this program. Patients will be more motivated to genetic screening when this results in better and more individualized treatment protocols for a (future) tumor.

The aim of the program is broad (recognition, diagnosis, therapy and prevention). Prevention may be a difficult one unless lifestyle interventions are studied in the context of avoiding tumor formation. AI is also being introduced in this program for the analysis of tissue samples, but it is unclear whether such data can be shared easily or whether protected networks must be developed.

The program presents both national and international leadership as illustrated by the involvement in European networks for Genetic Syndromes. The program not only excels by the number of top publications but also due to the national and international recognition of the group leaders from the program. The program itself is strongly organized and effective.

8.7 Recommendations

- Various group leaders will leave in the coming years due to retirement. A succession plan with a strong talent track program to find appropriate next generation talent is essential.
- For a program relying on patient materials, optimal access to these patient materials is critical. At Radboudumc, patients now have to opt-in to participate in scientific research with pathology tissue, while an opt-out approach (used across many UMCs) will improve patient accrual, a critical factor for genetic studies.

9 Gynecologic oncology

Gynecological cancer poses a significant and growing health problem for women worldwide, with an increasing incidence due to an aging population and its relationship with obesity, which is also on the rise. A key aspect that distinguishes gynecological (pre)cancer and its prevention from other cancers is that women in different phases of life, in particular the fertile phase versus post menopause, may experience different types of cancers, require different therapeutic approaches, and may suffer from different sequelae of treatment. The complex interplay of genetic and environmental factors throughout a woman's life that contribute to gynecological carcinogenesis requires a dedicated research approach.

9.1 Mission, vision and strategy

This research program aims to use knowledge regarding environmental and genetic influences throughout a woman's life to develop personalized prevention and treatment strategies within the program. The main goal of the program is to prevent gynecological cancer and deliver personalized care tailored to a woman's life phase.

The program has several subgoals, including the development, evaluation and implementation of personalized interventions to prevent gynecological cancer. Furthermore, the aims include to increase understanding of gynecological cancer development and tumor behavior with a focus on specifically female and environmental factors, and to develop personalized preventive and treatment methods. The program also works on approaches that preserve fertility and ovarian function in young women with cancer. Finally, the program aims to develop, evaluate and implement innovative tumor-oriented therapies and interventions to improve survival and personalized care, while simultaneously preventing late treatment effects.

The program is committed to extend its scientific impact beyond its specific field and stresses that the program has the potential to contribute to other areas of research. A well-attended research meeting is organized every two weeks in which different focus areas are scheduled. These strategic meetings ensure that researchers can easily meet and discuss research questions. In addition, the meetings are used by researchers to discuss collaborative grant applications and clinical trials, including patient involvement.

9.2 Research quality

This is an excellent, large and focused research program with nine RGLs in four subprograms who have worked together for many years. Several examples have been provided that demonstrate the impact of the research both at a national and international level. These include several high-impact and highly cited publications, memberships of researchers of the program in (inter)national research and guideline boards and personal awards and prizes.

The aims are clearly defined and ambitious. While the program is largely oriented towards clinical research, it also seeks the link with translational research *and* focuses on implementation. Therefore, the research program covers the entire 'translational research cycle'. While the link to translational science is successfully shaped in some cases (e.g., collaboration with Translational Immunology and AI research (Data Science) this could be further developed in the coming years. When this is achieved, the program could become an internationally leading research group. The research output is excellent with a high scientific and societal impact. All RGLs contribute to the total thematic research output. The program has a strategy in place to actively stimulate synergistic interactions between subgroups. This is done by regular research meetings, further enriched by a 'Research Garden' where PhD candidates can meet.

The program has yielded >20 PhD theses with 24 ongoing PhD trajectories. All four subthemes have demonstrated to be capable of acquiring considerable external funding (KWF, ZonMW, Health Holland). They have an excellent academic reputation and have demonstrated leadership in their field. Recognition of the quality of the program is supported by individual research prizes, and memberships of various members of the group in European research and guideline committees.

9.3 Societal relevance

The program has engaged in various investigator-initiated clinical trials and publications that may help improve the prevention and treatment of gynecological cancers, including the development of decision-making tools. The program has an extensive and exemplary patient involvement strategy. They received the Radboud patient involvement award in 2021. Overall, the societal relevance of the program is excellent.

9.4 Viability

Most research lines have been running successfully for many years already and are expected to also do so in the future. The RGLs in the program have different and complementary expertise. Still, the program would benefit from more clearly defined specific goals for each subprogram. In addition, the link between fundamental and clinical research is becoming increasingly important (e.g., see KWF strategy). Therefore, it may be prudent to develop a strategy aimed at actively connecting these scientific disciplines for each cancer type in the program, which ambition is already present within the program. For the financial viability of the program a broader range of funding opportunities may be investigated as most external funding currently is from KWF.

9.5 Future outlook

The future generally looks bright for this program that consists of researchers with complementary expertise who work well together and have done so for some time. Societal relevance is evident, and concerns a field that is growing, due to demographic developments. The program fosters a collaborative spirit that is also extended to the younger generation. More specific aims for each subprogram could be defined for the coming years, and a specific goal could be to further strengthen the role of fundamental/translational research in the program.

The are some potential risks and weaknesses. First, the link with fundamental research is not yet fully developed, and the external funding of the program is mainly dependent on one funding agency. Within this main funder of this program, the link between fundamental and clinical research is becoming increasingly important, as listed in its strategy.

9.6 Conclusion

The program is an excellent well-organized research program within RIMI, largely focusing on clinical research, but also actively seeking to strengthen their work using AI and including more fundamental research. The program has an excellent track record in terms of (clinical) scientific output, obtaining research funding, and generating societal impact. Its patient involvement strategy is exemplary. It is expected that the program will continue to perform well, as they have in the past years.

9.7 Recommendations

- To further develop focused fundamental and AI-based research lines within the program, in close connection with, and thereby enriching, the ongoing clinical research.
- For the financial viability of the program a broader range of external funding opportunities may be investigated

10 Breast cancer

This program studies breast cancer, closely examining both the characteristics of the women and the pathology's characteristics of breast cancers to reduce the burden of this common malignancy.

10.1 Mission, vision and strategy

The mission of the program is to optimize the entire pathway of breast cancer care, by collecting and integrating information on individual women and the characteristics of the pathology. The program aims to achieve this by personalizing screening, diagnosis, and treatment with the goal to lower morbidity and mortality, while simultaneously reducing the burden for healthy women and ensuring the use of sustainable, cost-effective interventions.
The program has subgoals to optimize breast cancer screening by improving imaging technologies and enhancing image interpretation through radiologists and AI, to support the transition from age-based to personalized, and risk-based breast cancer screening using new prediction models and tailored follow-up. Further subgoals are to develop and validate advanced imaging techniques for accurate diagnosis, lesion classification, and staging, and to personalize breast cancer treatment by testing minimally invasive therapies and refine imaging methods to precisely assess tumor status before and during therapy.

The research program takes a multidisciplinary approach. Both researchers and clinicians are involved, and the participation of numerous departments with diverse expertise is anticipated to create synergy within the program.

10.2 Research quality

This is a focused, high-quality but relatively small research program in academic breast cancer screening and personalized therapy, with strengths in radiology, diagnostic innovation, and use of national screening data. Important aspects are the close links with the Dutch screening program, patient involvement, and the potential to shape AI-supported breast cancer care on a national scale

The program shows strong expertise in diagnostic radiology, including advanced imaging such as 3D mammography and an ERC-funded line of work that serves as a clear anchor of excellence. Use of national breast cancer screening data, the aiREAD project, and several important clinical trials underline a solid track record and the potential for high-impact research on screening accuracy and personalized therapy.

10.3 Societal relevance

The program's societal relevance is evident from the program's focus on optimizing nationwide breast cancer screening and informing the implementation of AI in the Dutch screening infrastructure. Active involvement of a long-standing patient advisory board (PAR), which comments on research plans and provides letters of support, is exemplary and further strengthens the program's responsiveness to patient needs and ethical considerations, with ambitions to broaden representation to more multicultural perspectives.

10.4 Viability

At present, the program is relatively small, with its strongest assets in radiology and diagnostics and a clear dependence on collaboration with non-academic centers such as the regional hospital Canisius Wilhelmina Ziekenhuis (CWZ) to secure sufficient patient inclusions. An ERC grant provides a robust scientific and financial foundation, but the program would benefit from stronger clinical and

translational capacity and from more systematic integration with other institutional initiatives, particularly precision oncology.

10.5 Future outlook

The planned nationwide implementation of AI in screening by 2028 offers major opportunities but also raises the risk that some current diagnostic projects could become obsolete when they do not sufficiently anticipate the AI-driven future workflow. Key challenges include securing long-term investment in an academic breast cancer center in Nijmegen, managing the balance between local (Radboudumc) and external (CWZ and other non-academic hospitals) collaborations, and developing a coherent strategy for personalized therapies that goes beyond imaging.

There are some potential risks and weaknesses. The program is small, and dependent on regional collaboration. Furthermore, there is no clear integrative collaboration with aligned groups, e.g., precision oncology.

10.6 Conclusion

Overall, this is a promising and societally highly relevant program with clear strengths in diagnostic research, national-level data access, and patient engagement, but with limited critical mass and a rather narrow focus on radiology. Strategic decisions in the next years, especially regarding AI implementation, institutional embedding, and partnerships, will determine whether the program can grow into a visible, internationally competitive center in academic breast cancer screening and precision care.

10.7 Recommendations

- Consolidate and visibly support a single breast cancer center in Nijmegen (Canisius Wilhelmina Ziekenhuis with Radboudumc), with dedicated research time and shared governance, to secure patient volumes, translational pipelines, and long-term sustainability.
- Consider a formal merger or tight integration with the Precision Medicine program to link diagnostic excellence with molecular profiling, targeted therapies, and clinical trial infrastructure, thereby improving resource use and increasing internal visibility.
- Systematically align ongoing and planned projects with the national AI implementation timeline so that studies address questions that remain relevant after 2028 (e.g. AI validation, workflow integration, outcome impact), rather than duplicating soon-routine tasks.
- Deepen collaborations with oncology, surgery, pathology, immunology, and data science to build a more comprehensive research portfolio by expanding collaborations beyond radiology that covers the full pathway from screening to treatment, including immunological and metabolic aspects of breast cancer.
- Continue to support and diversify the patient advisory board, explicitly involving representatives from multicultural communities, and engage with (inter)national screening bodies to translate findings into guidelines and practice.
- Define recruitment, mentoring, and succession strategies around the ERC-anchored excellence areas to ensure continuity, to attract promising early-career investigators, and to consolidate the program’s role within RIMI and the broader Dutch breast cancer research landscape.

11 Prostate, bladder and kidney cancer

Urologic malignancies, such as prostate, bladder and kidney cancer have significant morbidity and mortality on a global level. When disease is diagnosed late, aggressive treatment may be required that, when successful, can have consequences that seriously affect quality of life. This research program studies urological cancers: cancers that affect the prostate, bladder or kidney to improve treatment results and reduce the burden on patients' lives.

11.1 Mission, vision and strategy

The vision of the program is to improve outcomes and quality of life for patients with prostate, bladder or kidney cancer. The program is aimed at enhancing patient care by discovering new biomarkers and creating personalized treatments and less invasive procedures. By introducing artificial intelligence and more effective therapies, the program aims to lower healthcare costs and build public trust in AI and new technologies.

The goals of the program include the identification of early diagnostic indicators to accurately identify patients with localized tumors while avoiding unnecessary or aggressive approaches, and the development and assessment of new diagnostic and treatment methods that improve efficacy and tolerability. Other goals are the identification of biomarkers before and during treatment to predict which patients will respond to specific therapies, enabling optimized outcomes by distinguishing responders from non-responders early on, the optimization of the benefit-risk ratio of available anticancer drugs, and the identification of host-related risk factors that inform primary and tertiary prevention strategies.

11.2 Research quality

This is a large, high quality research program with 11 research groups. Several examples have been provided and demonstrated the impact of this research program both at a national and international level. There are several high-impact and highly cited publications, which have given the group a solid position in the (inter-)national field, particularly for prostate and bladder cancer research and less so for kidney cancer research.
The aims are clearly defined and ambitious. There is a strong focus on clinical research, AI, and imaging, focusing on objectives such as enhancing clinical outcomes, identifying biomarkers, developing and evaluating diagnostic and therapeutic modalities, optimizing risk-benefit ratios, and pinpointing individual risk factors. These aims are highly relevant for improving patient care and advancing healthcare practice. As such the program offers significant benefits for patients and healthcare systems.

The program also reports on ambitions in fundamental preclinical research. However, specific goals are currently not clearly defined. It is advised that the program further develops this ambition by clearly defining topics and goals for the pre-clinical research program, including the way it is connected to and may further strengthen the ongoing clinical research.
The program has an extensive, strong 'funding portfolio' including national and European grants. Recognition of the quality of the program is demonstrated by prestigious individual grants, and participation of their RGLs in various international consortia. The program has a defined and effective strategy for stimulating interactions between groups and researchers within and outside the institute.

11.3 Societal relevance

The program has defined a clear and detailed impact pathway strategy and thereby a clear societal relevance. The program contributed to revising and shaping European guidelines for molecular imaging and theragnostic in prostate cancer. It is not immediately evident to what extent such defined outcomes and impact have already been generated for the other defined pathways. The program has

also yielded various products relevant to society, including implementation of new imaging modalities, guideline alterations and diagnostic and therapeutic products in collaboration with industry. While AI-algorithms have been evaluated and published in high impact journals by some of the program members, it remains unclear how these innovations will translate into medical devices for clinical applications. Furthermore, the program has a defined patient involvement strategy, including connections with 'Zorgprogramma urologische oncologie' and patient associations. Their work has had extensive coverage by traditional and social media. Clinical research directly benefits society by improving treatment protocols and lowering patient risk, thereby increasing the overall quality of healthcare delivery. Focusing on core clinical strengths will maximize both impact and effectiveness.

11.4 Viability

Most research lines have been running successfully for many years. Although the specific (common) goals for the coming six years have not been clearly defined in the self-assessment, generic goals and aims have been defined, and the viability of the program seems very good. However, it could benefit from more clearly defined specific goals for each sub-program in terms of scientific and societal relevance and their (inter-)national position. The leaders in the program have different and complementary expertise.

The program may benefit from a more clearly defined management structure, aiming to stimulate and foster collaborations between subprograms, defining (common) future research aims and identifying areas of synergy. In general, the link between fundamental and clinical research is becoming increasingly more important (e.g., see KWF strategy). Therefore, it may be useful to develop a strategy aimed at actively connecting these scientific disciplines for each cancer type in the program. The program is currently in a transformative phase with several RGLs retiring and younger talent rising through the ranks.

11.5 Future outlook

The program aims are not defined as specific research aims but rather as generic aims to achieve clinical and economic impact (e.g. less invasive procedures and lower HC costs). More specific research aims for each subprogram (disease entity) will help define and focus the program in the next 4-6 years, both in clinical and pre-clinical research. Having identified its own threats and weaknesses, the program may also develop a strategy for tackling and addressing the weaknesses and challenges and capitalize on the opportunities.

There are some potential risks and weaknesses. First, there is a lack of specific goals for some of the ambitions. Furthermore, there is too little cohesion between clinical and fundamental research

11.6 Conclusion

Prostate, Bladder and Kidney cancer is a strong research program within RIMI, largely focusing on clinical research, AI and imaging. The program has a very good track record in terms of (clinical) scientific output, obtaining research funding, and generating societal impact. It is expected that the program will continue to perform as such.

11.7 Recommendations

- To install a management structure to stimulate and foster collaborations between subprograms, to further define research aims, and to identify areas of synergy.
- To initiate a system for regular self-evaluation.
- To develop a strategy for dealing with the defined weaknesses and challenges and capitalizing on the opportunities.

- To further develop the pre-clinical research program in close connection with, and thereby enriching, the ongoing clinical research.

12 Thoracic oncology

The research program on thoracic oncology studies lung cancer, one of the most diagnosed and deadliest cancers in the Netherlands, with around 14,000 new cases each year. In about half of these cases, the diagnosis occurs at an incurable stage when the cancer has already spread, significantly worsening the prognosis. This puts a burden on patients, healthcare systems and the environment.

12.1 Mission, vision and strategy

The vision of the program is to make lung cancer a curable disease for most patients. To reach this goal, the program aims to decrease the number of patients diagnosed at an advanced stage, allowing lung cancer patients to live longer, healthier lives with improved quality of life, while also lowering the financial and environmental burden of lung cancer care. The program studies the various causes that underly the negative impact of lung cancer: late presentation with advanced stage disease, late recognition of symptoms and diagnosis, lack of personalized treatment and follow-up, suboptimal treatment responses and inefficient organization of lung cancer care.

To find solutions, the program uses an interdisciplinary approach that emphasizes personalization, minimally invasive methods, and a focus on the tumor microenvironment. The goals of the program are to achieve early diagnosis and precise risk assessment before, during, and after lung cancer, to provide evidence, guidelines and recommendations for personalized screening and follow-up, to develop, validate and implement innovative minimally invasive treatments for lung cancer, to enhance treatment effectiveness while reducing risks during treatment and follow-up, to build a comprehensive, multimodal data register to drive ongoing improvements in care, and thereby establish sustainable healthcare networks to enhance lung cancer management.

12.2 Research quality

The program has an ambitious mission-driven approach aimed at improving lung cancer outcomes with a long-term effect by improved screening, diagnostics and risk assessment accuracy, as well as treatment. These goals set the bar high and good progress has been made during the evaluation period. However, the success of several of these goals is difficult to assess now due to long-term follow-up requirements as well as lack of data presented in the self-assessment report (indicators for improved early detection, such as shifts in stage distribution, set in international context; improved treatment precision by improved outcomes etc.). Where this program is really outstanding at a high internationally competitive level is the radiology and imaging-based tissue analysis including related computational analysis developments. Also, methods development such as that on navigation bronchoscopy is impressive. These advances are found in areas such as relapse risk monitoring, treatment efficacy monitoring and implementation such as image guided bronchoscopy. This is evidenced by top publications and continued external funding. Additionally, important research is performed on anti-cancer treatment dose reduction strategies.

12.3 Societal relevance

The societal impact of the program is good, given the importance of the field. Activities include training healthcare professionals nationwide on focus areas with expertise such as imaging. National networks, cooperative projects with primary care providers and patient involvement contribute to societal impact. Also, the program has been very active on disseminating research results through media and policy makers. There is no screening program nationally or regionally for lung cancer so the potential for social impact and improved overall survival is high.

12.4 Viability

The mission driven approach of the program has connected researchers to form improved collaborative networks committed to long term health outcomes instead of fragmented project focus research. This is a positive development, and the group aims to promote and develop this

collaboration across groups and disciplines further. On core areas of the research, funding and impact on national and European arena is very good which makes this constellation viable. The program's activities to continue to build an even more coherent program and focus areas do not seem fully structured yet. A defined meeting structures and junior faculty interaction program may be needed.

12.5 Future outlook

The goals of this program have led to successful aggregation of expertise in imaging and related data analysis; weaker within the current program is the molecular pathology (omics-based analysis). This is a crucial area to materialize the precision medicine goals of the program. There are great opportunities to convert imaging-based discoveries to improved molecular understanding and, further down the line, new treatment options by connecting molecular profiles to imaging data. This could effectively connect the strong imaging and related AI expertise to molecular precision medicine diagnostics.

It is not straightforward to develop and report measurable outcomes of the mission driven program. It would make a big impact when the description of the progress could be coupled with measurable improvements in early diagnosis, improved outcomes, lower side effects and better quality of life of patients measured over time. The organization furthering the translational ambition of the program is excellent and should continue to promote overarching ecosystem development.

The are some potential risks and weaknesses. First, the absence of a strong link with -omics platform may hinder further development. Furthermore, the ambition to be active in many areas may spread the program too thin. Finally, the inability to produce measurable clinical progress may lower appreciation of the program.

12.6 Conclusion

Generally, this is well-performing and focused research program with a mission driven approach to improve thoracic oncology situation. The scientific ambitions are high, and in parts the quality is already excellent. Societal relevance is evident from the importance of the program, and the active involvement of various parties. There are no major concerns on the viability of the program, which is in its formative state. The program could consolidate the governing structures and strategic collaborations on molecular precision medicine area.

12.7 Recommendations

- We recommend developing and reporting measurable outcomes (KPIs) of the mission driven program. It would make a substantial impact when the description of progress could be coupled with measurable improvements in early diagnosis, improved outcomes, lower side effects and better quality of life of patients measured over time, for which key performance indicators (KPIs) could be developed.
- The program could try to strengthen connections with molecular pathology and current omics-based precision medicine efforts.
- An internal road map with specific goals of the mission driven improvement in thoracic oncology, could be helpful, by inclusion and exclusion of focus areas and define where additional collaborations are needed to complement the strategy to reach the goals. The program is currently small, and strategic choices may be necessary to focus on areas of strength.

13 Treatment improvement for severe hematological diseases

Although many hematological diseases are rare, together they are common. Hematological malignancies rank number five in the list of most frequently occurring malignancies in the Netherlands. Although improvements have been implemented in treating hematological diseases, there still are many unmet clinical needs, and knowledge gaps on the development from clonal hematopoiesis to hematological malignancies.

13.1 Mission, vision and strategy

There is an urgent unmet need to develop preventive, diagnostic, therapeutic, and quality of life enhancing modalities. With the program's choice for a disease and patient-centered program approach, it creates coherence between professionals from different departments who play a role in all stages of these diseases. The program aims to unravel the mechanisms of disease and understand the biological consequences, to improve diagnostic and monitoring modalities and prevent disease progression, to develop novel forms of precision medicine and perform investigator-initiated phase I/II trials, to improve quality of life by avoiding treatment-related toxicity and prevent disease progression, and to enhance patient engagement and shared decision-making by offering e-Health-based care platforms.

The program creates synergy by integrating complementary expertise in technical (genetics, molecular, cellular, immunological) and clinical (chemotherapy, immunotherapy, transfusion, infection, supportive care, eHealth) aspects.

13.2 Research quality

The aims of the group cover a wide breadth of modalities across the entire spectrum of research areas, from understanding disease mechanisms and a focus on diagnosis and monitoring, to the development of novel therapeutics, early phase clinical trials and improved patient outcome. The overall research program has generated important scientific findings and advances, with manuscripts published in a wide range of high impact factor journals. The research quality of the program is excellent, with clear areas of national and international strength. An evaluation per subarea shows that the focus on unravelling the mechanisms of disease and understanding the biological consequences is a significant area of strength, with key publications in high-ranking journals in the field. Outputs include innovative work on clonal hematopoiesis, the identification of clonally selective treatments for myeloproliferative neoplasms, mechanistic studies in B-cell lymphoma and findings on the characterization of genetic defects in inherited bleeding disorders. The area to improve diagnostic and monitoring modalities and prevent disease progression shows impressive work on improved diagnosis and disease monitoring in hematological malignancies including multiple myeloma. Various new molecular tests have been implemented locally, but it is unclear if there is potential for expansion of the use of these tests more widely. The area on the development of new forms of precision medicine with investigator-initiated phase I/II trials is another real strength of the program, with impressive work on CAR-NK/CAR-T cell therapies and the design of PROTACS (proteolysis targeting chimeras) against hematological malignancies. The group is well-positioned to guide this preclinical research through clinical evaluation. The area focused on improvement of quality of life by avoiding treatment-related toxicity and prevent disease progression deals with an important area of research in a setting where many older drugs are still used with often serious toxicities. This highlights important collaborations at a local and national level to provide guidelines in areas including CAR-T therapy and rare bleeding disorders. The efforts to enhance patient engagement and shared decision-making by offering eHealth-based care platforms contains relevant aspects, such as the CMyLife platform and an eHealth tool for drug dose reduction which has been adopted nationally.

The RGLs are involved in leading international scientific societies, which international outlook is important as progress requires international collaboration and clinical trials. With a total of 11 RGLs listed for the program the total grant income is relatively modest. Larger grants will need to be brought in to develop some of the promising preclinical findings to early phase clinical trials.

The publication record is strong, and highlights involvement in clearly important international consensus documents. There is clear involvement in the generation of treatment guidelines, both local and internationally, across a range of hematological diseases. This shows impact across a broad range of research areas, including preclinical and mechanistic work, through to studies with societal relevance. There are more limited examples of involvement in early phase clinical trials, although some promising preclinical work may lead to phase I/II studies in the future.

The group shows a solid and diverse membership, including senior leaders with good international standing and reputation, alongside promising young theme leaders who have entered the Talent Track system. The visibility of the group also appears to be strong, as highlighted by journal editorials published alongside publications from the group. There appears to be limited grant income at a European level. Several group leaders also have roles on boards of scientific societies, both at the national and international level.

13.3 Societal relevance

The program has excellent societal impact in terms of the development of products including CAR-T and CAR-NK cells for patients with hematological malignancies and the clinical development of new therapies for patients with acute myeloid leukemia and myelodysplasia. In addition, the CMyLife project and involvement in the development of national and international guidelines provides evidence of enhanced patient treatment and care. A clear list of themes has been identified for developing societal relevance further, with the group seemingly well positioned to develop programs and tools to allow patients to better manage their conditions and positively impact quality of life. In terms of education the provision of a defined master's course focusing on 'therapy development in hematology, from concept to cure' is to be commended.

13.4 Viability

The program's vision suggests a sound foundation for future success, combining a focus on the current strengths of the program and research teams. A key strength in this area relates to the further development of technologies towards a wider clinical utility. For some of the projects, grant income will need to increase to advance promising preclinical discoveries to the clinical setting, which will require significant funds. This could result from increased involvement of RGLs in international collaborations and consortia. As well as increasing international collaborations, capacity building and succession planning will be important, with the inclusion of early career researchers leading specific projects. Internal grant review processes represent a viable approach to maximize success rates.

13.5 Future outlook

The research grouping is well positioned to address its defined aims and is highly likely to maintain its publication record and impact on patient care. However, a less all-encompassing and more focused approach on the current areas of strength may be more successful than the current broad approach. A focus on the strengths in translational research relating to the development of innovative therapies may be advisable. To further develop some of the promising preclinical findings through to the clinic, significant funding and major grants will need to be obtained. A focus on increasing the international standing and visibility of the group, through increased involvement in international collaborations and consortia, is likely to be advantageous. The program may benefit from consolidating equipment and technology expertise in terms of their relationship with the core facility, alongside integration of pharmacy and academic drug development involvement in the program.

There are some potential risks and weaknesses. First, the increase of regulatory complexity and excessive costs may be a barrier for clinical translation. Second, the broadness of the research field in the program may be difficult to maintain, and strategic choices may need to be made. Finally, the dependency on large grants to reach the stated translational aims is a risk.

13.6 Conclusion

This is an excellent research program which is clearly well positioned to further develop its areas of strength moving forwards. There are some very strong areas which will require a strong funding performance in the coming years to progress to clinical utility. With the clear strengths and reputation of the group this is something that will be achievable if a clear strategy is put in place. It is expected that the program will continue to exhibit strong societal impact at a national level, with the potential for an increased international reputation.

13.7 Recommendations

- To consider the feasibility of maintaining such a wide and diverse expanse of research areas, as compared with an increased focus on areas of major strength.
- To consider integration of pharmacy and academic drug development expertise in the program.
- To give serious consideration to capacity building and succession planning.
- To involve younger program members in international groups to ensure the future success of the research program.

14 Precision medicine in patients with solid cancer

Precision medicine plays a pivotal role in advancing cancer treatment by tailoring therapies to individual patients. However, there still is a need for more precise cancer phenotyping and the ability to account for its dynamic evolution, particularly under selective treatment pressure. Furthermore, multimodal diagnostics with integrative analysis provides future opportunities. This research program aims to address these aspects.

14.1 Mission, vision and strategy

The program aims to enhance outcomes for patients with solid cancers, particularly those treated with targeted immunotherapies, by advancing innovative technologies such as molecular diagnostics, AI, and integrative data analysis. With this approach, the program is committed to generate more precise genotyping, phenotyping, improved prediction, and early assessment of treatment response, with a better detection of minimal residual disease.

The program wishes to advance precision medicine by advancing molecular diagnostics and by supporting the development of novel biomarkers and integrative analyses. These ambitions also require improving non-invasive sampling methods such as liquid biopsies, as well as refining genomic analysis techniques and bioinformatic pipelines to enable more accurate and comprehensive tumor profiling.

The program's core goals and principles focus on bridging scientific research and clinical practice, with the aim of accelerating the translation of breakthrough discoveries into real-world applications. The program approaches this by fostering multidisciplinary collaboration to develop and validate tumor-agnostic precision biomarkers and translate patient-focused research into clinical practice, promoting biomarker implementation through cross-departmental collaboration, with the ultimate aim to improve survival and quality of life for patients with solid cancers by enhancing personalized treatment allocation and ensuring timely access to the most effective therapies, and, finally ensuring the sustainability and affordability of precision medicine by integrating health-economic evaluations into the program.

14.2 Research quality

This is a large program with eleven RGLs across multiple cancer types and research focus areas. The team has produced impressive results according to their set goals. Under the goal on genotyping and phenotyping of solid tumors the team has adapted current genomics technologies for wide clinical use and research and proceeds to use new technologies. The track record on genome driven precision medicine and introduction of new technologies, such as long read sequencing, is very strong. The phenotype part is less intensely researched and seems to be mainly about clinical outcomes rather than molecular and imaging phenotypes.

Also, in predicting outcomes and toxicity related to treatment such as drug dose, this research program has made significant progress on well-crafted clinical cohort analysis. Important work has been done on targeted and immunotherapy dosing to allow development towards future combination treatments. In treatment response evaluation and detecting minimal residual disease the program has also used the current genomic and transcriptomics technologies and demonstrated added value on several areas.

It is unclear from the self-assessment report and discussions on site how the goal on systematic standardized biobanking (to allow strong future research on early response and multidrug resistance) is organized and how widely this is applied across solid tumors. This is an overarching area, ideally, with a need to harmonize efforts across all cancer types.

14.3 Societal relevance

The research effort has led to several implementation studies on national level and revisions of guidelines, national infrastructures as well as new clinical trials. This can be considered as an excellent success. However, it is not fully clear which of the research discoveries has been implemented into clinical care. Further, the strategy to implement new markers and methods in clinical practice is insufficiently described.

14.4 Viability

The good track record in publication has ensured significant grant funding, and the financial viability seems solid. The structure to obtain clinical samples, related data and new genomics methods is well placed so that these can be applied continuously, for cutting edge research and clinical trials. Through its meeting structure the program looks coherent and interactive, with many of the activities driven by junior faculty.

14.5 Future outlook

The plan to continue and focus on successful translational research, including trials and implementation effort, is good. The continued focus on program-wide activities including or driven by junior faculty is also a great asset of this program. This is an internationally competitive area and requires entire workflow to be in place from samples, technologies to clinical trials and hence careful considerations of focus areas.

There are some potential risks and weaknesses. First, the range of solid tumors is broad, and there is a risk of ineffective transfer of knowledge and methods across tumor types and expert groups. Furthermore, several other programs focus on solid tumors or relevant areas such as genomics or immunotherapy, which can create silos with insufficient connection, reducing the effectiveness of the research. There is substantial risk with a single focus on genomics and transcriptomics with a lack of molecular phenotyping (currently there is no proteomics and metabolomics; and relatively little connection to imaging in true integrative manner). In coming years this gap will be difficult to bridge due to lack of expertise and sole focus on nucleic acid-based biomarkers.

14.6 Conclusion

This is a well-functioning program, with ability to migrate methods and information across several tumor types. The active and interactive research environment has led to impact via new findings and implantation of there to guidelines. Research quality and societal impact are strong.

14.7 Recommendations

- Consider adding molecular phenotype layers such as proteomics and metabolomics analysis to the research or broaden phenotypic foci in another manner.
- Lay out, in the genomics driven precision medicine, strategic choices for a 5–10-year period.
- The active multi-disciplinary research community is an asset that should be continued vigorously.
- Develop strategies to interact with other relevant programs in terms of what is needed to strengthen the program and when.

15 Non-/minimally invasive oncology

Procedures in cancer treatment, particularly surgical cancer treatment, can be mutilating and have long-lasting consequences that affect a patient's quality of life. Hence a shift to non-invasive or minimally invasive procedures that can be equally effective but have fewer negative consequences. The program focusses on developing such procedures.

15.1 Mission, vision and strategy

There is a clear need to invest in developing new and improving existing technologies for non-invasive or minimally invasive oncology. Therefore, this research program brings together Radboudumc's expertise, experts and infrastructure to accelerate the development and clinical implementation of innovative non-/minimally invasive diagnostic and therapeutic tools to improve cancer care.
The program aims to develop, implement and evaluate innovative tools for personalized non- or minimally invasive therapeutic and diagnostic procedures that will change practice, improve quality of care, and remain cost-effective and affordable. In the program, innovation is approached by identifying practice-changing non-/minimally invasive technologies, providing a toolbox of "test facilities", accelerating clinical implementation and supporting a process of continuous evaluation through an assessment and improvement cycle.

The program describes that their next step is to achieve valorization, creating value from the acquired knowledge by making it suitable and available for economic and societal use. The program envisions addressing the growing pressure on oncological healthcare quality, accessibility, and affordability, and is committed to contribute to mitigating these societal challenges and delivering appropriate cancer care.

15.2 Research quality

The research quality of this program is impressive. There is active involvement in various clinical trials, particularly those employing an upfront radiotherapy approach followed by a "wait and see" strategy prior to surgery. The significance of the nation-wide studies focused on organ preservation is clearly visible, with an impressive 40% of rectal cancer patients benefitting from non-surgical management. The successful acquisition of KWF project funding further demonstrates the program's research excellence and commitment to advancing clinical care. The publication record is strong, with publications in high-ranking journals. Furthermore, the multi-center study examining the effectiveness and quality of life outcomes associated with focal treatment for prostate cancer, is highly relevant, and currently involves six collaborating centers. This collaborative effort highlights the program's dedication to improve patient-centered outcomes through innovative and minimally invasive therapies.

There is pioneering research in theragnostic for prostate cancer, particularly the investigations into Lutetium-based therapies combined with anti-PMSA targeting. The ongoing trial, which explores the potential of introducing these treatments earlier in the disease course, raises important scientific questions, such as the underlying reasons for the observed strong response in approximately 25% of patients. Collaborative efforts between radiotherapy and theragnostic teams can be encouraged.

15.3 Societal relevance

The societal impact than can be expected from this program is of high standard. Non-invasive and minimally invasive surgery offers important societal benefits that extend beyond clinical outcomes. Surgical innovations that reduce physical trauma while maintaining or improving effectiveness are highly relevant to patients, healthcare systems, and society at large, with macro-benefits regarding health care expenditure. At the patient level, minimally invasive oncologic surgery may significantly

improve quality of life, with earlier recovery, and fewer surgical sequelae. This has, for example, been demonstrated with the so-called MICE procedure for esophageal cancer, which has substantially reduced post-operative pneumonia. From a healthcare system viewpoint, these approaches contribute to efficiency and sustainability and may translate into substantially reduced overall healthcare costs. This cost-effectiveness is crucially important now that the cancer incidence is increasing due to an ageing population. The involvement of patients is not formalized.

The program aims both to increase early detection of cancer, or cancer recurrence, which may enable non-invasive or minimally invasive treatments, and positively affect morbidity, mortality and quality of life. The program's commitment to cost and environmental technology development through health technology assessment (HTA), is important, and to some extent unique as this is often not considered by other parties. The integration of early HTA, including the evaluation of quality of life as part of the assessment, is exemplary and demonstrates strategic foresight. This early HTA not only informs the scientific direction of research but also enhances the broader impact of the program. To be successful in impacting clinical care for cancer patients, the program should be able to develop techniques that will, in some cases earlier than in others, in non-academic settings.

15.4 Viability

The program is medium-sized, with 10 RGLs, and is closely connected to clinical departments and tumor-specific programs, as well as programs involved in health technology assessment (HTA). It is relatively young. It has become increasingly coherent and interactive, with regular meetings of involved researchers, though a formal structure for these interactions has yet to be fully established. The members of the program have a complementary background in, amongst others, radiotherapy, imaging, surgery and intervention radiology. The value of fellowships in supporting and enhancing interactions among program members is high. The access to data collected within the various departments involved in the program will be an important strength. However, the program does experience barriers related to legal and privacy regulations, which is not limited to this program, and therefore of wider importance. The program has clear views on education and the training of early career researchers in the field. Importantly, it includes two individuals in the Talent Track program. Overall, viability prospects are good, because the program is rooted in relevant and diverse departments and the access to technologic infrastructure. Viability can only increase when the program succeeds in harnessing the societal demand for these kinds of treatments.

15.5 Future outlook

This is a relatively new program that has all the features that allow a positive future look. It combines members from various groups with a strong publication and funding record, it has a solid portfolio of grants, and it actively works to promote cohesion, and possible expansion of the program. It uses state-of-the art technology and has sufficient access to data and computational facilities.

There are some potential risks and weaknesses: There are groups with diverse backgrounds involved in the program, and maintaining coherence requires continuous attention. Barriers to data sharing due to legal and privacy regulations are a given, but may prove difficult to overcome. The application of new approaches to non-academic settings may pose new hurdles.

15.6 Conclusion

The program non-/minimally invasive oncology is new and original, but can already be seen as excellent in terms of scientific quality, societal relevance and viability. It is an excellent example of the joining of forces and complementary expertise that lies at the basis of the introduction of the system of research programs by RIMI. Its use of technology is excellent. The program is organized along sensible and sustainable lines. The research quality and societal impact are excellent. There are no doubts about the viability of the program, however, given that the program is still young, this can be further developed.

15.7 Recommendations

- At an institute-wide level, or optimally in collaboration with other academic centers, RIMI may strive to remove legal and privacy regulations related barriers to data use and sharing.
- Build alliances with non-academic hospitals to ensure a wide uptake of new approaches, when this becomes possible.
- Continue and expand activities that strive to cement the cohesion of the program.
- Intensify activities to career development of younger clinicians and scientists to solidify the base for the future.
- As a minor suggestion, change the name into an esthetically more pleasing form, such as ‘non-invasive and minimally invasive oncology’.

16 Cancer immunotherapy – a pan-cancer program (CI-app)

Immunotherapy is currently the standard-of-care for over 20 cancer types. However, the response rate in the eligible patient population is estimated at only 10 percent. Medically, immunotherapy is associated with a risk of severe toxicity and it imposes a high economic burden on society. Therefore, there is an urgent need for further research in the field of cancer immunotherapy to improve efficacy and reduce toxicity.

16.1 Mission, vision and strategy

The mission of the research program is to unravel the underlying mechanisms of tumor-immune attack and resistance in a wide variety of cancer types, and to contribute to improved clinical outcomes for cancer patients treated with immunotherapy. The program is an interdisciplinary network for cancer immunotherapy research at Radboudumc that aims to expand and strengthen the current collaborations across different disciplines and tumor types, and meet regularly to warrant fruitful interactions, from research ideas to implementation. The program develops immunotherapeutic strategies for clinical applications. This is done by initiating preclinical in vitro and animal experiments and starting phase I/II clinical trials at a new multidisciplinary phase I unit (CANTO).

The aims of the Cancer Immunotherapy – a pan-cancer program – are to unravel the underlying mechanisms of the tumor-immune attack and resistance. With this, the program aims to understand the tumor micro-environment at a (sub)cellular level, adjust the function of immune cells to improve tumor killing and circumvent tumor-induced resistance, and to improve the use of currently available immunotherapies. This is done by developing biomarkers to select patients, by improving efficacy, and by investigating toxicity and toxicity costs.

16.2 Research quality

The program has three main goals that move from fundamental research to application (bench-to-bedside). Firstly, understanding the tumor micro-environment and modifying immune cells to improve tumor immunotherapy; secondly, identifying biomarkers as predictors of successful immunotherapy and with the aim to limit toxicities, and, thirdly, testing new immunotherapy approaches in preclinical and clinical systems including Phase I/II studies. Various examples are part of impactful publications from the group. Important positive points are the use of various strong Radboudumc platforms and the interaction with the Sanity program, which brings in radiotherapy and radiology.

Parts of the program are nationally leading but must compete with large international activities. These include the work on the tumor microenvironment and on microbiota. The dendritic cell vaccination approaches are internationally leading, and the team must be admired for the enormous investment in bringing this work from bench to bedside. Also, the question of limiting the toxicities by lower dosing of immunotherapy is important. In general, this is a good team whose work on immunotherapy in cancer is broadly recognized. Yet, it is somewhat heterogeneous, and the question is whether some streamlining would further improve their international position.

This program is highly valuable, demonstrating success not only through its publications but also in the clinical domain, with several established clinical trials. There is an excellent collaboration with the Department of Molecular Biology in the Faculty of Science, which highlights the commitment and capability of the group to utilize available resources effectively. While immune responses to cancer and immunotherapy are certainly overarching themes, it may be worth considering a focus on fewer cancer entities to enhance power and deepen the impact of ongoing research.

16.3 Societal relevance

Immunotherapy of cancer is a relatively new and successful but not perfect therapy. Many cancer patients do not respond to this therapy, and the question is whether it can be improved and made less toxic. This is generally considered an important field in oncology and immunology. This is also recognized by funding bodies and patients alike. Further illustrations of societal impact are that the team executes several investigator-initiated trials, participates in several multicenter trials, has written clinic practice guidelines and has generated a new product that is patent protected. The work on dendritic cell vaccination resulted in the Huibregtsen Award, which illustrates the societal relevance for the work within this program

16.4 Viability

Cancer immunotherapy will remain an important cancer therapy that certainly requires further improvements as it is still poorly understood why particular patients respond unlike others. Also, only a limited number of tumors are immunogenic and can be expected to respond. The program is broad and of high quality. They will contribute to this field, and this field will remain important for many years to come. The program harbors groups working on fundamental questions and on more applied questions. There are several relatively unique activities within the program including vaccination with peptide loaded DCs, radio-immunotherapy and immune dysregulation in hematologic malignancies. The fundamental research is essential to feed translational research. Further streamlining of research would help with visibility but possibly with funding as well. There is a healthy funding base provided by EU, ERC, KWF and other major sources. Until now the funding of the program is excellent, and it is anticipated that this will not change the coming times, albeit that KWF has altered the funding somewhat at the disadvantage of fundamental research.

16.5 Future outlook

The program has a clear and feasible vision of the future that follows the research lines currently running (in other words, these are realistic). They aim to broaden their collaborations across different disciplines and expand the number of tumors. The program wants to unravel underlying mechanisms of tumor-immune attack and resistance in a wide variety of cancer types, and to contribute to better clinical outcomes for cancer patients treated with immunotherapy. They also want to evaluate the cost-effectiveness of immunotherapy (which is an interesting issue!) by lowering doses. Investigator initiated trials will be started to define the best and most cost-effective trail. This may be challenged by the providers of the antibodies/drugs, certainly when better drugs become available. The overall aim is to make advanced cancer treatments more affordable and accessible to a broader population. This will be an important selling point of the program

There are some potential risks and weaknesses. First, the sustainability of the expensive facilities run by dedicated personnel may prove difficult. The same facilities can be used for other cell-based therapies which may mitigate these concerns. Second, it is possible that it may prove difficult to maintain this as an academic activity. Yet, academic research is critical for the further development of cancer immunotherapy. Finally, this program is presented as a ‘pan-cancer program’. This implies some heterogeneity as to the different projects that are included within the program, which may lead to fragmentation.

16.6 Conclusion

The Cancer Immunotherapy program at RIMI is unique and world leading in various aspects. It also includes unique facilities such as clean rooms to produce specific dendritic cells for vaccination purposes. The analysis of the biodistribution of dendritic cells is of high quality, as this type of information may explain failure or success of treatment. The program has a long history and started before the checkpoint antibodies came into the clinic. The program is highly visible internally and externally and well-funded. The complexity of establishing and running clean rooms for ATMPs with all the regulatory challenges is usually poorly appreciated. The fact that RIMI has a long history of successfully running such a facility is something they must be applauded for. It requires having multi-disciplinary teams working under GMP conditions and their activities are usually less visible and recognized. The program is built on a long history of developing DC based immunotherapies for the treatment of melanoma and other cancer patients. Now CAR-T cells may enter the field of autoimmunity, and the demand for clean rooms may further expand.

16.7 Recommendations

- The clean rooms are mainly staffed by personnel on soft money. That makes this essential part of the program fragile. A more solid financial construction is recommended, also to ensure that personnel remain working in this program.
- Some focusing within the program may be of interest. This requires the definition of the ‘common goals’ of the program followed by focusing on how to achieve these.
- The interactions with other analogous RIMI programs such as SANITY could be strengthened to help secure stable funding for the clean rooms and its personnel. With most people currently on soft money, the situation may be considered not sustainable. The combined knowledge of the program may also evoke interest from companies in running Phase I trials that may offer support for the program.

17 SANITY: Synergistic combinations of ablation and immunotherapy in cancer

Physical tumor ablative therapies are a mainstay of cancer management, offering unique treatment plans for individual patients. A second pillar in cancer treatment is immunotherapy, a personalized treatment that enables the patient's own immune system to fight cancer. Combining physical tumor ablation with immunotherapy has shown great potential to improve treatment efficacy, which is the research topic of this research program.

17.1 Mission, vision and strategy

The mission of the research program is to achieve long-term survival for cancer patients by bridging the medical physics of ablative interventions and immunotherapy to enable individualized cancer care. The team has four goals, of which the first is to gain a fundamental understanding of the mode-of-action of ablative technologies focusing on immunological and Tumor Microenvironment (TME) effects. The second goal is to develop innovative immune modulatory therapies for in vivo programming of (innate) immune cells and fibroblasts for combination therapy. The third goal is to develop (early) clinical feasibility and translational studies, guided by early health technology assessments to ensure responsible research and innovation. The final goal is to train next generation of professionals to bridge the medical physics of ablative interventions and immunotherapy.

The program brings together Radboudumc clinicians, scientists, physicists, and their collaborators to develop new and optimize existing immunotherapy combinations with minimally-invasive, high precision tumor ablation technologies, such as MR-guided radiotherapy (RT) to treat loco-regional tumor lesions with photons, High-Intensity-Focused-Ultrasound (HIFU) to destroy tumor lesions with ultrasound waves, and radionuclide therapy for intra-tumoral or systemic treatment using radionuclides emitting alpha or beta particles. By crossing disciplinary borders, the program is committed to gain momentum to achieve durable local and systemic cancer immunity for multiple tumor types.

17.2 Research quality

The program harbors RGLs at international top level and many of national top level. The program's mission to achieve long-term survival for cancer patients by bridging the medical physics of ablative interventions and immunotherapy to enable individualized cancer care, is very strong and to some extent fills a gap in the research done on tumor-immunotherapy, since ablative therapies are usually not considered in the immunotherapy context. The four goals are feasible, although some overlap with goals in other programs (i.e., tumor immunology).

The interaction with the other relevant programs appears to be good. Research output on all research goals is of high quality. In the provided 'key publications' were not many examples yet of the proposed integration of immunotherapy and medical physics, which is notwithstanding the considerable opportunities to provide novel aspects to the broad field of immunotherapy. Further integration of research lines (i.e., focusing on a clear shared theme) would be helpful to increase research Impact even further.

17.3 Societal relevance

Improving tumor immunotherapy is of broad societal relevance. The checkpoint inhibitors are used by around 15,000 cancer patients in the Netherlands annually. The program also includes studies on therapy cost assessment, which is important. The team members have produced products for radiotherapy and participated in clinical trials. They collaborate with various industries and have patents on various aspects of radio and immunotherapies. They participate in advisory organs for

different funding organizations and provide courses for the community. Advertising the program and prospects of the combination of immunotherapy and medical physics would improve recognition.

17.4 Viability

The program has taken steps to ensure longer term viability by including four talent or Tenure Track researchers in addition to 12 RGLs. This shows excellent long-term planning. When the program succeeds in further integrations of the different research lines to generate a visible 'radioimmunotherapy' line of research that moves from evaluating the effects on the TME and the resulting immunotherapy, this may further viability. The excellent facilities at Radboudumc will help to support this development. A stronger integration and visibility may prove critical in obtaining grants

17.5 Future outlook

It is obvious that both radiotherapy and immunotherapy will remain cornerstones in cancer treatment. immunotherapy will be further improved but this field is highly competitive field, and even the focus of other programs within Radboudumc. The combination of the two fields in an environment where the facilities provide state-of-the-art technologies may provide a unique position. This requires more focus in this radioimmunotherapy field by various groups with the potential to improve tumor(immune)therapy.

There are some potential risks and weaknesses. The most important is the lack of synergy with programs with similar aims. Furthermore, the interaction between scientists and clinically active individuals may become insufficient to fully harvest the benefits of synergy.

17.6 Conclusion

The program is strong and integrates immunotherapy understanding with that of radiotherapy and other techniques of ablation. Obviously, such treatments affect the local tumor microenvironment, with poor understanding as to the effect of immune- (or chemo) therapies. It is surprising that while the treatments are combined, the short- and long-term effects of tissue ablation treatments are poorly understood.

While this program is interdisciplinary by nature, there is a limited number of 'cross-over' publications where the work has been integrated, which may be related to the program being relatively young. The program has many interactions with other activities within RIMI that can support scRNA sequencing, microscopy and many other high-end technologies. Also, the animal facility is fully equipped for this work. There is a clear vision to integrate these interdisciplinary research lines. Leadership is shown through the selection of young faculty to expand the different research lines. The fact that an HTA analyses group is included in the program is excellent idea.

17.7 Recommendations

- The interaction between scientists and clinicians may be further enhanced.
- A further form of integration of radiotherapy with immunotherapy may be investigated to further strengthen the program. While of high quality the research is also rather diverse. Some structuring around broad themes could be of help here.
- The HTA analyses to define early during development of a clinical research line the costs vs the benefits is a great development. This activity may be more broadly applied across various clinical translation processes within RIMI.

18 Cellular adaptive immunity

This research program studies the cellular adaptive immune system, which consists of B-cells and T-cells. These are essential for defending us against infectious diseases and cancer, but they can also lead to pathology, as seen in inflammatory diseases. A key aspect of T- and B-cells is their ability to respond to antigens expressed by pathogens or by host cells, which can be studied for diagnostic purposes and manipulated to treat disease.

18.1 Mission, vision and strategy

The aims of the program are to advance knowledge of the biology of adaptive immunity and its clinical applications in the context of vaccination, infection, autoimmune diseases, and cancer. It includes the development of new methodologies to study the adaptive immune system and develop improved diagnostic tests and treatments, such as personalized immune interventions to treat cancer.

The program consists of clinical, biomedical, technical, and data analysis dimensions of cellular adaptive immunity. Various specialized groups focus on the complementary areas of expertise. The mission of the research program is to bridge disciplines by uniting clinicians, wet-lab scientists, and computational biologists to translate mechanistic immune insights into clinical applications, innovate methodologically through development of novel technologies (e.g., co-culture hydrogel models, single-cell analytics), and study immune cell interactions and signaling. Furthermore, the program mission includes engaging national and international partners (e.g., Netherlands Cancer Institute (NKI), Immuniverse network, Radboud University), industry collaborators (e.g., Philikos), and patient panels (such as STAP) in designing and guiding research, all of which to deliver clinical impact by transforming immune biology into actionable tools for diagnostics, prognostics, and therapeutic innovation.

18.2 Research quality

Despite its relative youth, the program has already demonstrated strong scientific potential by combining cutting-edge experimental platforms with translational applications. The horizontally structured approach encourages collaboration across disease contexts, shared technology development, and integration of both junior and senior researchers, creating an environment conducive to innovation and learning. The research covers the core biology of T- and B-cell responses, including clonal expansion, tissue localization, effector function, and regulatory mechanisms. These fundamental insights are actively translated into diagnostic and therapeutic innovations, with high-quality publications and patents demonstrating scientific impact. Key examples include the identification of disease-driving T-cell subsets, leading to a patent and a spin-off (Philikos) developing a therapeutic candidate; antiviral immunity post-pertussis vaccination; clinical immunotherapy trials in melanoma that combine immunology, microbiome research, and oncology; the SurfaceID platform which enables high-throughput immune profiling; computational tools to facilitate modeling of immune responses, multi-omics integration, and interpretation of complex trial data.

The focus on tool and technology development, alongside translational applications in cancer and auto-immune diseases, represents a clear strength, although questions were raised about scaling assays for broader clinical studies. Currently, the program integrates seven research group leaders, two tenure-track researchers, and three clinicians, providing a balance of fundamental and translational expertise. Horizontal organization allows sharing of technologies and platforms to address mechanistic immune questions across diverse disease areas.

In terms of collaborative outputs, the program has generated many publications since 2020, numerous shared grants and coordinated clinical trials, highlighting strong internal and external networking. While the program is currently well-balanced in size and supportive of junior researchers, greater clarity on mutual expectations, structured strategic planning, and coordinated grant support would further strengthen interdisciplinary integration.

The program's broad disease coverage enhances translational potential but presents risks for cohesion and methodological harmonization.

The program has developed several unique platforms to facilitate research and translation, which form the backbone of the program, allowing it to interrogate fundamental immune mechanisms while simultaneously developing diagnostic and therapeutic strategies.

18.3 Societal relevance

The program's societal impact is impressive, extending from health policy to contributions to clinical applications, but may be improved regarding public outreach measures that are currently not visible. Examples of the societal impact include the Philikos spin-off**,** developing targeted immunotherapies for systemic sclerosis**;** clinical immunotherapy trials**,** including PRECIOUS-01, NEODOC, and MIND-DC, applying single-cell and pathway analyses to predict treatment response**;** human challenge trials in pertussis and malaria, which influence vaccine development and regulatory policies.

The program collaborates with major pharmaceutical and biotech partners, demonstrating active knowledge transfer and industrial engagement**.** Public-private partnerships (e.g., DETECTIVE, ImmuneHealthSeed, and Immune Health XL) illustrate how academic discoveries are integrated into broader innovation ecosystems. Researchers also engage patients directly in research design (e.g., the STAP panel for rheumatoid arthritis) and participate in public outreach.

The COVID-19 pandemic has underscored the critical importance of adaptive immunity. The program's contributions to understanding vaccine responses in immunocompromised patients (RECOVAC study) and cross-disease immune regulation position the program as a national leader in immune health research. Further, the coordination of Immune Health XL**,** a national platform uniting academia, industry, and health foundations, amplifies the program's potential to impact policy, healthcare, and innovation.

18.4 Viability

The program's viability is strong, underpinned by its funding and collaborative structure. The program has secured impressive base funding over the few years since its formation, which provides financial sustainability. Funding benefits from a robust mix of funding sources, including public and private funding. Whereas the funding acquisition is impressive, it is assigned to selective RGLs and often listed in several research programs. Acquisition of collaborative funding with the prime focus on cellular adaptive immunity should be considered.

The program's team structure is young and diverse, and creates a self-sustaining, synergistic environment. Regular meetings foster collaboration and joint grant writing ensures continuity of innovation. The close link with other Radboud programs (e.g., Innate Immunity, Chronic Inflammatory Diseases, Cancer Immunotherapy) further strengthens viability through shared expertise and infrastructure (e.g., Radboud Single Cell Center). Noteworthy, various leaders of the program participate in several research programs, which may be a risk of dilution of focus and energy.

18.5 Future outlook

This recently founded program has already established a strong foundation in technical innovation and translational applications. In the coming years the program will have the potential to expand its impact by scaling high-throughput immune profiling technologies, such as the SurfaceID platform, to support broader clinical studies and cross-disease comparisons, by deepening integration between adaptive and innate immunity research, and leveraging shared molecular pipelines to uncover crosstalk mechanisms relevant to infection, autoimmunity, and oncology. Translational pipelines can be strengthened from mechanistic discovery to patient-centered interventions.

Despite its promise, there are potential risks and weaknesses. Absence of harmonized molecular pipelines across disease areas may limit comparability of data and hinder cross-disease translational applications. The overlap with other programs raises the question whether merging with related

initiatives (e.g., biomarker discovery) could enhance impact. Parallel research in innate immunity is not yet fully integrated, highlighting opportunities for crosstalk between adaptive and innate lines. Scaling high-throughput assays and translating technical advances into clinical studies remains a critical hurdle. Future directions emphasize strategic planning, prioritization of translational applications, and clearer structuring of expectations across RGLs to maximize cohesion and efficiency. With RGLs involved in multiple research programs, the mission may become fragmented, potentially reducing the strategic coherence of the program. While some horizontal and vertical collaboration exists, structured frameworks for joint strategy planning, grant coordination, and mutual expectations among RGLs are still developing. Existing outreach is fragmented, and broader initiatives to engage patients and the public consistently are required to strengthen societal impact.

18.6 Conclusion

The program is a state-of-the-art initiative with clear strengths in technical innovation, translational application, and interdisciplinary collaboration. Its horizontally structured approach creates an environment that supports learning, innovation, and method development. The program has already achieved high-quality publications, patents, spin-offs, and clinical trial involvement, demonstrating significant potential for translational impact.

At the same time, the program is still young, with a mission focused primarily on methodological and technical developments rather than broad-scale disease outcomes. While it demonstrates high scientific quality and strong translational potential, there is room for improvement in several aspects. Strategic focus, program-level integration, and expanded clinical translation pathways will be key to reaching the next level.

18.7 Recommendations

- Enhance program integration by developing structured frameworks for RGL coordination, shared molecular pipelines, and harmonized cross-disease data analysis.
- Reassess the value of having RGLs affiliated with several programs.
- Prioritize the translational focus by aligning technical innovations with specific disease contexts where clinical impact is maximized, including oncology, vaccinology, and autoimmunity.
- Strengthen junior researcher support and establish clear career pathways, grant mentorship, and opportunities for independent funding to retain and develop early-career talent.
- Expand clinical and patient engagement by Integrating clinicians more closely in experimental design and actively involve patients in study planning and societal outreach.
- Focus mission scope by maintaining a balance between breadth and coherence, to ensure that cross-program collaborations do not dilute the program's primary objectives. The allocation of RGLs across several research programs should be reviewed and likely reduced to concentrate efforts and create a true hotspot.
- In public and societal outreach consistent initiatives could be developed for communication and engagement with the public to highlight societal relevance and translational impact.

19 Innate immunity in health and disease

Innate immunity is one of the two major components of the immune system. It is essential for defending against infections, supporting immune surveillance, and enabling tissue repair. Furthermore, it plays a key role in homeostasis and pathophysiology of nearly all major disease types.

19.1 Mission, vision and strategy

The mission of the research program is to deepen the understanding of mechanisms of innate immune responses in health and disease. With this knowledge, patient outcomes can be improved through the development of new diagnostic and therapeutic strategies targeting innate immunity. The four main goals to achieve this mission are to study innate immune responses at the population level, to understand the role of innate immune responses in health and diseases, to improve vaccines using innate immune memory, and to explore and optimize innate immunity-based immunotherapy. The program creates impact on multiple levels, by uncovering key mechanisms in pathophysiology underlying major diseases (including infections, inflammatory and autoimmune disorders, cancer, and neurodegenerative conditions), enabling new diagnostic and therapeutic approaches, uniting Radboudumc researchers in a highly dynamic research area, and providing an excellent training environment for the next generation of scientists.

19.2 Research quality

The program, established in 2007, is a large, multi-disciplinary program with a clear and ambitious mission: to advance understanding of the mechanisms that modulate innate immune responses in both health and disease, with the goal of translating this knowledge into improved diagnostics and therapeutics for patient benefit. The program's objectives include leveraging systems biology to study immune responses at a population level, elucidating innate immune mechanisms in infections, inflammatory diseases, and cancer, and developing innovative strategies—such as trained immunity—to enhance vaccine efficacy and design novel immunotherapies.

Over the past six years, the program has demonstrated outstanding research quality and leadership at national and international levels. It has fundamentally shaped current understanding of innate immune mechanisms and has contributed with conceptual breakthroughs and clinical innovations. Among its most influential contributions is the discovery and clinical development of *trained immunity*, an epigenetically mediated memory of innate immune cells that represents a major paradigm shift in immunology. The program has made significant contributions to development of 'personalized immunotherapies' against severe infections and cancer.

A hallmark of the program's success is its mission-driven and integrative approach, combining deep immunological phenotyping with cutting-edge cross-omics analyses. This strategy has led to numerous high-impact publications. The program's visibility is further reflected by four researchers ranked in the top 1% most cited scientists globally (Web of Science) and by its leadership of landmark international initiatives such as the Human Functional Genomics Project (HFGP) and the International Trained Immunity Consortium, both of which unite multiple institutions across four continents. The program unites eighteen RGLs and over twenty senior scientists across disciplines including immunology, clinical medicine, systems biology, microbiology, and engineering. This ensures a dynamic and interdisciplinary environment, complemented by international partnerships with leading institutions. The program's training and mentoring record is equally impressive: over 150 PhD theses were defended between 2018 and 2024, reflecting a strong educational framework.

Despite its overall excellence, certain institutional and operational challenges persist. Data storage, security, and integration remain bottlenecks, particularly given the program's extensive cross-cohort collaborations. The administrative complexity of large, multi-institutional projects occasionally strains

resources and slows the translation of discoveries into clinical applications. Addressing these infrastructural and administrative constraints will further enhance the program's efficiency and impact.

19.3 Societal relevance

The program demonstrates societal relevance across health, economic, and educational domains. By addressing fundamental mechanisms of innate immune responses in infections, inflammation, and cancer, the program directly contributes to advances that improve patient care, inform public health strategies, and strengthen biomedical innovation. The program's discoveries have had a profound clinical impact, translating mechanistic insights into tangible health benefits. Its research has contributed to the development, regulatory approval, and global implementation of immunotherapies for COVID-19. The discovery and characterization of primary immunodeficiencies, such as TLR7 and STAT1-GOF variants, have led to improved diagnostics and personalized treatment strategies for rare immune disorders. Trained immunity, a paradigm-shifting concept pioneered by the program, has enabled immunotherapy trials aiming to improve the treatment of severe infections and cancer. The program is also involved in major international efforts to use experimental human infections for the development of new vaccines and therapies. The societal importance of the program extends globally, reflecting the universal relevance of innate immunity in nearly all major disease groups. The inclusion of diverse population cohorts across Europe, Africa, and Asia supports equitable scientific progress and globally applicable health solutions. Education and mentorship are central pillars of the program's societal relevance. Through comprehensive PhD training, interdisciplinary clinician-scientist mentorship, and postdoctoral development, the program has produced a new generation of scientists, many of whom now hold leading positions.

The program's translational success has stimulated collaboration with the biotechnology and technology sectors, including initiatives in AI-driven diagnostics, next-generation vaccine platforms, and precision immunotherapies. While the program's discoveries have yielded substantial health and societal impact, valorization potential remains partly underexploited. Public outreach is reflected by experimental human infection studies, patient-centered research, and transparent communication through public–private partnerships. Nonetheless, further investment in structured public outreach activities could strengthen societal visibility and engagement with diverse communities.

19.4 Viability

The program demonstrates high viability for the coming six years, supported by its outstanding scientific quality, strong societal relevance, effective leadership, and comprehensive resource planning. The program's mission aligns with global health priorities such as infection control, vaccine innovation, cancer immunotherapy, and preparedness for emerging pathogens. This strategic positioning ensures both scientific and societal demand for its continued development.

The program's leadership exhibits clear foresight and adaptability. Early adoption of systems biology, multi-omics integration, and AI-based analytical approaches has positioned the program at the forefront of technological innovation in immunology. Continued success in highly competitive grant schemes demonstrates financial resilience. A culture of collaboration and open data sharing reinforces the program's institutional and scientific viability. Strong international partnerships extend the program's sustainability and reach, ensuring access to complementary expertise, diverse patient populations, and advanced technologies. This collaborative model enhances both research productivity and institutional stability.

The program's human capital is well-balanced, encompassing established principal investigators, dynamic early-career researchers, and a steady influx of PhD candidates and postdoctoral fellows. The proactive mentoring and career development structure supports continuity and mitigates the risk of talent drain, while fostering the emergence of new research leaders. While overall human resource

sustainability is strong, limited tenure-track opportunities and international competition for top talent remain challenges that will require continued institutional attention.

19.5 Future outlook

The program is well-positioned to remain a global leader in innate immunology research over the coming decade. Its integration of deep clinical insight with omics-driven systems immunology, innovative translational approaches, and the coordination of major international cohorts and consortia provides a robust foundation for sustained scientific excellence and societal impact. This strategic environment enables rapid adoption of emerging technologies, a timely response to global health threats, and a continued stream of high-impact discoveries that bridge fundamental mechanisms and clinical application.

Strategic collaboration with University of Technology Eindhoven for harnessing opportunities of nanoengineering in the development of new vaccines and nanodrugs will further expand translational potential. Integration of precision medicine, machine learning, and population-level genomics will allow the program to bridge mechanistic insight with individualized patient care.

Despite its strong foundation, the program faces some potential risks and weaknesses. Scaling and integrating large, multi-cohort omics datasets require sustained institutional investment in secure, harmonized, and interoperable data infrastructures. As data protection regulations evolve, robust governance structures will be essential to ensure compliance, transparency, and sustained international collaboration. The large size and highly interdisciplinary nature of the program provide stability and strong collaboration opportunities but also increase the risk for loss of focus and low cohesion.

19.6 Conclusion

With its proven adaptability, strong infrastructure, and culture of collaboration, the program is very well-equipped to sustain its leadership in the rapidly evolving field of immunology. Its strategic integration of systems biology, AI-based computational approaches, and global collaboration ensures continued capacity to address the most pressing biomedical challenges of the coming decade while maintaining high societal and scientific impact.

The program has excellent scientific output, funding success and international collaborations. However, as a large program, its overall research vision is less clear. The programs' societal impact via clinical applications is very good and is expected to further increase in the coming years through focus on systems immunology and AI-based approaches, as well as large global collaborations creating valuable data sources.

19.7 Recommendations

- The cohesion of the research program, with a clear shared research vision, may be improved.
- Assess ways to increase patient engagement and public outreach.
- Enhancing skills for valorization may improve entrepreneurship.

20 Chronic inflammatory diseases

Chronic inflammatory diseases (CID) are common: the prevalence is estimated at 1 million patients in the Netherlands. CID include rheumatic diseases, systemic auto-immune diseases, inflammatory skin diseases, and inflammatory bowel diseases (IBD).

20.1 Mission, vision and strategy

This program has the aim to improve treatment outcomes for patients with chronic inflammatory disorders, implement novel therapies, and foster curiosity-driven translational research. This requires close collaboration between laboratories and clinical departments, to enhance individual patient care, prevent disease progression, and lower healthcare costs.

Current diagnostic criteria are integrated with clinical measurements, imaging techniques, and biomarker analysis. Personalized treatment responses are assessed through stratification by sex, age, and specific situations such as pregnancy and family planning. Strategies investigating safe dose reduction are applied to reduce medicinal costs. Alongside clinical research, the program includes experimental preclinical studies aimed at disease mechanisms, also to identify novel drug targets through the development of immunocompetent models, disease endotype models, drug screening, and drug repurposing.

20.2 Research quality

The program focuses on improving treatment outcomes and patient quality of life for - amongst others, rheumatoid arthritis, chronic inflammatory skin diseases (e.g., psoriasis and atopic dermatitis), inflammatory bowel disease, and systemic autoimmune diseases through early detection, disease stratification, biomarker discovery, and innovation in therapeutic monitoring. The program's integration of data registers, home monitoring, and sex- and age-inclusive research directly addresses societal and clinical priorities in sustainable healthcare and personalized medicine. While its focus on translational applications and patient-centered strategies ensures societal value, the overarching goals are more practice-oriented than conceptually pioneering. Given the limited size of the program (six RGLs and associated members) and the wide range of disorders studied, it remains unclear how the groups benefit from the program and how the program prioritizes the focus to gain sufficient depth along the "pipeline" from molecules to implementation. The overlap of diseases, model systems and use of technologies with other research programs creates opportunities for further collaboration.

The research quality of the Chronic Inflammatory Diseases program is good and scientifically relevant. Over the past six years, the program has chosen an interdisciplinary, cross-disease approach to address major challenges in rheumatology, dermatology, immunology, and gastroenterology. The main scientific outputs include the early detection of pulmonary function decline by home spirometry in patients with systemic sclerosis-associated interstitial lung disease, the identification of sex-differences in inflammatory profiles and pain, and the description of costimulatory molecules as key regulators of cytotoxicity-driven pathology in systemic sclerosis.

The program has built a research pipeline from innovative preclinical human models to state-of-the-art immune profiling and real-world clinical registers. Its academic reputation benefits from visible clinical translation, participation in large public-private partnerships (IMI/IHI, Hippocrates, Immuniverse), leaderships in major nationally funded programs (BIOMAP, NGID, ImmuneHealthSeed/ ImmuneHealthXL), and frequent guideline contributions (EULAR, ECCO, ASAS). The longstanding integration of patient perspectives, collaboration across medical and scientific departments, and active efforts to replace animal models with relevant human systems highlight a forward-looking strategy.

20.3 Societal relevance

Societal relevance is multifaceted, rooted in its direct impact on public health, patient well-being, and healthcare system sustainability. Its research addresses a pressing societal need. Through precision diagnostics, dose optimization, home monitoring and personalized care strategies, the program demonstrably improves quality of life, work participation, and long-term health outcomes, as well as reduces healthcare expenditure.

Data from registers and multicenter trials, such as the BeNeBio and RASSc studies, have informed new guidelines on biologic tapering and cost-effective drug use. These outputs exemplify how the program translates scientific insight into practical solutions for healthcare sustainability.

Public engagement and patient partnership are key elements of the program's impact. Patient organizations are co-creators in the multiple research consortia, including BIOMAP and NGID, influencing study design and dissemination. The outcomes of the program are disseminated in international guidelines and in the public domain through educational media, podcasts, and public lectures.

20.4 Viability

The viability of the program is good but not without risks. Its mission to enhance diagnosis, monitoring, and personalized treatment of chronic inflammatory diseases remains highly relevant in the face of increasing global disease burden and the need for sustainable healthcare systems and ensures continued potential for societal and clinical importance in the coming decade.

The program benefits from a solid infrastructure within Radboudumc's Clinical Center for Inflammation, Immunity and Infection (COIA), with close integration among clinical specialties, experimental labs, and computational teams. Leadership demonstrates foresight in aligning with major international consortia and leveraging public–private partnerships, which ensures robust funding and translational opportunities. The program's multi-level collaborations and clinician-scientist workforce provide a strong foundation for continuity and interdisciplinary innovation.

However, future viability depends on addressing several structural and strategic challenges. The limited number of group leaders and growth opportunities for early-career researchers pose a risk to talent continuity. Sustained success will require formal career development pathways, recruitment of next-generation leaders, and retaining a critical mass. The number of group leaders is relatively small.

Additionally, while the program excels in clinically informed and translational research, it would benefit from further attention to experimental preclinical capabilities in frontier areas, such as computational biology, AI-based stratification, and advanced imaging, to remain competitive internationally.

20.5 Future outlook

The outlook for the program is built upon a solid interdisciplinary foundation spanning rheumatology, dermatology, gastroenterology, and immunology. The program's emphasis on early diagnosis, biomarker discovery, and cost-effective treatment strategies ensures continued societal and clinical relevance as healthcare systems shift toward sustainability, digitalization, and individualized care.

Looking forward, the program is well positioned to contribute to guideline development, real-world evidence, and disease prevention through initiatives such as the NGID consortium and the Immune Health XL platform. Its integration of home monitoring technologies, AI-assisted imaging, and sex-differentiated research underscores a forward-looking approach that aligns with both patient engagement and policy priorities. Strong institutional embedding within Radboudumc's Center for Inflammation, Immunity, and Infection provides structural stability and collaborative momentum.

There are some potential weaknesses and risks. First, it is of crucial importance to ensure generational renewal, talent retention, and maintenance of critical masses. Second, computational and systems immunology expertise remains critical to the program. Finally, the small number of group leaders brings the risk of limited cohesion between the groups given the spectrum of diseases studied.

20.6 Conclusion

This program demonstrates good research quality. Its interdisciplinary, cross-disease strategy has produced a coherent translational pipeline from mechanistic discovery to clinical implementation. The research is scientifically sound and internationally connected, with visible outputs in biomarker discovery, dose optimization, and guideline contributions. While primarily practice-oriented rather than conceptually groundbreaking, the program's clinical and translational quality is consistently high.

Societal relevance is clearly visible because the program delivers tangible benefits for patients and healthcare systems. It enhances quality of life, supports cost-effective care, and influences international clinical standards. Patient engagement and public outreach further strengthen its societal impact. The viability of the program is supported by strong institutional embedding, interdisciplinary collaboration, and active participation in European consortia.

Overall, the program is recognized as a dynamic, clinically embedded research environment with clear translational value and a well-defined path toward future excellence in chronic inflammatory disease medicine.

20.7 Recommendations

- Investigate possibilities to align or integrate the research activities with other research programs.
- Strengthen talent renewal and career development to ensure long-term leadership continuity and critical mass.
- Invest in computational, AI-based, and systems immunology expertise to enhance mechanistic and predictive research capacity.
- Maintain focus by prioritizing research lines that best exploit the cross-disease approach and available translational infrastructure or by selecting specific diseases.
- Further integrate preclinical innovation with digital and clinical research pipelines.
- Continue fostering patient involvement and cross-program collaboration to sustain societal impact and institutional synergy.

21 Optimal infectious disease care and outbreak response

Preventing, accurately diagnosing, and effectively treating infections is vital for ensuring health and wellbeing for people of all ages. This program focuses on usual care of infectious diseases as well as outbreak situations.

21.1 Mission, vision and strategy

The program aims to secure sustainable access to high-quality infection prevention and control, diagnostics, and antimicrobial therapy. The mission of the program is to reduce the incidence and impact of infectious diseases through a combined approach of antimicrobial and diagnostic stewardship, infection prevention and control, and early and effective case management. While focused primarily on hospital care, the program also seeks to strengthen the links across the healthcare system and public health to address global threats such as antimicrobial resistance and infectious disease outbreaks.

At the patient level, the program aims to improve infectious disease care through evidence-based prevention, diagnosis, and treatment. At the population level, the program strives to contribute to the reduction of hospital-acquired infections, outbreaks, and antimicrobial resistance.

Key objectives of the program include the development of innovative prevention measures, diagnostic strategies, antimicrobial treatments and outbreak response strategies, the integration of proven innovations into standard care, policy, and guidelines (implementation science), the translation of research into education and training (educational research) and the advancement of research methodology and data collection across these areas.

21.2 Research quality

The research line aims to converge two separately operating programs, with one focusing on hospital care and one focusing more on outpatient populations. The research program is composed of RGLs from six different departments who all contribute to either optimizing in-hospital infectious diseases care or reducing antimicrobial resistance and preparing for outbreaks. Areas of strength are the work on antibiotic stewardship, outbreak preparedness and response, and high containment patient care. This is a broad focus, seen as essential because of the need for continuity of infectious disease outbreaks in the health care system, and therefore the need for an integrated approach to infection and outbreak diagnosis, treatment, and prevention.

The combined expertise brought together in this research team is quite unique and therefore offers great potential for innovative research. The choice to combine the different areas of the care system into a joint research line is strategic, and requires a longer-term vision, given its complexities. The current umbrella is broad and comes across as a strategic program that provides ‘a Christmas tree’ of interesting projects, that all seem to fit under the same umbrella, but may lack coherence. There is a strong emphasis on implementation and training, also on international projects, and this is where the current strength of the research line lies. There is substantial enthusiasm visible, with clear plans delineated, but the interaction between the public health department and the clinical departments may need strengthening.

21.3 Societal relevance

The program does address an important societal challenge, which is the continued threat of infectious diseases and the rise of antimicrobial resistance. Societal relevance is a strong aspect of this program, particularly the training and teaching aspects developed through historic programs and currently supported by international funding. Given the weight of the research line’s focus on implementation,

it would be interesting to explore whether some of the international training programs can be coupled with implementation research projects.

21.4 Viability

The group so far has been successful in securing funding, but funding for preparedness and infectious diseases is under threat, both nationally and internationally. Currently, the talent program is underdeveloped.

21.5 Future outlook

This program addresses an important problem in healthcare research, bringing together different silos of the healthcare system in its ambition to reach a collaborative infection prevention research agenda. With long-term vision, the research quality can remain of good quality, whereas societal relevance is not likely to diminish.

There are some potential weaknesses and risks. First, the program would benefit from further specification of its joint research ambitions and a clear long-term vision. This should include a need for translation of the high-level vision into concrete and focused collaborative programs. Second, the innovation aspect is not very visible. Links with biologists and molecular sciences are important and should be developed. Finally, continued funding may be at risk, which calls for sharpening the strategic vision.

21.6 Conclusion

The committee considers the research quality, which is mostly implementation research, important and a clear strength. However, the question remains what the ambition is for new research, based on lessons learned from the group's expertise and experience in outbreaks nationally and internationally. The program has major societal impact through training, outreach, public engagement, and work with low- and middle-income countries.

Currently, the program is viable. For the future, a clear strategy is required. The innovation aspect is less visible and tangible from what has been provided. The group is strong in implementation research, but it would be good to develop a vision on the bidirectionality of translational research.

21.7 Recommendations

- The team is encouraged to take the strategic discussions on the joint research lines a step further.
- The program should answer the key question whether it is possible to come up with some research lines that truly connect the different pillars of the care system.
- The innovative science part of the program should be better developed and defined.
- Links with other programs, such as academic drug therapy development and controlled human infection models, should be explored.

22 Human challenge models

A human challenge model is a deliberate infection of humans with a pathogen. This is done under strictly regulated conditions, with oversight from ethical and regulatory authorities, and based on thorough risk-benefit assessments at both individual and population levels. In this research program, infection, inflammation, immune response and transmission are studied in vivo, with human models.

22.1 Mission, vision and strategy

The program focuses on three main goals. First, it aims to drive methodological innovation by developing new challenge models. This is done by improving study designs, advancing simulation and mathematical modeling, and enhancing biomarker development followed by validation. Second, the program seeks to increase efficiency in healthcare by increasing collaboration to address gaps in human capacity and infrastructure. The third goal of the program is to build capacity by establishing and evaluating effective governance models, training young researchers at Radboudumc and partner institutions, and expanding the international network. The program adopts an interdisciplinary approach, offering an interactive framework that integrates clinical development, methodology, ethics, societal impact, and the support of emerging talent.

22.2 Research quality

The program entails innovative, high-quality and complex research using human challenge models of infectious diseases. The research quality of the program is high, and the human challenge models have been pivotal in several important discoveries in recent years, e.g., in phase 1 trials for vaccines and novel adjunctive treatments in infections. This strength is particularly visible in the longstanding malaria work, and in the bacterial pathogens. The program brings together researchers from internal medicine, pharmacology, intensive care, medical microbiology, laboratory medicine and IQ Health. The collaboration of the RGLs within the program ensures optimal use of the challenge models, a joint approach to troubleshooting and regulatory and administrative processes, and provides a strong link to basic immunology research. Expertise on viral infections has been added through interaction between the research program members.

Methodologically the program is very strong, and because of the complexity of human challenge models it has a unique position within the Netherlands (and abroad). The researchers in this program are performing research initiated by researchers from other programs or industry but also have their own aims at a different level. These are: improving the methodology and efficiency of the human challenge models and maintaining sufficient capacity. The input of this research program to the performed studies is sometimes difficult to weigh as the RGLs in the program are also involved in (multiple) other programs.

22.3 Societal relevance

The societal impact of the program is excellent, with a clear scientific impact of the performed work, strong public engagement with visibility in (inter)national media and during music festivals, and many examples of connecting with policy makers and grant providers (NIH, ZonMW, etc.). Studies are both investigator-initiated and industry-commissioned. Challenge studies are also performed in conjunction with international partners, increasing the impact of the work. The program has invested in policy advice by writing a roadmap on controlled human infection studies. The regulatory aspects are clearly well-covered, and scientific outreach is achieved through articles in newspapers and television programs. The group has increased its societal impact by implementing the experience in human challenge models in lower- and middle-income countries, where the relevance of the models is even greater. The program participates in InFECT-NL to meet needs in the preparedness research field. Within the InFECT-NL consortium this research program focuses on the human challenge models, and integration with research from four other UMCs.

22.4 Viability

The overall viability is very good, with multiple ongoing projects, successful acquisition of grants for new projects and a broadening array of diseases that are modelled in the human challenge models. The research infrastructure is of high quality and there is excellent access to participants and expertise. The presence of the insectary at Radboudumc ensures that human challenge models can continue to play a key role in the vector borne disease research. Collaboration within the institute, and on a national and international level, is excellent as well.

The researchers in the program benefit from being together and sharing expertise and knowledge on regulations and ethical aspects of human challenge models. However, a question that does arise is whether a research program is the best format for such interaction. The research on the models itself (efficacy, sustainability and capacity building) is currently limited and perhaps not sufficient to exist as a research program.

22.5 Future outlook

The human challenge models in infection are a unique asset of RIMI and deserve full support from the institute as it facilitates high-quality, unique experiments that drive innovation in several areas of research including vector-borne diseases, sepsis and respiratory infections. The program functions well with monthly meetings, a top-notch research facility and a team of dedicated scientists who interact actively. The complexity of the models, ethical aspects, potential changes in regulations and geopolitical situation present ongoing challenges that require constant vigilance from the team.

There are also potential risks and weaknesses. First, research questions and funding are mainly driven by other research programs such as the vector borne disease program and innate immunity program. There are no examples of studies or funding presented to the committee that contribute to the aims of the program (improving methodology). Sharing the expertise on human challenge models does not necessarily need to be in the form of a research program. Second, there are upcoming renewed regulations for human challenge research, and the facilities may currently not meet the requirements. Third, performing human challenge models abroad is vulnerable to geopolitical changes, e.g., due to travel restrictions. Finally, legal support needs to be timely to maintain the flexibility of the program.

22.6 Conclusion

The human challenge models research program presents a unique, high-quality research modality that pushes innovative research in several key research groups in RIMI forward and has contributed strongly to scientific breakthroughs in the past years. The research quality is very good with high impact. The RGLs and other research program members form a strong community around the theme of the human challenges models and help to improve each other's projects, with a strong link to basic immunology. The program demonstrates a strong drive for further interaction with other RIMI investigators, but also nationally and internationally the necessary links for collaborative projects are in place. The societal impact of the program is exemplary for other research programs. The viability is very good although there is continuing threat of high costs of the models, potential changes in regulations, and ethical aspects of human experimentation. These threats are adequately identified by the research program members and incorporated in the long-term strategy.

22.7 Recommendations

- The RGLs could consider another format such as being a core facility or part of a clinical trial facility rather than a research program, as this may free up other types of support from RIMI. If continuation of the research program in its current form is preferred, more emphasis on the described goals of model improvement and capacity building should be visible in the output and grant applications.
- The program is still young and further development in the coming years is required to develop a shared grant strategy to initiate research projects specifically tailored to the aims of the

program. These may include cross-model studies on innate and adaptive immune responses to different stimuli, including e.g. transcriptomic, proteomics or clinical biomarkers. Cross-research program coordination may need to be formalized to connect the results from human challenge models to patient cohort data, in vitro, organoid and animal experiments and vice versa.

- Currently, there is involvement and engagement of public and patients, and active participation of previous participants, but these interactions should take place at every step of the experiments including the human challenge model design, evaluation of the models, and the analysis and dissemination of the results.
- There are no program members on the career track. A clear strategy for attracting talented researchers from outside the institute would be valuable.
- Interaction with industry may be increased as an alternative source of funding. This can have a bidirectional effect when discoveries in the program can be commercialized through public-private partnership.

23 Vector-borne diseases and zoonoses

This research program studies vector-borne diseases, illnesses caused by parasites, viruses, or bacteria transmitted through infected vectors such as mosquitoes, and zoonoses, infectious diseases that originate in non-human animals and have been transmitted to humans.

23.1 Mission, vision and strategy

The core mission of the research program is to conduct transformative research on vector-borne diseases and zoonoses to enhance the knowledge on disease pathogenesis and transmission, develop innovative interventions and maximize the public health impact of both new and existing strategies. Through translational and applied research, the program is committed to develop innovative interventions and prevention strategies and aims to enhance their impact on public health. To this effect, epidemiologists, computational scientists, molecular biologists, pharmacists, and clinicians collaborate on studies in regions heavily affected by vector-borne diseases.

23.2 Research quality

The program represents an internationally leading research effort with a long-standing track record of excellence. Its success is built on a powerful combination of basic, translational, and clinical research, supported by one-of-a-kind experimental infrastructure and deep partnerships in endemic regions across Africa and Asia. The program has demonstrated a sustained capacity to generate high-impact discoveries, drive methodological innovation, and translate fundamental insights into interventions with global relevance.

The program's scientific output is of high quality, with multiple examples of fundamental discoveries that have reshaped our understanding of vector and pathogen biology, such as the discovery that endogenized viral sequences in mosquitoes can provide heritable antiviral immunity, the development of biteOscope, BuzzWatch, and SpitGrid, combining AI-driven imaging, computational modeling, and entomological precision, and last but not least the identification and clinical testing of monoclonal antibodies and transmission-blocking vaccines against *Plasmodium falciparum*. The success of the program is rooted in a deeply interdisciplinary approach that integrates molecular virology, vector biology, immunology, epidemiology, pharmacology, clinical medicine, and computational sciences. This wide-ranging expertise allows research questions to be addressed across biological scales, from molecular mechanisms to population-level dynamics, and enables the development of interventions grounded in real-world transmission processes. The ability to conduct early-phase intervention studies in endemic areas is a direct result of decades-long partnerships, which exemplify the program's international credibility and its commitment to equitable global collaboration. The program excels in attracting both talent and competitive funding. The team combines experience with a youthful demographic, creating a fertile environment for innovation. At the same time, several structural bottlenecks affect talent development—particularly for female scientists.

While the program title includes "Zoonoses," this component is currently underdeveloped, inconsistently represented, and not well integrated into the main scientific program.

23.3 Societal relevance

The program's societal impact is multidimensional, extending from health policy to community engagement, with a high global health impact, addressing diseases (malaria, dengue, Q-fever) that collectively cause immense morbidity and mortality. Further the program directly informs WHO guidelines, national policies, and European clinical standards (e.g., Q-fever, malaria elimination, dengue vaccination). The program is strong in diagnostic innovations already implemented in hospitals in Burkina Faso and the Netherlands, improving surveillance and rational treatment. Clinical deployment of vaccines and monoclonal antibodies represents a direct pathway to disease elimination.

The program achieves community and citizen engagement. Projects such as Mosquito Magnet integrate public participation and science education, bridging the gap between academia and society. In addition, active involvement of patient associations ensures that research aligns with societal needs. Team members have policy influence as they hold key leadership roles in WHO, ESCMID, LCI/RIVM, and the Netherlands Health Council, shaping national and global health strategies.

23.4 Viability

The program's viability is strong, underpinned by infrastructure, funding, and partnerships. It has world-class malaria and vector laboratories, including the only European facility for infected mosquito production. Advanced AI-based behavioral tracking systems and transgenic mosquito facilities create competitive advantages. The program has a sustainable funding base. Active grants include those from ERC, NWO, Gates Foundation, NIH, Horizon Europe, and others. Team members have deep, long-term partnerships across Africa (Mali, Uganda, Burkina Faso, Ethiopia, Tanzania) and Asia (Indonesia). There are cross-appointments and joint programs with Pasteur, LSHTM, UCSF, University of Tübingen, and others ensuring international integration. The program's human capital is strong, with a young, dynamic, and increasingly diverse research team. However, equal gender representation has not yet been reached.

23.5 Future outlook

The next decade offers major opportunities for the program to expand its global leadership in vector-borne (and zoonotic disease) research. Key directions include expanding translational research pipelines, integrating vector, pathogen, and host data using AI, machine learning, and multi-omics approaches to create predictive models for transmission and outbreak dynamics, responding to global environmental change,

There are potential risks and weaknesses. First, bridging timelines between discovery and implementation through translational pathways require long-term, cross-sectoral collaboration beyond traditional academic timelines. Second, it is important to maintain infrastructure flexibility. Third, continued success depends on attracting, mentoring, and retaining a diverse pool of researchers in a highly competitive global research environment and supporting them to follow their careers to a senior level.

Despite the presence of strong female early-career researchers, career progression pathways are constrained by limited senior-level positions and insufficient opportunities for young women to independently pursue major grants. Effective re-use and standardization of complex datasets (behavioral, clinical, genomic) remain a logistical and ethical challenge.

23.6 Conclusion

The program stands as an internationally leading center of excellence distinguished by outstanding research quality, transformative scientific discoveries, and a deeply embedded global health mission. Its integration of basic, translational, and clinical research, supported by unique infrastructure, enables a full continuum of innovation from molecular insights to real-world implementation.

The program's societal impact is equally impressive. Its research informs WHO guidelines, national policies, and clinical standards across Europe, Africa, and Asia, and its diagnostic and interventional innovations are already deployed in hospitals and clinical trials. Furthermore, the program maintains long-standing, equitable partnerships with institutions across endemic regions, ensuring that research advances are grounded in local needs and promote capacity strengthening. Parallel efforts in citizen science, community engagement, and patient involvement underscore the program's commitment to societal trust, communication, and relevance.

The program's viability is supported by a robust and diverse funding landscape and a dynamic cohort of young researchers. Its strong international network- spanning public health agencies, academic

institutions, and global health organizations, creates a highly connected ecosystem capable of sustaining long-term scientific and societal impact.

23.7 Recommendations

- To maintain its momentum, the program may consider revisiting aspects of its strategic definition. particularly the role of zoonosis research. If zoonoses are to be a meaningful part of the program, substantial investments are required.
- Given the program's dependence on high-maintenance vector and pathogen facilities, continued institutional support is required to ensure stability and technological competitiveness.
- Continued progression of monoclonal antibodies, transmission-blocking vaccines, and diagnostic tools toward late-stage clinical validation and deployment should be prioritized. Strengthened collaborations with regulatory agencies, industry partners, and international trial networks will help bridge the gap between laboratory breakthroughs and global health implementation.
- The program would benefit from unified data governance frameworks and shared platforms for integrating behavioral, genomic, clinical, and epidemiological datasets.
- Greater involvement of clinicians and active participation of patients in study design, implementation, and evaluation will help align research priorities with real-world health needs and increase the societal relevance and impact of the program's work.
- Expanding citizen science initiatives, community participation projects, and policy engagement mechanisms may strengthen public trust and ensure alignment with societal needs.

24 Fungal diseases

Fungal infections are common, partly due to the number of vulnerable individuals, such as those with a weakened immune system and or underlying lung conditions. Fungi present a significant public health threat, driven global travel, climate change, and emerging drug resistance. Treatment is difficult, as there are limited resources and only three classes of antifungal drugs currently available in clinical practice.

24.1 Mission, vision and strategy

The overall mission of the program is to advance the understanding, prevention and treatment of fungal diseases, especially those with high morbidity and mortality. The program aims to contribute to reducing the global burden of fungal diseases, enhance patient outcomes through precision medicine and raise public awareness. Key objectives of the program include identifying host vulnerabilities and underlying mechanisms of pathogenicity for targeted treatments, developing new diagnostic and therapeutic approaches, improving global surveillance of emerging fungal threats and antifungal drug resistance, and fostering interdisciplinary collaboration to bridge critical research gaps. Fundamental research, clinical studies and applied methodologies are integrated in the program. Through a focus on translational research and global collaboration, the program is committed to reduce the impact of fungal diseases and improve outcomes for those affected.

24.2 Research quality

The program has an outstanding track record, with projects and outputs that range from mechanistic insights, clinical insights and results of therapeutic trials. The collaborative outcome is more than the sum of parts, with strong global visibility for the individual parts. An interesting focus is on clinical treatment and diagnosis using pan-fungal testing by next-generation sequencing. This work is done with cohorts from across the country.

24.3 Societal relevance

Fungal diseases are an increasing and increasingly recognized problem. This research program can take credit for raising awareness of the importance of fungal infections, which is an important aspect of societal impact. Members of the program are involved in guideline development, which have clear impact.

24.4 Viability

While the program has had a strong track record with long-established specialists who are well recognized in the field, both nationally and internationally, it is less clear whether there is a longer-term outlook on continuity of the program. The junior team members are mostly clinical scientists, which does not reflect the multi-disciplinarity that the track-record of this research program was built on. The integrated research ambition is not clearly defined in the financial and viability outlook of the self-assessment report, which seems to steer more towards commercial trial funding. While this is understandable and a trend observed in many medical centers of universities, it also is a clear risk regarding the future of this research program.

The program report mentions that '*Sector plan initiatives are not fully utilized within the field of drug development. Need to strengthen pharmacological knowledge for lead identification and product development.'* This could help in diversifying funding, but it is not clear whether this is a viable option for the future.

24.5 Future outlook

The combined clinical expertise in the fields of microbiology, molecular pharmacology, clinical pharmacology, are relevant for rigorous execution of clinical trials and the focus on inflammation and

health policy. The emphasis seems to be towards clinical activities, whereas the mechanistic research is less clear.

There are also potential risks and weaknesses. First, from the presentation of the research line, it appears there is a strong clinical focus with less clear strategy or vision towards more basic research. Second, several RGLs retire soon, which calls for succession plans. Finally, the innovation potential is not fully secured.

24.6 Conclusion

The research quality is high, particularly in translational research, but the link with innovative and basic research could be strengthened. Regarding societal impact, the committee considered it excellent, observing that the program is consulted for clinical treatment guidance from outside the hospital and that members are involved in guideline development. Viability is generally good but requires attention regarding strategic choices.

24.7 Recommendations

- The basic research elements of this research line should be strengthened to retain a translational research program. Currently, the balance, including with incoming researchers, appears to be mostly on the side of clinical research.
- It is important to also engage in new research to build insights into future clinical excellence as well. It was not obvious where the team sees the opportunities for innovative (mechanistic) research.
- Identification of junior talent with basic and mechanistic research expertise is needed who would be eligible for competitive funding to secure long-term viability and replacement of retiring RGLs.

25 Treatment optimization for mycobacterial diseases

Tuberculosis (TB), the main mycobacterial disease, is caused by mycobacterium tuberculosis, and is the leading infectious disease killer worldwide. In addition, non-tuberculous mycobacteria (NTM) are emerging and causing infections, leading to global health problems. Diagnosing and treating TB and NTM diseases is difficult, with additional barriers at the policy and implementation levels. This research program addresses these aspects.

25.1 Mission, vision and strategy

This research program's mission is to optimize treatment and outcomes of mycobacterial diseases, as a national and international referral center for mycobacterial diseases.

The goals of the research program are to develop diagnostic approaches that enable personalized treatment of mycobacterial diseases, and to create, refine or repurpose drugs that improve treatment outcomes. The program aims to integrate these innovations into health policy and clinical practice, with the patient perspective central to the research, and strengthen human and infrastructural capacity to support international research efforts. The program is committed to train the next generation of talented researchers in the field of mycobacterial diseases.

To reach these goals, program members have adopted an integrated, multidisciplinary strategy built around three interconnected areas of activity: (1) preclinical research, (2) clinical research, and (3) health policy and implementation research. These domains form a translational chain designed to lead to output and generate outcomes that improve the treatment of mycobacterial diseases. With this strategy, the program has the ambition to deliver societal impact both at Radboudumc and globally.

25.2 Research quality

The committee assesses the Mycobacterial Therapy Optimization research program as a strong program that combines translational, clinical and implementation research in a coherent way. The program is highly visible nationally and internationally and benefits from a strong international network, which is essential in a field where the disease burden and clinical trial capacity largely resides outside the Netherlands. The program has delivered high-quality scientific output, including several impactful randomized controlled trials.

The program addresses clinically relevant problems across the treatment continuum: rapid detection and characterization of drug resistance, host–pathogen interactions, optimization of drug combinations and dosing to improve outcomes and reduce adverse events, and improved understanding of paradoxical reactions using multi-omics approaches. The committee considers this approach of linking mechanistic insights to clinical outcomes and implementation questions an important strength.

Over time the program's scope appears to have become broader than 'treatment optimization'. The program reports a clear shared strategy across seven research group leaders from multiple departments.

25.3 Societal relevance

The societal relevance of the program is high, both nationally and globally. Tuberculosis continues to be an enormous global health burden, while non-tuberculous mycobacterial disease represents a rising clinical burden. In line with its aims, the program demonstrates a strong ability to translate scientific insights into patient benefit through an integrated approach that links mechanistic and translational research to clinical studies and implementation. The committee recognizes clear pathways to impact through high-quality clinical research that informs clinical practice, as well as contributions to guidelines and engagement with policy-relevant stakeholders. Capacity building and

long-standing collaboration with partners in high-burden regions further strengthen the program's societal reach, ensuring that research questions, trial conduct and eventual uptake are connected to the contexts where improvements in treatment are most urgently needed. The committee notes that part of the program's broader societal ambitions, particularly in health policy and implementation, are still developing. While strengthening this dimension could enhance uptake and sustainability of impact, the program should strive to make deliberate choices about how far to expand into health policy research versus prioritizing and consolidating its current strengths in translational science and clinical trials.

25.4 Viability

The committee considers the program's goals to remain scientifically and societally highly relevant, given persistent global challenges posed by tuberculosis and NTM disease. The program has demonstrated strong viability through effective acquisition of external funding, including leadership in international initiatives such as UNITE4TB, and its track record and international network are likely to keep it an attractive partner for future consortia.

Two of the seven research group leaders are retired, and it remains unclear how replacement will be secured and whether future leadership will be developed from within the talent pipeline or primarily via external recruitment.

25.5 Future outlook

The committee sees a strong outlook for the program, given its international visibility, impactful clinical and translational research, and role in major global initiatives. Future success will depend on maintaining focus and integration across diverse lines of work so that mechanistic, modelling, clinical and implementation components yield coherent outputs.

There are also potential risks and weaknesses. The funding landscape is changing, driven by shifting (inter)national political priorities and reduced attention to poverty-related and infectious diseases. Leadership continuity and talent development constitute a key vulnerability. Two research group leader positions are currently vacant. Only one junior researcher has entered the Talent Track.

25.6 Conclusion

The committee concludes that the program demonstrates high research quality, characterized by a strong international profile and an extensive global network that supports high-quality translational and clinical output. Societal impact is judged to be excellent, reflected in clear pathways to patient benefit through influential clinical studies and guideline contributions, active involvement of patients, and effective international collaboration. Viability is underpinned by a strong funding track record and consortia leadership, but global funding for poverty-related and emerging infectious diseases appears to be under pressure, making diversification and adaptation increasingly important. Sustaining leadership will require a clear and proactive strategy for developing and retaining young talent.

25.7 Recommendations

- A key recommendation is to sharpen and communicate the program's positioning (including whether the name should reflect its broader scope), and to demonstrate integration and scientific synergy across the seven RGLs.
- The program should develop an explicit succession and talent strategy, clarify strategic choices on specific capabilities, and articulate an adaptive funding strategy in response to shifting political priorities, including diversification of funding sources.
- The program should make choices on the extent of expansion into health policy and implementation, ensuring that any added expertise is clearly embedded and supports uptake without diluting existing strengths.
- In several research areas within the program strategic choices can be made explicit (e.g., the role of quantitative PK/PD modelling in tuberculosis and non-tuberculous mycobacteria research), and such capabilities should be built within the program or reached through strategic partnerships (e.g., hollow-fibre infection model) .

26 Cerebrovascular disorders

Cerebrovascular disease (stroke) affects one in five people during their lifetime in high-income countries, and almost one in two in low-income countries. Stroke has a global prevalence of over 100 million and an annual incidence of more than 12 million individuals. The prevention of cerebrovascular disease will have the greatest impact on these staggering figures, but complete eradication through prevention is unrealistic in the foreseeable future. Therefore, optimizing recovery in the acute, subacute and chronic post-stroke phase is of crucial importance.

26.1 Mission, vision and strategy

The mission of this research program is to reduce the burden of stroke. To fulfill this mission, the program defined three common goals. The first is to prevent stroke, through investigating the effects of both primary (preventing first stroke) and secondary (preventing recurrence) prevention on cerebrovascular disease and dementia. Secondly, the program has an etiologic aim and investigates inflammation in subarachnoid hemorrhage, intracerebral hemorrhage and cerebral small vessel disease (SVD), causes and consequences of cerebral amyloid angiopathy (CAA) and stroke in the young, and the role of atrial fibrillation in ischemic stroke. Finally, the program aims to improve the acute treatment of stroke, prevent incident vascular disease by innovative therapies, and to develop and implement home-based personalized rehabilitation strategies, all to ameliorate the prognosis for patients with stroke, and their quality of life.

26.2 Research quality

Overall, the research quality covered by this program is very good. This is a relatively small team, but with an excellent reputation as illustrated by impactful publications and grant acquisition. The unit operates internationally in collaborative research efforts, such as multinational randomized controlled trials and meta-analyses on relevant topics (funded, amongst others, by EU Horizon) and nationally with grants from the Netherlands Heart Foundation and ZonMW. Whereas the research output is of high quality, it is to some extent more aimed at refining the existing knowledge base than searching for true innovations and new interventions. Genetic markers and genomic technologies may be an avenue to explore in this context.

26.3 Societal relevance

The incidence of stroke makes this an area with clear relevance to society. The contributions to Dutch and European guidelines are important to shape the care for patients with stroke. Regional strengths include integrated neurology–neurosurgery–rehabilitation care pipelines, enabling rapid recruitment and implementation. There are three main pillars in the program, i.e., preventing stroke, identifying causes of stroke, and improving stroke prognosis. What might be considered missing is an aim on explicit implementation and driving change, which would particularly serve a societal relevance of improving outcomes across the globe within a range of different health economies. The program is actively involving patients, and the creation of patient advisory boards is commendable. Also, the reference to health service delivery is particularly relevant to society, especially in the context of how much society is prepared to pay for stroke prevention and care. However, there is little about how the program might raise awareness of stroke in the wider population and how to prevent and detect early signs. Furthermore, while engagement is deep within clinical and patient communities, broader societal dissemination, such as partnerships with industry, policymakers, and preventive public health initiatives, could be further strengthened. The impact on economic and educational domains is not fully developed.

26.4 Viability

Longer term viability of the program seems secure, based on its impact, relevance, quality and funding. The group has ample experience as a collaborative team, which creates trust for a viable future.

Expanding links with commercial bodies might stimulate research into novel areas with the potential to significantly improve outcomes for patients.

26.5 Future outlook

This program covers an important area of research that has clear relevance for patients and serves one of the largest medical problems. Based on the group's track record, with impactful science and adequate funding, as well as international collaborations, the outlook for the future is positive. The acquisition of a 14T MRI scanner by the Radboudumc will offer new opportunities to perform studies on small vessel disease.

There are several potential risks and weaknesses. The program has many subprograms, which do not fully operate as a unified entity. There is some overlap with related programs, i.e. Atherosclerosis and Thrombosis, which may lead to competition. The research, while of high quality, lacks to some extent a drive for innovation.

26.6 Conclusion

The Cerebrovascular disorders program produces high quality research with international impact. The program is highly relevant to society and has a good future outlook. As a program, this constellation is quite recent, and hence efforts are to increase synergy. Effective collaboration will be essential to ensure an enduring, world-leading endeavor. Without this, there is a risk that the program will fragment and potentially become absorbed into other research programs, losing the important focus on the brain.

26.7 Recommendations

- Establish a clear process for agreeing research priorities, with input from all relevant parties. This will help provide alignment, focus and avoid duplication and fragmentation of effort.
- To avoid detrimental overlap with other programs, notably Atherosclerosis and thrombosis, either by shaping the overlapping area in one of integrated collaborations, or by agreeing on delineating which group is active in which area, i.e., primarily assign cerebrovascular research to this program Cerebrovascular disorders. A merger of the two programs is another option, which on the one hand is the most logical, but might also be inadvisable since the combination may become unwieldy large. RIMI is advised to thoughtfully assess which approach is best.
- Focusing the research on new emerging areas, for instance genomics, or imaging.
- Extending communication beyond academic and clinical audiences to demonstrate how stroke prevention can be embedded within public health to strengthen societal benefit.

27 Dementia

Dementia forms a significant societal challenge. There are many types and subtypes of dementia, each of which is often multifactorially determined, shows heterogeneous clinical courses, and, with advancing scientific insights, has shifting disease definitions. Adding to this complexity is that many patients have a combination of several types of dementia. This complexity of dementia complicates healthcare systems and underscores the urgent need for improved prevention, diagnostic strategies and treatment. The societal impact is profound, affecting patients, families, and the broader healthcare infrastructure.

27.1 Mission, vision and strategy

The mission of the program is to reduce the burden of disease and economic impact of dementia on patients, caregivers, and society. This is aligned with the overall goal of the WHO Global action plan on the public health response to dementia 2017-2025.

The program spans the full range from fundamental to applied clinical research. For example, the program's fundamental research focuses on understanding disease mechanisms and developing intervention strategies by identifying new biomarkers for cerebral amyloid angiopathy (CAA) and Parkinson's disease/Lewy body dementia (PD/LBD), discovering mechanisms and biomarkers for cognitive and psychosocial resilience, and investigating blood-brain barrier (BBB) dysfunction in Alzheimer's disease (AD) and vascular dementia (VD). Additionally, the program aims to determine the impact of interventions on BBB integrity using translational neuroimaging studies and uncover mechanisms underlying known risk factors for dementia. In this way, deeper insights can be gained into the molecular and clinical aspects of dementia, leading to more effective diagnostic tools and therapeutic interventions.

The program's research can be summarized in four main themes with each theme having its specific goals (aims). Each research line is further organized into complementary research projects, in which several departments of the Radboudumc collaborate towards a shared objective and associated set of defined results.

27.2 Research quality

The research program has pursued a research strategy spanning mechanistic studies, biomarker development, prevention, and care in line with its mission to reduce the burden of dementia. Over the past years, this has generated scientific contributions at multiple levels in high-impact journals: fundamental insights into links between obesity, hypertension, sleep, and dementia, biomarker studies in Alzheimer's disease and cerebral amyloid angiopathy, randomized controlled prevention trials, and innovations in dementia care models such as DementiaNet. Nationally, the program has established a visible role in the Dutch Alzheimer Center, the National Dementia Strategy, and updates to the multidisciplinary dementia guidelines. Internationally, its work is competitive, contributing to EU-funded projects (H2020, JPND) and advisory roles (e.g., European Medicines Agency). These activities confirm academic reputation and recognition within the field.

The structured impact pathway of the program, linking biomarker discovery, mechanistic studies, and resilience frameworks to defined outputs and clinical translation, illustrates the program's research aims. It remains unclear how the stated aims (goals and subgoals in the impact pathway) will be achieved, and how its position in the national and international context is.

27.3 Societal relevance

The research program has demonstrated strong societal relevance, well-aligned with its mission to reduce the burden of dementia on patients, caregivers, and society. Its research has clear implications for healthcare systems, given the projected rise in dementia prevalence and associated economic

costs. Concrete contributions include the development and long-term evaluation of DementiaNet, which facilitates integrated primary dementia care and shows measurable patient and caregiver benefits, as well as randomized trials of mobile health interventions for dementia prevention in diverse populations. These initiatives directly address pressing public health needs and contribute to more sustainable care models.

The program maintains a close partnership with Alzheimer Nederland via the Radboudumc Alzheimer Center, ensuring bidirectional exchange between research and patient needs. This connection enhances dissemination, implementation, and alignment of research with real-world challenges. Program members have also contributed to national guideline updates (e.g., biomarker use, lifestyle interventions) and to policy through roles in professional organizations, the National Dementia Strategy, and the European Medicines Agency, underlining their influence on healthcare practice and regulation.

Educational outreach is another strength, with training for healthcare professionals, caregivers, and the public, complemented by strong media visibility in newspapers, television, and radio. These efforts enhance societal awareness and support inclusion of people living with dementia.

27.4 Viability

The research program is supported by a strong multidisciplinary team of nine RGLs and eight additional senior researchers across geriatrics, neurology, imaging, and primary care, complemented by senior researchers in translational neuroscience, rehabilitation, and health sciences. This breadth ensures coverage of the program's aims, from mechanistic studies and biomarker discovery to prevention and care innovation. The program's goals for the next six years, biomarker validation, prevention interventions, and resilience-based care models, remain highly relevant considering the rising dementia prevalence and align with both the WHO dementia action plan and the Dutch National Dementia Strategy.

The program has demonstrated its ability to secure competitive funding, including H2020, Joint Program in Neurodegenerative Diseases and National Dementia Strategy grants, and leading large global consortia. Institutionally, the program is well embedded within Radboudumc and the Donders Institute, giving access to infrastructure and local collaborations.

27.5 Future outlook

The program is well positioned to advance dementia research through its multidisciplinary structure, strong translational focus, and integration with national and international policy initiatives. Its strategic emphasis on biomarker discovery, prevention, and resilience-based care aligns with global priorities and provides a coherent framework for long-term societal impact. Stronger synergies with the other neurodegenerative research group (PD) and alignment with pharmaceutical and translational therapeutic development may become necessary to maintain and extend viability in the next six years.

There are some potential risks and weaknesses. First, a clear strategy for leadership is not presented. Furthermore, several programs may be highly dependent on a single RGL. Finally, synergy with other groups needs to be optimized.

27.6 Conclusion

The Dementia program demonstrates high research quality, producing influential work across mechanistic research, prevention, and innovative care models. Publications in leading journals and involvement in EU-funded consortia underscore strong academic recognition. The program's research portfolio is comprehensive, covering vascular, metabolic, and neurobiological contributors to dementia, and extending into pragmatic care innovation. However, the overarching strategy

connecting these diverse themes is insufficiently articulated, and the integration between foundational mechanistic work, biomarker discovery, and clinical cohorts remains unclear.

The program's societal relevance is very good, reflecting deep alignment with national and international priorities in dementia care and prevention. Initiatives such as DementiaNet and mobile health prevention trials address major public health challenges and demonstrate real-world impact. The program meaningfully influences clinical guidelines, regulatory discussions, and national dementia strategy development, supported by strong partnerships with Alzheimer Nederland and public-facing outreach. These achievements illustrate a research program that engages effectively with patients, caregivers, practitioners, and policymakers. The societal narrative could be strengthened by more explicit evidence of implementation outcomes and by outlining how emerging interventions—particularly those related to biomarker-informed diagnostics or Alzheimer pharmacotherapy—will be evaluated within care pathways.

The program shows solid viability, supported by a multidisciplinary team with wide-ranging expertise from basic neuroscience to primary care and ethics. Its goals for the next six years are scientifically relevant and aligned with international trajectories. Sustained competitive funding and integration within Radboudumc and Donders provides a stable institutional foundation. Nevertheless, the program's dependence on a small number of highly central RGLs raises concerns about long-term leadership continuity. Limited collaboration with the Parkinson's Disease program—despite shared biological themes—suggests untapped potential for synergy. Engagement with industry partners, particularly in the context of emerging Alzheimer disease treatments and biomarker translation, is largely absent from the current strategy and represents a gap.

The future outlook is promising, with clear strengths in prevention research, resilience frameworks, and personalized care models. The program is strategically aligned with global dementia policy priorities and positioned for significant societal impact. To maintain and enhance this trajectory, greater integration with related neurodegenerative programs, clearer articulation of translational pathways from laboratory to clinic, and the establishment of a leadership succession plan will be essential. More explicit engagement with therapeutic development and implementation, including the evaluation of newly approved Alzheimer treatments, would further strengthen the program's relevance.

27.7 Recommendations

- Enhance collaboration with the Parkinson's Disease program in shared domains (e.g., α-synucleinopathies, PDD, vascular risk, sleep) to exploit complementary strengths.
- Address leadership succession plans by articulating a strategy for developing future senior investigators and distributing responsibilities more broadly.
- Increase engagement with pharmaceutical and therapeutic implementation research, especially given the changing landscape of Alzheimer treatments and associated societal needs.

28 Parkinson & other movement disorders

In 1990, 3 million people were diagnosed with Parkinson's disease worldwide. Nowadays, that number exceeds 11 million and projections are that this rise will continue over the next years. Against this background, this research program studies Parkinson's disease and other neurologic movement disorders.

28.1 Mission, vision and strategy

The program aims to reduce the incidence, progression and burden of Parkinson's disease (PD) and other neurological movement disorders. By identifying risk factors, facilitating early diagnosis, implementing preventive measures, and developing disease-modifying interventions, the program aims to limit the disability experienced by affected individuals, reduce healthcare costs, and alleviate pressure on the healthcare system.

Goals for the next decade are to lay the foundations for a zero growth in the worldwide incidence of PD and to contribute to development of the first disease-modifying strategy to slow down disease progression, either in the preclinical or clinical stage, for PD and specific other movement disorders. Specifically, the program aims to generate new insights into the pathophysiology of movement disorders, develop innovative biomarkers, leverage AI-driven tools, and develop innovative treatments in both the symptomatic and disease-modifying domains, thereby advancing scientific research and fostering innovation in the field of neurology.

By developing and implementing novel symptomatic therapies and diagnostic tools, and by developing and applying novel remote monitoring technologies, the program seeks to enhance personalized patient care, leading to improved quality of life and better clinical outcomes for individuals affected by these disorders. Additionally, the program's research findings will inform the development of evidence-based public health policies and interventions aimed at reducing the incidence, prevalence and impact of movement disorders. The program's aim is to identify environmental risk factors that are contributing to the rapid worldwide rise of PD and other movement disorders. The program also focuses on affected patients, with an emphasis on promoting patient-centered care, empowering individuals to actively participate in healthcare decisions, and enhancing clinical practices to deliver more effective care.

28.2 Research quality

The research program has delivered research of high quality and international standing over the past years, well-aligned with its ambitious mission. The unit has produced highly relevant publications in the field of Parkinson's and other movement disorders (e.g. ataxia) across genetics, (digital) biomarkers, non-motor and motor symptoms, and integrated care models.

Overall, the program's research studies span a wide spectrum of Parkinson's disease stages, from individuals at-risk but still asymptomatic, through different phases in the disease after established diagnosis. The program's quality is also evident in its outputs beyond publications. For instance, the Personalized Parkinson Project has become a unique platform for high-quality longitudinal data collection, secure data sharing, and the integration of clinical, digital, and biological information in Parkinson's disease, and is now being extended through partnerships with the Michael J. Fox Foundation. Moreover, PRIME Parkinson received third-party funding and represents an integrative care model that is evaluated in the Netherlands (PRIME-NL study) using nationwide healthcare claims data and patient, caregiver, and professional surveys, offering both a rigorous assessment of patient-centered care and a template for evaluating complex healthcare interventions in dynamic environments. Recognition of scientific excellence is visible in the program's ability to attract competitive funding across career stages (VENI, VIDI, NWA-ORC, ZonMW, Horizon Europe) and in prestigious prizes and distinctions, including the NWO Stevin Prize and national honors for its leaders.

There is little interaction with basic neuroscience, which is a barrier for the aim of discovering pathophysiological mechanisms and developing disease modifying treatments. The program's major strengths lie in patient-related scientific research, but a translational approach is not evident beyond imaging and neurophysiology limiting the potential to discover groundbreaking insights in disease mechanisms (e.g. biobanking for genetics or toxin research).

28.3 Societal relevance

The research program has demonstrated outstanding societal relevance by translating research into innovations that have influenced care for Parkinson's Disease. The program initiated ParkinsonNet, a novel scalable healthcare concept that has shown to reduce disease complications and healthcare costs, and is now being extended to ataxia. Investigator-initiated studies such as Park-in-Shape, PD-PEST, and Slow-SPEED provide new evidence for lifestyle-based prevention, while PD-PAL advances palliative care strategies. A major strength is the focus on patient-centered care, also on underrepresented groups of PD patients.

The group has influenced European pesticide policies, contributed to national and international clinical guidelines, and pioneered digital biomarkers through the AI for Parkinson ICAI-lab. Societal recognition is reflected in public expert roles, strong patient engagement, and national honors. Collectively, these achievements show that the program not only produces high-quality science but also consistently delivers innovations that improve healthcare and shape policy, confirming its societal relevance as excellent.

28.4 Viability

The research program shows excellent viability. Its mission to reduce incidence, progression, and burden of Parkinson's disease remains highly relevant considering the growing prevalence of neurodegenerative disorders, and its aims and strategy are well aligned with expected scientific and societal developments. The program has strong and stable leadership, with multiple senior investigators in permanent RGL positions, complemented by a dedicated Research Support Team that strengthens trial capacity, data management, and financial oversight. The infrastructure, including the physical co-location of clinical care and research, nationwide ParkinsonNet, and public–private partnerships such as the AI for Parkinson ICAI Lab, provides unique opportunities for rapid translation and large-scale recruitment. The project has acquired strong funding with sustained success in acquiring national and international multi-year grants.

The research program shows thematic overlaps with the research program Dementia, particularly regarding cognitive decline in PD and biomarker discovery for Lewy body/α-synucleinopathies. Synergies are bridged by a common RGL, who contributes to translational neurodegeneration research across both programs. Nevertheless, the flagship publications of the program display little to no overlap in co-authorships with those of the Dementia program. This can stand for effective complementary work, but could also indicate missed opportunities of stronger integration. In addition, the lack of experimental model systems to test the different hypotheses is an aspect that may prevent easy moving from correlation to causality.

28.5 Future outlook

The program is well positioned to maintain international leadership through its strong clinical integration, unique longitudinal cohorts, and emphasis on prevention and personalized care. Its alignment with societal trends, such as lifestyle-based prevention, digital biomarkers, and integrated care models, supports continued relevance and impact.

There are some potential risks and weaknesses, which the program's limited interaction with basic neuroscience and experimental model systems that constrains its ability to advance mechanistic discovery and develop disease-modifying interventions. Dependence on a small number of highly

visible leaders raises questions of future succession and continuity. Moreover, the strong focus on environmental and lifestyle determinants introduces strategic vulnerability if major hypotheses (e.g., pesticide exposure) do not yield expected results.

28.6 Conclusion

The Parkinson's Disease and other Movement Disorders program delivers exceptional research quality, with internationally recognized contributions across digital biomarkers, genetics, motor and non-motor symptomatology, and innovative care models. Landmark outputs—including the Personalized Parkinson Project and PRIME Parkinson—demonstrate the program's unique ability to generate, integrate, and translate multimodal longitudinal data at scale. However, limited interaction with basic neuroscience and mechanistic laboratory work weakens the translational pathway from hypothesis generation to causal testing, and some research foci—particularly the emphasis on pesticides—may be overly narrow relative to the multifactorial etiology of Parkinson's disease.

The program demonstrates outstanding societal relevance, having shaped clinical practice, healthcare policy, and patient-centered care both nationally and internationally. ParkinsonNet remains a flagship example of scalable innovation, now extended to Ataxia. Lifestyle-based prevention trials, digital biomarker initiatives, and palliative-care innovations highlight broad societal engagement and relevance. To enhance clarity for stakeholders, the program's explicit prioritization of environmental, lifestyle, and organizational determinants, rather than pharmacological or device-based interventions, could be more clearly articulated.

The program shows strong viability, supported by stable leadership, robust research infrastructure, effective public–private partnerships (e.g. ICAI Lab), and a proven track record in large-scale grant acquisition. Cohesive clinical–research integration enables efficient recruitment and high translational potential. At the same time, greater synergy with the Dementia program could unlock additional opportunities in biomarker development and shared neurodegenerative mechanisms. The program's future outlook is good, with strong foundations in prevention, personalized care, and digital health.

28.7 Recommendations

- Consider approaches and infrastructure to support disease-modifying research.
- Enhance collaboration with the Dementia program, particularly around α-synucleinopathies and shared risk-factor research, to exploit thematic synergies.
- Consider strengthening the mechanistic research base, diversify etiological investigations beyond pesticides, and distribute leadership to ensure resilience. Enhanced integration with basic neuroscience and translational laboratories would support the development of disease-modifying strategies and help bridge the current gap between observational findings and causal interventions.
- Work on succession plans and continuity of leadership.

29 Neuromuscular disorders

Neuromuscular disorders are conditions that disrupt the communication between nerves and muscles, leading to symptoms like muscle weakness, atrophy, pain, twitching, and breathing difficulties. Inherited neuromuscular disorders display a variety in nature and degree of clinical symptoms. This research program studies neuromuscular disorders and their heterogeneity.

29.1 Mission, vision and strategy

The mission of the program is to make a significant impact on care and therapy for patients with neuromuscular disorders by understanding disease heterogeneity. To address this heterogeneity, the program designs trials and implements personalized evidence-based interventions.

The program's focus is on four major neuromuscular disorders (NMD): Myotonic Dystrophy (DM), Facioscapulohumeral dystrophy (FSHD), Duchenne muscular dystrophy (DMD), and Congenital myopathies & Metabolic myopathies (CM&MM). This selection is based on their prevalence, available expertise in care and research, and the outcome of a nationally agreed specialization in the six neuromuscular centers in the Netherlands ('Spierziekten Nederland'), acknowledged as UMCnl/VWS centers of expertise. With this focus, the program is well positioned to translate newly identified (digital, imaging and molecular) biomarkers, novel therapies (small molecules, antisense oligonucleotides and cell therapies), and rehabilitation strategies into clinical care and evaluate their effect on quality of life. In this, the program implements a reverse translation: from patient (needs) to the laboratory and back. The program acknowledges the importance of a "holistic" view on patient well-being (starting from the strategic theme of "Meaningful and value-based care") and a personalized approach in care, rehabilitation and other interventions.

29.2 Research quality

The research program has focused on four (rare) genetic neuromuscular disorders for which a wide range of aspects are studied: in the lab using cell lines, genetics and biomarkers, in clinical cohorts describing the natural history of disease, describe patient related outcome measures, and ancillary investigations, and finally rehabilitation strategies. This gives a profound insight in the pathophysiology of disease and creates trial readiness facilitating randomized controlled trials with future antisense oligonucleotides or CRISPR-CAS technology. The research quality is very good, with examples of innovative research in several cutting-edge developments, either within the research program or in (inter)national collaborative projects. There is excellent expertise in small population trials and a clear vision on publication strategies. The nature of genetic neuromuscular diseases (NMD) makes it a niche research area, but within this niche the group performs world-leading research. There is clear collaboration with other groups in the Netherlands and worldwide within the research community of researchers in these topics.

A clear vision on how the findings in these diseases may contribute to identification of general principles or research strategies that may be applicable beyond these four disease areas is not presented. This could increase the impact of the research program.

29.3 Societal relevance

This group excels in societal impact by interacting with patients, patient advocacy groups and other relevant stakeholders through organization of mixed patient-research conferences, involving patients in research proposals and policy makers. Good examples are the 'Spierenraad', participation in advisory boards of patients' organizations, guideline development and connections with regulatory bodies. Furthermore, the 'Serious request' donation campaign in December 2025 will have led to a high level of attention for neuromuscular research. It is not clear how the research program will

capitalize on such campaigns and whether there is a strategy on how to present themselves to the public.

The interaction with other medical professionals is clearly present, given the number of involved rehabilitation physicians and pediatricians. Also, the organization of workshops, development of guidelines and conferences with researchers and physicians exemplifies excellent knowledge utilization.

29.4 Viability

Overall viability of the research program looks very good, with three researchers in Talent Tracks, a clear research domain and strategy for the future, and the outlook on future therapeutics in these rare diseases. The latter is, however, also a risk, as there is a large dependency on the industry to develop these new treatments. Working towards repurposing trials mentioned by members of the research program may be a way out of this dependency.

The lack of staff scientists may pose a threat to the viability of the group. The staff scientists' program will be started by RIMI in 2026, which may alleviate this matter. The tension between clinical work and research is not unique to this program and the interaction between disciplines is also a clear strength of this type of research.

Funding appears to rely on the Prinses Beatrix Fonds and 'Spieren voor Spieren', which provides some reassurance for stability of funding of future projects. The aims of the research program are mostly relevant and achievable. In the funding strategy, no specific grants are mentioned such as the ERC program or Veni/Vidi/Vici tracks. Developing long-term funding strategies will increase the viability of the group.

29.5 Future outlook

The research program benefits from existing long-term collaborations between RGLs and other members of the program. The research topics and strategies are clearly delineated, but to some extent may limit the innovation potential. Regular interaction between RGLs/research staff in the program such as the Radboud Muscle Network and an annual strategy meeting ensures optimal use of the different techniques and perspectives on the diseases. The division of research areas within neuromuscular diseases research community in the Netherlands and collaborations on research technology enables the program to have access to the selected patient populations and thereby excel internationally in clinical research. The excellent interaction with stakeholders in the community is an important asset of this program and is exemplary for other research programs.

There are some potential risks and weaknesses. First, the level of bioinformatics support for the group may not be sufficiently secured. Second, although the matrix of diseases and disease elements provides a holistic view of the different neuromuscular diseases, it is unclear how the application of different methods across diseases is operationalized as (PhD) projects tend to focus on one aspect of one disease. Third, a clear vision on how the findings in these diseases may contribute to the identification of general principles or research strategies that may be applicable beyond these four disease areas is not present.

29.6 Conclusion

The neuromuscular program demonstrates a very high research quality, by focusing on all aspects of a focused number of genetic muscular disorders, spanning from cell line experiments, genetics, biomarkers, natural history studies, patient related outcome measures, trial readiness to rehabilitation strategies. Within the field of myotonic dystrophy, facioscapulohumeral dystrophy, Duchenne muscular dystrophy, and congenital myopathies and metabolic myopathies, the research program is among the international top and world-leading in several aspects such as having executed

the largest international clinical trial in myotonic dystrophy. The program is a perfect example of translational research. Strategic alliances with other academic research groups in the Netherlands, Europe and the rest of the world are important features of this research program.

The societal impact is excellent with patients and patient organizations involved in many aspects of the research, and exemplary for other research programs. The participation of RGLs in regulatory bodies, development of clinical guidelines, and generation of media attention are further proof of the societal impact of the research program.

The viability of the neuromuscular research group is very good, with three researchers in Talent Tracks. There is a steady flow of funding through funding agencies specifically funding muscular disorders such as the Prinses Beatrix Spierfonds, Spieren voor Spieren, Vereniging Spierziekten Nederland *etc.*, but also RGLs in the program have been awarded personal grants (Vici) or participate in consortia (Horizon 2020).

29.7 Recommendations

- Develop a clear roadmap that connects the program's pillars into a coherent set of overarching research questions and milestones. Further implementation of research methods and treatment modalities across diseases will enhance the impact of the research group.
- Several junior research group leaders have recently been admitted to the Talent Track program, and a strategy for grant applications should be developed for them.
- Formalize strategies for recruiting, integrating, and supervising machine-learning and data-science experts, including co-supervision models between clinical and computational PIs. Encourage development and sharing of open, well-documented code (e.g. Jupyter notebooks) and best practices for explainable, privacy-conscious AI in healthcare.
- Develop more dynamic and user-friendly web pages that give a clear, up-to-date overview of program members, expertise, projects, and key outputs, increasing internal and external visibility.
- Continue to support projects like buddy4caringparents and outreach activities that incorporate people with lived experience, ensuring that research questions remain grounded in real-world needs. Use the program's expertise in resilience and positive factors to contribute to destigmatization and to develop strengths-based narratives around NDDs in collaboration with patient organizations and policy stakeholders.

30 Stress and mental health

500 million people worldwide suffer from stress-related mental disorders such as anxiety disorders, depression, obsessive-compulsive disorders, addiction and substance use disorders. Along with this high prevalence, the burden of these disorders is exceedingly high. Over the past few decades, our understanding of the brain, and of how stress impacts its structure and function, has expanded exponentially. However, it remains a major task to translate this fundamental knowledge into effective solutions for these disorders.

30.1 Mission, vision and strategy

The mission of the program is to tackle one of the greatest public health challenges of this time: decreasing the vast burden of stress-related mental health problems, both in psychiatric and somatic illnesses.

To achieve this, the following four goals have been formulated: to advance mechanistic understanding of how stress affects brain structure and function by integrating insights across levels from molecules to neurocognitive systems and behavior, and across animal and human experimental models. The program will use state-of-the-art measurement techniques and mechanistic proof-of-concept interventions; to identify genetic and environmental factors that confer risk and resilience to stress, and to uncover the transdiagnostic disease and resilience mechanisms that operate across timescales – from immediate responses to life episodes and across the lifespan. This includes understanding how these mechanisms shape neuroplasticity, learning, and (mal)adaptation, to ultimately determine development of stress-related mental health symptoms, exacerbate or accelerate development of somatic/neurological diseases, or promote maintenance or quick recovery of mental health; to develop individualized and targeted interventions for the treatment and prevention of transdiagnostic stress-related symptoms or the mitigation of somatic disease symptoms, based on mechanistic, genetic, developmental, and computational understanding. Interventions address the full spectrum, from normative populations to individuals at risk and those experiencing psychopathology, targeting both multi-scale individual mechanisms and environmental modifications aimed at enhancing adaptation. The efficacy of these interventions, including their combinations, will be evaluated in randomized controlled trials, and the program will promote their implementation in (preventive) healthcare settings; and finally, to advance analytical data science approaches for investigating quantitative (bio)markers (including neuroimaging, -omics, population registers, satellite remote sensing, and offline as well as real-time behavioral phenotyping) for stress responsiveness and resilience, including the development of new algorithms. The program will make these techniques, tools and protocols available to consortia and the broader research community.

30.2 Research quality

The Stress and Mental Health program aims to reduce the global burden of stress-related mental health problems, which are among the leading causes of disability worldwide. It started 10 years ago as a bottom-up initiative and continued successfully in the theme phase, and now as a program. The program focuses on four highly relevant main objectives: advancing the mechanistic understanding of stress and resilience at genetic, biological, and behavioral levels; developing prevention and early intervention strategies for at-risk populations; improving treatments through innovative, mechanism-based approaches, and bridging the gap between science and clinical practice by implementing evidence-based solutions.

Strong points of this program are its broad interdisciplinary approach focusing on circuits, systems, and cognitive neuroscience, that combines psychology, behavioral science, and medicine, translational pathways, digital phenotyping and e-health approaches, and its computational pipelines. It emphasizes transdiagnostic mechanisms and seeks to unravel the complex processes underlying

stress and mental health. A less developed step in the program's translational chain is molecular neurobiology, which the program aims to strengthen through collaboration with other programs. The program has several internationally leading experts, a strong track record, with more than 60 completed PhD projects, numerous open-access publications, high impact papers, and national and international recognition through prestigious awards. It participates in major national and international consortia and networks such as Stress-NL, Stress-EU, DynaMORE, and ENIGMA, and contributes to large-scale cohort studies such as the Healthy Brain Study. The program describes ambitious, but sound, impact pathways for its various domains that do interact.

Overall, the research quality of the program is excellent. There are, however, some points that deserve attention and could strengthen the program. Development of new algorithms in machine learning and bioinformatics is relevant for identifying novel predictive patterns in mental health. Research or connections into this direction are not clearly delineated yet and could be a weakness for future translational work. In general, the report lacks details on potential omics analyses and digital tools to monitor mental health more effectively and comprehensively. In addition, achieving the program's stated objectives, which include gaining a mechanistic understanding of disease and developing targeted mechanistic interventions, will require a substantial molecular neuroscience component. Currently, molecular neuroscience appears underdeveloped or absent, representing a potential critical gap.

30.3 Societal relevance

The societal relevance of the program is high, as stress-related disorders are a leading cause of reduced quality of life and work disability. By developing faster and more effective treatments, supporting secondary prevention, and reducing health inequalities, the program improves mental health outcomes on a broader scale. There is close interaction with various stakeholders (patient organizations, healthcare providers, and industry partners) to improve the implementation of research findings. The program is committed to citizen science and open science.

30.4 Viability

The program's viability is also high: it has a strong interdisciplinary team of internationally leading experts from different backgrounds and sound structure and strategies. It has a good funding base, including institutional support, personal grants such as VENI, VIDI, as well as large consortia and public-private partnerships. Strategic collaborations with healthcare institutions and international partners further strengthen their viability and long-term impact. The demerging of the Radboudumc and the Radboud University, however, poses challenges for intra-institute collaborations. This concerns financial and legal matters, and there is also a clear need for RIMI to stimulate harmonization and uniform guidelines.

30.5 Future outlook

The program's documentation points at the strength of the program and the relevance of stress related mental health problems, with as a weakness the position of molecular neurobiology in its translational chain and threats being the limited funding for intra-institutional collaboration and the position of animal research in the Netherlands. The program aspires to enhance interdisciplinary integration for synergy, and its future goals align with Radboudumc's research domains (Discovery science, Health science, Innovation science and Data science). The program is depicted as local but well embedded in national and international networks and it collaborates with mental health institutions and industry partners to translate innovations into practice. The program perceives a striking lack of funding instruments for intra-institute collaborations. Its strategy is therefore to build a platform that promotes and supports applications for large-scale collaborative grants within the program.

There are some potential risks and weaknesses, which include a lack of digital tools to monitor mental health and underdevelopment of molecular neurobiology within the program.

30.6 Conclusion

The program started as a bottom-up initiative and has successfully continued into the current program. It has excellent research quality, with a strong interdisciplinary approach, high-impact publications, and active participation in major international consortia. It addresses a critical global health challenge and engages effectively with stakeholders. The program's viability is supported by a long-term involvement of research groups, a solid funding base, strategic collaborations, and alignment with institutional research domains. However, there are currently certain weaknesses that may limit achieving its ambitious translational goals, in particular the underdeveloped molecular neuroscience component and limited integration of advanced computational and omics approaches.

30.7 Recommendations

- To achieve its aims of achieving mechanistic understanding and targeted interventions, the program should establish and strengthen dedicated research groups or collaborations to address the current gap in molecular neurobiology. If such an expansion is not feasible, it is suggested to revise the program aims to align with existing available expertise.
- The program should also develop more bioinformatics and machine learning capabilities to support predictive modeling and personalized mental health strategies, while further incorporation of omics-based analyses and digital monitoring tools into research pipelines is also desirable.
- The program leaders should start a discussion with the RIMI board for the development of a structured platform to facilitate large-scale collaborative grant applications and harmonize guidelines across Radboudumc and partner institutes. Furthermore, new funding instruments specifically targeting cross-program and institute integration should be explored.
- Finally, the program should continue its diversifying of funding sources and reinforcing international collaborations to ensure its viability.

31 The brain across development in health and disease

Some well-known examples of neurodevelopmental conditions include ADHD, autism spectrum disorder, and intellectual disability. Difficult aspects in the treatment of these conditions include heterogeneity, high comorbidity and their complex multifaceted etiology.

31.1 Mission, vision and strategy

The common goal of the program is to have a significant impact on brain health and on healthcare related to neurodevelopmental disorders. The program aims to achieve this through innovative research to increase insights into the underlying mechanisms involved in risk and resilience of neurodevelopmental conditions, using cutting-edge methodology across explanatory levels from gene to cell, tissue, behavior, longitudinal outcome and societal context.

The program aims to innovate the phenotypic conceptualization and subtyping of neurodevelopmental conditions, increase the knowledge on mechanisms of risk and resilience, invest in translating findings from mechanistic and clinical studies into prevention strategies, exploit the shared etiology between brain and somatic traits, and enrich and guide the program's research through co-creation with diverse stakeholders.

This approach will facilitate stratification based on etiological understanding and inform personalized precision medicine approaches. Moreover, the program contributes to the international movement towards a new nosology of neurodevelopmental conditions, to facilitate treatment, reduce stigma, empower patients, and support a more balanced societal view of these conditions.

31.2 Research quality

The program delivers high-quality, innovative research at the interface of neurodevelopmental disorders (NDDs), metabolism, and precision psychiatry, e.g., it convincingly positions the insulin pathway as a mechanistic crosslink between NDDs and metabolic regulation, and conducts advanced work on synaptic identity during development, including transitional 'mixed synapse' states on the trajectory from immature to mature excitatory and inhibitory neurons derived from iPSCs (induced pluripotent stem cells). The integration of big-data modeling, normative approaches to resilience, and a predictive clinical neuroscience laboratory reflects a sophisticated and state-of-the-art strategy.

Methodologically, the program is very strong. It uses cutting-edge behavioral monitoring in real-time and in naturalistic environments, for example through smart-watch–based assessments, and it capitalizes on the Radboud assessment center to bring together researchers who work with similar types of data. The combination of cell-based models, normative modeling, and computational psychiatry places the program at the forefront of mechanistically informed, data-driven research on NDDs and related psychiatric phenotypes.

However, the program exhibits weaknesses in its overall approach, still being more a collection of strong individual projects than a cohesive whole in which the RGLs collaboratively pursue a translational axis. It will require time and visionary leadership to weave these individual projects together into a greater unified entity.

31.3 Societal relevance

Societal relevance is a major strength of the program. The work directly addresses the burden of NDDs across the lifespan, including both risk and resilience, and explicitly considers transdiagnostic dimensions rather than restricting itself to single categorical diagnoses. Projects such as buddy4caring parents exemplify a strong commitment to real-world impact, inclusion, and reduction of stigma.

The program also shows a clear awareness of the lived experience of people with NDDs and their families. Historical perspectives on NDDs focus on resilience, and engagement activities (workshops, outreach, integration of people with lived experience into program activities) create a robust bridge between research and society. This aligns well with broader aims of destigmatization, improving care pathways, and informing policy and clinical practice in a nuanced and person-centered way.

31.4 Viability

Overall viability is good, with a strong track record of scientific excellence, successful grant acquisition, and integration into the Donders Institute. Approximately half of the RGLs are affiliated with Donders, which provides an important network, access to seed funding, and a platform for interdisciplinary collaboration. Collaborative meetings including RGLs with complementary expertise have already helped catalyze new interdisciplinary projects. The members of the research program are enthusiastic, eager and looking for ways to make the program grow with integration of the various groups included in the program.

At the same time, there are structural vulnerabilities. Meetings of the research program are now in the format of workshops for which the initiative comes from the members of the program. A combination of longer meetings with regular meetings would secure further integration of the different research groups and development of long-term research strategies. The program relies on external structures (e.g., Donders) for seed funding and for some aspects of its administrative and collaborative infrastructure. Within RIMI, support structures are less clearly defined. Administrative tools such as room booking, shared calendars, and a dynamic web presence that clearly displays who is involved in which program, and with what expertise, are not yet fully implemented. Attention to these aspects will be important for long-term viability of the research program. Furthermore, attracting and retaining computational and machine-learning talent will be of fundamental importance to ensure viability.

31.5 Future outlook

The program is in an exciting developmental phase, actively working out how to move from excellent individual projects toward a truly integrated, overarching research agenda. Internal and external evaluations have already helped to initiate discussions on interdisciplinary collaboration and to lower barriers through informal workshops and joint meetings with clinicians and basic scientists, and cross-pillar seed initiatives. The use of internal targets for this evaluation cycle shows that the team is introspective and motivated to progress.

There are some potential risks and weaknesses. First, leadership and coordination across the program's different pillars is not formalized and a clearly articulated roadmap is lacking. Second, the recruitment, integration, and supervision of machine-learning and data-science experts require careful planning, especially given the demands of explainability, data protection, and clinical relevance in healthcare AI. Third, the relationship with other NDD-focused programs—particularly those that concentrate on monogenic disorders and therapeutic interventions— raises questions about complementarity, overlap, and shared strategy that should be addressed explicitly.

31.6 Conclusion

Overall, this program represents an excellent and forward-looking effort that combines mechanistic, computational, and clinical perspectives. It is grounded in strong scientific fundamentals enriched by innovative behavioral and big-data approaches. The program demonstrates clear introspection, openness to change, and a willingness to experiment with new formats of collaboration and outreach.

The current phase is one of consolidation and strategic definition. To fully realize its potential, the program will need to move from a collection of outstanding projects to a more clearly defined, overarching agenda with agreed priorities, mechanisms for coordination, and stronger internal

support. Given its strengths and the enthusiasm of its members, it is well positioned to become a model for interdisciplinary, mechanistically informed research on NDDs and resilience

31.7 Recommendations

- Develop a clear roadmap that connects the program's pillars (insulin/metabolism, synaptic development, precision psychiatry, resilience, and therapy) into a coherent set of overarching research questions and milestones.
- Establish a small steering group responsible for aligning individual projects with this roadmap and for monitoring progress toward shared goals, with regular meetings.
- Continue and expand collaborative seed funding mechanisms that require complementary expertise.
- Maintain and further develop workshops and joint events that allow in-depth methodological exchange and participation of clinicians and basic scientists.
- Formalize strategies for recruiting, integrating, and supervising machine-learning and data-science experts, including co-supervision models between clinical and computational researchers. Encourage development and sharing of open, well-documented code (e.g., Jupyter notebooks) and best practices for explainable, privacy-conscious AI in healthcare.
- Improve administrative and digital infrastructure. Develop more dynamic and user-friendly web pages that give a clear, up-to-date overview of program members, expertise, projects, and key outputs, increasing internal and external visibility.
- Articulate more explicitly how this NDD program complements other RIMI initiatives focusing on monogenic diseases and therapeutic development, identifying shared priorities and distinct contributions. Explore joint projects where mechanistic and precision-psychiatry approaches can feed directly into therapy-oriented pipelines, for example through shared biomarkers or stratification strategies.
- Continue to support projects such as buddy4caringparents and outreach activities that incorporate people with lived experience, ensuring that research questions remain grounded in real-world needs. Use the program's expertise in resilience and positive factors to contribute to destigmatization and to develop strengths-based narratives around NDDs in collaboration with patient organizations and policy stakeholders.

32 Therapy development for rare disorders of the brain

There are estimated to be around 7,000 different rare diseases, and combined these affect 350 million people worldwide. A significant portion of these rare diseases involve the brain, and this has devastating consequences, while only a minority of these diseases are treatable.

32.1 Mission, vision and strategy

The mission of the program is to bring new, effective, and affordable therapies to patients with rare brain disorders. The program has brought relevant clinical and preclinical experts in rare degenerative, developmental, and metabolic brain disorders together to jointly develop, test and implement disease-modifying, mechanism-based interventions. The program uses overlapping opportunities, shared infrastructure and tools, and complementary expertise to install and accelerate fully aligned preclinical to clinical therapy pipelines for a selected set of rare, genetic disorders of the brain.

Specific objectives include establishing preclinical model systems with predictive validity for candidate interventions, securing access to both disease-specific and generic clinical and surrogate markers that can serve as sensitive and patient-relevant read-outs in clinical trials, and the design and conduct of academic-led clinical n-of-1 or n-of-few trials for lead compounds.
The resulting expertise will be integrated in a public-private ecosystem for rare disease drug development at Radboudumc, currently being established by the Sector Plan team “Therapy Accelerator for Rare Diseases” with relevant internal and external stakeholders. The program’s combined and integrated expertise on powerful disease models, multi-omics profiling, molecular therapeutic strategies, outcome measures and biomarkers, stratification strategies, clinical cohort studies, and n-of-1 interventional trials will accelerate therapy paths across a prioritized set of twenty rare movement, neurometabolic, and neurodevelopmental disorders. Successful trajectories for specific diseases will showcase the translational development pipelines that serve as blueprints for other rare brain disorders within the program and beyond.

32.2 Research quality

The research quality of this program is strong. In line with its mission to develop mechanism-based, disease-modifying interventions, the program brings together preclinical and clinical expertise across rare degenerative, developmental and neurometabolic brain disorders, aiming to build aligned preclinical-to-clinical therapy pipelines, including preparation for academic-led trials. This is a coherent strategy, and the progress in utilizing complementary expertise, and international collaborations is commendable.

There are important scientific contributions along the translational trajectory from mechanism to therapy. The program has developed advanced patient-derived in vitro model systems and uses these to connect genotype to functional phenotypes and to explore candidate interventions. In parallel, it applies multi-omics approaches to deepen mechanistic insight and to identify biomarkers and outcome measures that can bridge preclinical studies and small-scale clinical evaluation. There is concrete progress in moving towards clinical translation through biomarker development and participation in early-phase therapeutic studies.

The program would benefit from a clearer definition of (i) how multi-modal data integration across preclinical and clinical studies is organized and which infrastructure is in place, (ii) what advanced computational expertise is available and whether capacity matches ambition, (iii) how collaborations with other RIMI programs (e.g., Academic Drug Therapy Development) operate in practice, and (iv) the longer-term strategy for benchmarking advanced in vitro models against clinical data, including the role of animal models and contributing to the advancement of regulatory considerations for small-n trials and industry collaborations.

32.3 Societal relevance

The societal relevance of the program is high. The program targets a major unmet need: effective therapies for rare neurological disorders, where patients often face limited treatment options. The program has a credible pathway to impact by accelerating translation from mechanistic knowledge and pre-clinical studies towards clinical interventions. The attention to patient benefit and health-system sustainability is valuable, as is the embedding in national initiatives such as RARE-NL and DCRT. Outreach and educational activities are good, but could be further strengthened and made more systematic.

The program public–private collaboration ambitions offer opportunities for uptake and scaling, but require clearer pathways of how academic independence will be safeguarded and how intellectual property (IP), data ownership and routes to commercialization will be managed. Given the importance of regulatory science in rare-disease translation, further integration of regulatory expertise is recommended so that evidence generation is aligned from the outset with regulatory and HTA requirements.

32.4 Viability

The program's goals to remain on the forefront scientifically and societally are highly relevant, given rapid developments in disease models, omics technologies and precision therapeutics and the persistent unmet need for effective treatments for rare brain disorders. A strong interdisciplinary team is in place, and the program has a diverse funding portfolio and solid participation in larger initiatives, which provides a good basis for continuity.

There may be a need for clear choices on governance and prioritization, particularly given the scale of the program (eleven RGLs). This includes specifying which domains are prioritized and why, how resources are allocated, and how leadership continuity is ensured through the talent pipeline. An explicit outlook on the European funding landscape may strengthen viability, including whether the program acts as a leader or partner in key networks and how it will respond if priorities shift.

Viability will also depend on effective technology transfer and IP management. The current approach may be overly conservative, and it is timely to review whether the program's strategy best supports timely translation while safeguarding independence and societal affordability.

32.5 Future outlook

The committee expects the program to strengthen its international profile and deliver meaningful therapies for rare brain disorders, building on strong translational science and collaborations.

There are potential risks and weaknesses, including maintaining a sufficient capacity of advanced computational expertise. Furthermore, there is no longer-term strategy for benchmarking advanced in vitro models against clinical data. The scale of the program may lead to fragmentation in the absence of clear governance and strategic choices, with sharper prioritization. Finally, the approach to IP technology transfer may be too conservative.

32.6 Conclusion

This is a strong program with high scientific quality and clear societal relevance. It brings together complementary preclinical and clinical expertise and is developing coherent translational pipelines that connect mechanism-based insights towards clinical interventions, supported by international collaborations and participation in national initiatives. The program has a solid basis for continuity through an interdisciplinary team and a diversified funding portfolio.

32.7 Recommendations

- Making explicit governance and prioritization choices across the RGLs, including defined priority domains, resource allocation, and a robust talent and succession pipeline.
- Strengthening and detailing the infrastructure and approach for multi-modal data integration and ensuring adequate embedded computational expertise.
- Clarifying how collaboration with other RIMI programs functions in practice and how preclinical models will be benchmarked against clinical data (including the role of animal models).
- Integrating regulatory expertise earlier and more visibly to align evidence generation with regulatory and HTA requirements.
- Developing clearer frameworks for public–private collaboration, including safeguards for academic independence and transparent approaches to IP, data ownership and commercialization, supported by an effective and fit-for-purpose Technology Transfer strategy.

33 Hearing & vision for all, from diagnosis to treatment

The program studies diseases associated with the dysfunction of two of our most important senses, hearing and vision. The commonality between dysfunctions in hearing and vision is the substantial overlap in their genetic causes, the molecular mechanisms underlying hearing and vision, the pathophysiology of the diseases, and the way that our brain interprets sensory input. Due to an aging population, hearing and vision impairment is a growing burden for society. Moreover, inherited forms of hearing and vision loss affect, besides adults, also children and adolescents worldwide. This disrupts the lives of many globally, as there are often few opportunities for intervention in many countries.

33.1 Mission, vision and strategy

The mission of the program is to combat severe neurosensory loss by elucidating the molecular and pathogenic pathways of sensory disorders, by opening targets for therapy, by developing functional models, and by identifying patient profiles amenable to intervention. The main goals are to preserve hearing and vision in individuals affected by inherited and multifactorial disorders, and to develop effective and safe therapeutic interventions to improve patients' quality of life. The program will combine mechanistic knowledge with designing, developing and implementing safe and effective therapeutic approaches and demonstrate their success. In parallel, the program will foster an environment that is attractive for the development of talented researchers to ensure the program's viability.

The program studies the entire spectrum of hearing and vision and is committed to employ innovation in several ways, e.g., clinical and molecular diagnosis, state-of-the-art DNA sequencing, disease relevant model systems and imaging tools. The program integrates fundamental, translational and clinical research to prevent the onset of vision loss and hearing impairments. Researchers actively collaborate not only in the Radboudumc nationally and abroad. There is a strong interaction with stakeholders in and outside the Netherlands and the program is internationally recognized, allowing it to have access to global funding sources.

33.2 Research quality

The program's overarching mission is to combat severe neurosensory loss, ultimately improving quality of life for large patient populations worldwide, which is operationalized through a clearly structured set of aims: elucidating molecular and pathogenic pathways, opening new therapeutic targets, developing functional model systems, identifying patient profiles amenable to intervention, and implementing safe and effective therapies.

Research quality is high, with a strong and well-coordinated portfolio spanning cognitive neuroscience, ophthalmology, otorhinolaryngology, and human genetics. Deep phenotyping and multi-omics are systematically applied to define disease mechanisms and modifiers, complemented by advanced functional disease models such as retinal organoids, organs-on-chips, and animal models that closely mimic human physiology. The program has particular strength in Usher syndromes and inherited retinal dystrophies, including mechanistic work including the elucidation of molecular mechanisms using nasal epithelial cells and long-read sequencing to reveal RNA defects, and it is actively involved in gene- and RNA-based therapeutic development, including ASO approaches and clinical trials using innovative designs such as paired-eye randomization.

33.3 Societal relevance

The societal relevance of the program is outstanding, as it addresses combined hearing and vision loss that radically affects autonomy, education, employment, and social participation, often beginning in adolescence. By focusing on conditions such as Usher syndrome, Leber congenital amaurosis, RPGR-associated retinitis pigmentosa, and other inherited neurosensory disorders, the program directly targets diseases with high unmet medical need and very limited treatment options. The work

is also of broad importance because the ear and eye are relatively accessible target organs, making them ideal systems to pioneer antisense oligonucleotides (ASO)-, RNA-, and gene-based therapies that can later be translated to other rare monogenic diseases.

The program engages closely with patients and families through symposia, meet-the-scientist events, patient profiling activities, and collaboration with patient foundations. This bidirectional interaction helps to align research priorities with patient needs and expectations and enhances awareness of ongoing trials and emerging therapeutic opportunities. The explicit focus on personalized medicine, using genetic and clinical profiling to identify those most likely to benefit from specific interventions, underlines the strong patient-centered orientation.

33.4 Viability

Viability is currently strong. The program comprises 14 RGLs with a good gender balance and benefits from an explicit talent development and mentorship plan that covers PhD candidates, postdocs, and junior group leaders. Several team members have led major national and international consortia (such as SYSCILIA and EYE-RISK) and hold visible roles in professional organizations as EURETINA, underscoring both scientific leadership and networking capacity. The program maintains robust partnerships with industry (for example, AbbVie and Roche), patient organizations, and spin-off companies such as Astherna, which originated from program investigators.

Clinical infrastructure is a major asset: the Department of Ophthalmology hosts a high-performing trial unit that runs a substantial portfolio of commercial and investigator-initiated trials, while the Department of Ear, nose and throat disease (ENT) and central trial units add further capacity. However, these structures are vulnerable due to staff shortages, occasional illness, and the highly specialized expertise required for rare disease trials. In addition, four senior researchers are expected to retire in the near term; although five promising young researchers are already being supported and the program has talent-track mechanisms in place, attracting and retaining additional mid-career investigators will be crucial to maintain critical mass and leadership.

33.5 Future outlook

The program has articulated a coherent future vision structured around three major goals. First, it aims to understand disease mechanisms by elucidating molecular and pathogenic pathways underlying auditory and visual impairments and identifying novel therapeutic targets. Second, it seeks to develop and apply functional disease models—using retinal organoids, organs-on-chips, animal models, and integrated clinical–molecular–imaging diagnostics (including OCT and other advanced imaging) to capture disease progression and test interventions under conditions that closely reflect human physiology. Third, it aims to advance personalized medicine by designing patient-specific therapies, such as ASOs that restore gene and protein function, and by using detailed genetic and clinical profiling to select patients most likely to benefit.

The long-term ambition is to have fully operational DNA- and RNA-based therapies, alongside neuroprotective and neuroregenerative strategies, available within roughly the next decade. To achieve this, the program will need to address several challenges. Succession planning is urgent, to ensure that new leaders can shape and expand the program's scientific agenda. Clinical trial capacity needs to be stabilized to develop proportionate frameworks for rare disease trials, where traditional large-scale phase 2/3 designs are often not feasible. Finally, the program would benefit from a more centralized, well-resourced institutional facility for AI-based image analysis and clinical endpoint development, building on existing collaborations with advanced imaging.

There are potential risks and weaknesses. First, a substantial number of researchers will be retiring soon. Second, there is fragmentation of the use of AI-based methodology. Finally, the clinical trial capacity may be a limiting factor.

33.6 Conclusion

This is an outstanding, highly focused, and internationally recognized program that integrates molecular diagnostics, cognitive neuroscience, and clinical units in an exemplary fashion. It fills a critical gap for patients with severe neurosensory deficits and has already made substantial contributions to understanding disease mechanisms and developing ASO- and gene-based interventions, particularly for Usher syndromes and related inherited retinal disorders. The combination of deep mechanistic work, innovative model systems, patient profiling, and early-phase clinical trials positions the program as a leading hub for translating cutting-edge molecular insights into tangible therapeutic options for patients with hearing and vision loss.

33.7 Recommendations

- Strengthen succession planning by rapidly converting the current cohort of five talented young researchers into clearly defined career pathways (e.g., talent tracks, junior group leader positions) and by actively recruiting additional mid-career investigators.
- Stabilize and scale clinical trial capacity by securing permanent, specialized staff for ophthalmology and ENT trial centers; exploring shared support structures with the central trial unit; and engaging national and international regulators to adapt trial requirements to the realities of rare disease research.
- Establish a centralized AI and advanced imaging facility that can support endpoint development, image analysis, and data integration across projects, leveraging existing collaborations but reducing duplication and improving efficiency and visibility.
- Further integrate cognitive neuroscience into the program's core themes, using its expertise to investigate cortical processing and adaptation in sensory loss and to develop innovative functional outcome measures that complement structural imaging and molecular readouts.
- Continue to nurture and expand national and international partnerships, including consortia (e.g., Dutch Center for RNA Therapeutics, RARE-NL), industry collaborations, and patient organizations, to accelerate translation from mechanistic discovery to accessible therapies and to ensure that the program remains at the forefront of global developments in neurosensory genomics.

34 Academic drug therapy development

The pivotal role of academic pharma has become increasingly evident in the development of affordable drugs, especially in the field of orphan drugs. This program is a recent collaboration within Radboudumc to support accelerating academic drug development across disease-focused programs from the preclinical to post-marketing setting.

34.1 Mission, vision and strategy

The mission of the program can be summarized along the following lines: to combine the right expertise early in drug development, to improve public-private partnerships in a societally healthy relationship, to acquire long-term funding and reach sustainable implementation in global clinical networks, to proactively apply available knowledge of regulatory pathways, and to contribute to the innovation of study designs. The program's mission is to be value-driven and conduct research where there is yet insufficient commercial incentive. The overarching aim is to develop innovative pharmacotherapeutic treatment strategies and drug development strategies.

Subgoals of the program are manifold and ambitious, including establishment of a well-functioning academic research program and ecosystem that disseminates academic drug development knowledge, and developing novel pharmacotherapeutic and repurpose treatments aligned with the respective research programs. Furthermore, the program has the goal to develop alternative and optimized dosing strategies for existing treatments including novel model-informed dosing and drug development methodologies, as well as new drug production platform technologies and affordable and accessible pharmacotherapeutic treatments, by explicitly improving clinical trial design and guiding regulatory decision-making on (academic) drug development.

The program is new, bringing together research groups that have strong research track records of their own and that share the vision that combining these strengths can help grow academic drug development.

34.2 Research quality

The program Academic Drug Therapy Development has assembled relevant and broad scientific expertise across drug therapy development, with activities ranging from support for preclinical and clinical development of therapeutic modalities, to optimization of existing therapeutics, and biomarker-oriented research. The program is still developing its identity and program-level track record, but already demonstrates the potential of this program in academic drug development. Positive energy and commitment within the team are recommendable.

Showcased examples included dendritic cell vaccination approach in Lynch syndrome patients and a monoclonal antibody strategy targeting parasite–mosquito interactions, supported by PK/PD modelling. These examples suggest an ability to connect mechanistic understanding, quantitative pharmacology and clinical development in a way that is competitive in the (inter)national landscape of academic drug development. This program adds value by bringing in complementary expertise areas. Importantly, embedding of the program in disease-focused ("vertical") programs is in place.

The program currently appears as between an internal expertise/capability service function and an independent research program, with a mix of being a core facility and performing research, without a clear own research agenda. Several elements of the drug development pipeline are essential and often not available within academic environment, but are not inherently innovative. It is therefore important that the program more explicitly articulates where it primarily applies established approaches and where it aims to drive methodological or conceptual innovation, for example in quantitative translational strategies, biomarker qualification, or other design innovations. This

distinction is also critical for demonstrating academic leadership and building a coherent body of scholarly contributions aligned with the aims of this program.

The current scope of the program is very broad, which offers flexibility but risks fragmentation and diluted visibility. There is an apparent mismatch between ambition and available staff and resources; without prioritization and sufficient capacity, there is a risk that scientific depth and continuity may suffer. Overall, the program's research quality is promising and has potentially high impact, grounded in strong expertise and with initial examples of impactful and relevant results.

34.3 Societal relevance

The focus on development and optimization of drug treatments is of high societal relevance, particularly where commercial incentives are limited, e.g., for rare or orphan diseases and other underserved patient populations. This aligns well with the ambition to contribute where commercial drug development has not materialized and where affordability, access and appropriate use are concerns. There are credible indications of societal uptake through contributions to clinical practice and policy, including model-informed dosing approaches and dose-optimization strategies that have informed guideline development and implementation efforts. Societal relevance is further strengthened by the program's attention to cost-effectiveness of expensive therapies, and by its capacity to support translation of advanced therapies, including academic-initiated trials and access to enabling infrastructure. Patient involvement is not formalized. There is potential for the program to bridge the development gap between early Radboudumc discoveries and later-stage translation (including spin-out readiness), and to catalyze participation in external initiatives and consortia, provided this bridging function is made explicit and operationalized through visible pathways for internal researchers and external partners.

34.4 Viability

The program is a timely and important initiative, with goals that are likely to remain scientifically and societally relevant given continued developments in complex therapeutics, data-driven development strategies, and increasing pressure to improve affordability and appropriate use of medicines. Still, there are serious concerns about the program's viability in its current form. The program is still under development, and its viability appears highly dependent on close collaboration with other RIMI programs, combined with uncertainties regarding its positioning, resourcing and funding model. It is crucial that the intended objectives of this program are sufficiently clear: should it function as an independent research program or primarily as a structured clustering of key expertise and capabilities that can be accessed by other research groups? Both models can be viable, but they require different governance, success indicators and resource allocation. Without a clear choice, there is a risk of diluted focus, limited visibility and difficulties in building a coherent track record. The committee therefore urges the program to define the niche it can credibly claim in the Dutch landscape and to specify where it is unique and competitive versus where it intentionally serves as a local RIMI resource.

A viable strategy must further articulate how the program will secure sustainable funding, including an explicit approach to collaborations with companies and public–private partnerships, particularly given its interface with translation and potential spin-out trajectories. Talent development and succession planning at all levels is as important as ensuring that staffing and resources match their ambitions. Without additional investments and sharper strategic choices, it is questionable whether the program can deliver on its ambitions over the next period.

34.5 Future outlook

There is clear potential for Academic Drug Therapy Development to become a strategically important enabler of Radboudumc's translational pipeline, building on the team's positive energy and the existing (and expandable) embedding in disease-focused vertical programs. The main and urgent task is focus under constrained resources: the current ambition to cover all modalities and a wide span of

activities risks overextension and diluted visibility. Explicit strategic choices are in order by prioritizing a limited set of flagship themes aligned with the needs of the vertical programs, clarifying what expertise is offered (and via which access routes), and articulating where the program will contribute genuine methodological innovation rather than primarily applying established approaches. A clear choice is also needed between operating as a strictly defined core facility or as a research capability program with its own cross-cutting agenda.

The potential risks and weaknesses further include a lack of own research agenda and sharp thematic focus. The broad scale of the program risks fragmentation or insufficient focus. There is a dependence on other RIMI programs and lack of strategy to secure adequate funding.

34.6 Conclusion

Academic Drug Therapy Development is a timely and societally important initiative with clear potential to become a strategic enabler of Radboudumc's translational pipeline. The program has assembled broad and relevant expertise and has provided promising early examples of academically embedded drug therapy development that can add value beyond disease-focused programs, particularly for areas with limited commercial incentives. There are serious concerns about viability in its current form: the program's scope is broad, its positioning yet unclear (i.e., independent research program versus core capability/expertise center), and there is a mismatch between ambitions and available resources, which risks fragmentation, limited visibility, and difficulty in building a coherent track record.

34.7 Recommendations

- A main recommendation is to sharpen strategic focus and clarify the operating model. The program is urged to make an explicit choice between (i) a strictly defined core facility/capability function with clear access routes and service levels, and (ii) an independent research capability program with a limited number of flagship themes and a demonstrable innovation agenda. In either model, the program should specify where it aims to deliver methodological or conceptual innovation (versus applying established approaches), further strengthen its embedding in vertical programs through well-defined collaboration pathways, and articulate a sustainable funding strategy including a clear approach to public–private partnerships and translation/spin-out interfaces.
- To be a viable and visible program, the program leaders should work to define a cross-cutting research agenda with a limited number of flagship themes and corresponding deliverables, rather than an apparent ambition to cover the entire pipeline across many areas simultaneously
- Staffing and resources should be aligned with prioritized goals, strengthening talent development and succession planning, and securing targeted investments to ensure the program can deliver on its ambitions.

35 Biomarkers for (health)care

Biomarkers are used for diagnosis and prognosis of many diseases, as well as to monitor disease progression. In addition, biomarkers help predict which therapy may be effective, and allows monitoring the efficacy of treatment. Not all biomarker-related discoveries result in tangible health benefits. Important determinants of this are the focus on technology rather than patient needs, few incentives to validate biomarkers after the discovery phase, and difficulties in finding sufficient expertise to implement biomarkers into clinical practice.

35.1 Mission, vision and strategy

The mission of the program is to advance the understanding of disease mechanisms by developing innovative biomarkers that address unmet clinical needs, by using cutting-edge technologies and multimodal data integration to identify personalized targets for intervention. The program aspires to improve health and healthcare by translating these insights into robust biomarkers, driving precision medicine through scientifically validated, economically viable, and socially responsible solutions. The program aims at impact in two areas: diagnosis and prognosis of disease, and prediction and monitoring of therapy efficacy. The program's goal is to unite expertise across molecular biology, analytical and clinical chemistry, preclinical and clinical models, data integration, artificial intelligence (AI), health economics, and ethics to identify and develop biomarkers for personalized diagnosis, prognosis, prevention, therapeutic prediction, and monitoring.

As a horizontal research program, the program focuses on advancing laboratory techniques and data and AI methodologies. Through collaboration with clinical research programs the program strives to enhance the quality and efficiency of biomarker development, translating disease mechanisms into clinical biomarkers. The program's goal is to reduce research waste and to accelerate the translation of new discoveries into clinically impactful biomarkers.

35.2 Research quality

The program has successfully developed, discovered and validated novel biomarkers, demonstrated their clinical utility, and progressed toward commercialization and clinical adoption. In addition, it has catalyzed high-quality sample workflow in plasma analysis that effectively bridge clinical routine with research and development activities, as well as established technology test beds to support the transition from single-analyte assays to multi-marker panel assays. The program has produced several high-quality publications that effectively document the biomarker research process and demonstrate the development of the program as a cohesive whole, rather than as a collection of isolated single-biomarker projects.

Still, the program's selection of focus areas and individual projects lacks some clarity. While the program aspires to be driven by clinical needs, its alignment with other strong research area programs that define future clinical demands appears limited. This raises concerns regarding coherence and prioritization of topics in which RIMI has established excellence. Furthermore, clinical decision-making increasingly relies on multimodal data integration, whereas the program appears to have placed limited emphasis on such integration. Clinical reporting seems largely confined to traditional clinical chemistry outputs, rather than integrative analyses that combine, for example, pathology, genetics, imaging, and clinical data.

35.3 Societal relevance

The biomarker program has a broad and highly relevant focus, advancing biomarker domain expertise and associated research from multiple perspectives. The program has generated biomarkers with clear clinical relevance and significant commercial potential, thereby creating societal impact across multiple dimensions. This impact is demonstrated through successful integration of biomarkers into

clinical practice, assessments of added clinical value, and active involvement and training of both healthcare professionals and patients.

The long-term benefits, such as reduced mortality, improved quality of life, and health economic gains, are inherently complex and resource-intensive to evaluate. However, such assessments could, for example, be undertaken by analyzing the value of transitioning assays from single-analyte measurements to multi-marker analyses. Overall, this type of evaluation represents a critical area for strengthening the added value and could be more clearly defined and monitored through key performance indicators (KPIs).

In addition, the program has made substantial efforts to raise awareness and engagement through dissemination activities. However, patient involvement is not well-developed. The program has also contributed meaningfully to education and capacity building within the biomarker field and has influenced national guidelines for biomarker use.

35.4 Viability

The program has successfully brought together a critical mass of researchers and secured substantial external funding. There is clear outreach effort aimed at consolidation and long-term continuation of the initiative. In particular, the “Meet the Biomarker Expert” initiative is an effective mechanism for engaging researchers and healthcare professionals and for disseminating a shared “biomarker perspective” across disciplines.

The program could further benefit from a more explicitly multidisciplinary approach, for example by incorporating health economics and broader patient and population perspectives, as demonstrated in the hepcidin project. Such efforts should be more systematically linked to relevant research areas, including ethical considerations and factors influencing patient willingness to participate.

In addition, several programs within RIMI are engaged in biomarker research and implementation, creating clear opportunities for synergy. A broader application of the program’s biomarker implementation–focused approach across the university and hospital settings could further strengthen impact and efficiency.

The program’s dependence on infrastructure is another important consideration that is not fully elucidated. It is unclear how access to and renewal of cutting-edge biomarker technologies are ensured. Much of the research appears to rely on “spare-time” access to instrumentation. Furthermore, data science and AI expertise do not appear to be sufficiently embedded within the program, despite being essential for this research area, especially with respect to multimodal data integration and analysis.

Finally, the funding model, combining clinical development funding and research funding, remains somewhat unclear. Nevertheless, the research component clearly provides valuable research and development capabilities that support clinical routine, and this synergy should be explicitly recognized and further endorsed.

35.5 Future outlook

The program includes several notable success stories. However, the process for selecting and prioritizing future focus projects, particularly in alignment with the broader RIMI strategy, remains insufficiently clear. It is not evident how next-generation projects are designed to systematically build upon these successes by iterating proven success factors while introducing methodological or conceptual improvements.

To date, the biomarker program has been highly successful in addressing specific unmet clinical needs using single or limited numbers of biomarkers. However, the field is increasingly moving toward

system-level approaches within precision medicine, where multiple components, from assay development and data integration to regulatory considerations, become interconnected and interdependent. Going forward, the program would benefit from complementing its strong 'traditional' clinical chemistry–based operational model with a systems biology-oriented biomarker framework. Such a shift would enable the transfer of accumulated expertise and lessons learned toward next-generation biomarker development and implementation in precision medicine.

There are some potential risks and weaknesses, including limited connections with groups that determine clinical applications. Furthermore, there is a lack of integrative analyses incorporating pathology, genetics, imaging, and other phenotypes. Finally, there is a lack of structural access to machinery.

35.6 Conclusion

The biomarker program demonstrates substantial scientific, clinical, and translational strength. It has successfully developed and validated biomarkers with clear clinical utility, established high-quality workflows bridging clinical routine and research, generated impactful publications, and progressed toward commercialization and clinical adoption. The program has also built a critical mass of expertise, secured significant funding, contributed to education and national guidelines, and created meaningful societal impact through dissemination and stakeholder engagement.

However, the program's strategic focus and project selection processes are not always clearly articulated, particularly with respect to alignment with the broader RIMI research strategy and future clinical needs. In addition, limited integration of multimodal data, insufficient embedding of data science and AI expertise, and unclear infrastructure and funding models constrain the program's ability to fully transition toward next-generation, systems-level biomarker development.

35.7 Recommendations

- Establish a transparent and coherent process for selecting and prioritizing focus areas and projects, explicitly aligned with the overall RIMI strategy and emerging clinical needs.
- Complement the strong clinical chemistry foundation with systems biology–based biomarker frameworks, including multimodal data integration across pathology, genomics, imaging, and clinical data as a "collaborative system" across multiple programs.
- Integrate data, bioinformatics, and AI competencies as core components of the program to enable advanced analysis, reporting, and decision support.
- Broaden the program to more systematically include health economics, ethical considerations, and patient and population perspectives to support evaluation of long-term societal impact.
- Secure and articulate infrastructure and resources: Clarify access to, renewal of, and strategic planning for cutting-edge biomarker technologies to reduce reliance on ad hoc instrumentation use and mitigate execution risks.
- Develop clear performance indicators to quantify clinical, economic, and societal impact, including assessments of transitions from single analyte to multi-marker assays.
- Actively promote collaboration and knowledge transfer across RIMI programs, the university, and the hospital to maximize efficiency and impact of biomarker implementation efforts.
- As a minor point, the brackets in the name of the program seem neither necessary nor esthetically pleasing.

36 Genomics for rare disease

Each of the 6,000-8,000 rare diseases of which we are currently aware are individually rare, however, collectively, they are common and present a significant healthcare problem. Of these rare disorders, more than 80% are thought to have a genetic cause. This research program studies the genomics of rare diseases.

36.1 Mission, vision and strategy

The research program and affiliated RGLs work at the forefront of rare diseases gene and mechanism discoveries, aiming to enhance understanding and diagnostics through comprehensive data sharing, the use of advanced genomic technologies, and the functional interpretation of genetic variation. The overall aim of this program can be categorized in four aims, i.e., creating access to cohorts with comprehensive genetic and phenotypic datasets, creating new and improved genetic technologies, understanding genetic variation and mechanisms of disease, and translating discoveries to patients' lives and clinical practice

The aims range from centralized data collection to impacting the lives of patients with rare disorders. The program's efforts are therefore a prime example of personalized, precision medicine, with the ambition to be a global leader in rare diseases research, diagnostics, and care. To achieve this ambition, the program has set up a multidisciplinary network of experts across a selection of Radboudumc departments.

36.2 Research quality

The transition from a disease-oriented structure to a horizontal research program is a clearly positive development, as it now allows the group to work on technologies across disease boundaries and to develop a genomics program that cuts across several other programs. The portfolio covers interpretation of genomic variation, single-cell and long-read sequencing, allele and haplotype resolution, epi-signatures on the DNA level, and patient phenotype analyses using AI, demonstrating a technically advanced diagnostic and research profile. The program actively uses the expertise and model systems of other research programs to establish its own biological programs and collaborates widely: Several RGLs participate in different programs, with daily interactions and particularly strong links to groups working on neurodevelopmenta, immune, sensory and movement disorders, as well as rare familial cancers.

The team's past performance is impressive, marked by great engagement of its investigators in international conferences, active participation in scientific advisory boards and committees, involvement as reviewers, and robust collaborations with life science companies. The unit successfully acquired both national and international grants. Among the highlights are major successes in disease gene discovery and significant contributions to technology development (such as optical genome mapping and long-read sequencing), with several landmark publications emerging from broad trans-European collaborations. The unit has also provided important insights into the analysis of comorbidities among neurodevelopmental disorders (NDDs).

Despite this, the program has not yet fully risen to its full potential. Cutting-edge topics in genome medicine, such as RNA biology and modification, DNA structure, and the roles of sex, gender, and clinical variability and others, are not visibly addressed. Therefore, without a broader strategic orientation, the program may risk limiting its future development when it continues to concentrate predominantly on diagnostic applications rather than comprehensive and ambitious research activities. Also, bioinformatics and data science are not yet sufficiently visible or articulated as core strengths of the program, which is of relevance in such a data-intensive field and may contribute to

the impression that the computational dimension is less dynamic than would be expected of a leading genomics hub.

36.3 Societal relevance

Clinicians are fully integrated into the program, with the clinical genetics care center financing a high-throughput research program, allowing researchers to align close to patient care. The program focuses on interpretation rather than mere generation of data and offers machine capacity to internal and external scientists, thereby supporting a broad range of translational and clinical projects beyond its own portfolio. This configuration directly targets major healthcare challenges in rare diseases by combining comprehensive genomic and epigenomic characterization with functional assays and detailed phenotyping, which is strongly aligned with frameworks for high societal impact in health care.

The group leads large European consortia in rare diseases, while in more narrowly disease-specific tracks others may take the lead, which fits well with its horizontal mission. The unit's diagnostic innovations have had a significant positive impact on patient care, supported by close interactions with patient support groups and participation in large consortia. However, structured discussions of documenting outcomes such as diagnostic yield, healthcare cost savings, or pathway changes are largely lacking.

36.4 Viability

Viability is currently strong but critically dependent on specific institutional conditions. The program enjoys baseline funding from clinical departments, is very successful in securing large European grants that align with its philosophy of addressing multiple rare diseases, and benefits from an infrastructure model in which diagnostics pre-finances new sequencing machines through a structure that is described as unique in the Netherlands. This prefinancing scheme is considered essential for maintaining the scale and technological edge of the research program.

Training programs for young investigators are a strong point, demonstrating successful talent development. The unit has excelled in securing collaborative grants for large-scale projects, confirming its capacity for effective teamwork. The program risks overestimating its robustness: while baseline and consortia funding look healthy, there appears to be no clear contingency plan for infrastructure funding. There is also strategic ambiguity around whether certain areas, such as hereditary cancer, should remain separate vertical programs or be more tightly integrated into the horizontal genomics umbrella to avoid duplication of efforts.

36.5 Future outlook

Taken together, the combined evidence describes a huge, enthusiastic, and clinically embedded genomics diagnostics program with excellent technology, cutting-edge research, strong funding, and impressive potential for real-world impact in rare disease medicine, but also one that appears slightly complacent about its limitations and overly reliant on a fragile infrastructure arrangement. To maintain and strengthen its position, the program, together with the institutional leadership, should further refine its strategic priorities, with particular attention to anticipatory genome medicine, bioinformatics, and the long-term sustainability of key infrastructures.

There are potential risks and weaknesses. First, the program is dependent on the prefinancing scheme. Second, there is a lack of a visible computational backbone.

36.6 Conclusion

The program has a longstanding reputation for excellence in disease gene discovery, technological innovation, and multidisciplinary collaboration. Its work has significantly advanced diagnostics and precision medicine for rare diseases, resulting in extensive international engagement, high-profile

collaborative publications, and substantial grant success. The unit has positively impacted patient care and contributed to understanding the genetic basis of neurodevelopmental disorders.

There are some potential risks and weaknesses. There is a risk that, when the focus remains predominantly on clinical applications and on pathogenic variants in coding regions, the program's development could plateau over time. At the same time, the strong commitment to training and collaboration provides an excellent foundation, and further progress is likely to depend on broadening the research portfolio to encompass a wider spectrum of questions in genome medicine.

36.7 Recommendations

- Articulate a medium- to long-term vision as a clear scientific spearhead in which the program can evolve and embrace innovative approaches that will enable it to address the key questions shaping the future of genomic medicine.
- Establish or formalize a robust core facility-like structure for bioinformatics, engineering, and AI that can underpin variant interpretation, multi-omics integration, and service activities for internal and external users as well as can provide a state-of-the-art data storage and management facility according to FAIR criteria.
- Work proactively with Radboudumc and RIMI leadership to maintain the KGC prefinancing model or develop an alternative mechanism (e.g. hospital-backed infrastructure calls), backed by quantitative evidence of diagnostic and economic value.
- Implement routine impact monitoring (diagnostic yield, time to diagnosis, cost offsets, pathway changes) using established health research impact frameworks to systematically document societal impact and to guide strategic choices.
- Maintain the horizontal identity of the genomics program while clearly defining complementary roles and collaboration models with disease-specific vertical programs such as hereditary cancer, ensuring synergy rather than duplication and benefitting from cross-disease insights.

37 Obstetric and pediatric clinical pharmacology

Over 70% of women use medication during pregnancy to treat chronic conditions, short-term illnesses, pregnancy-related diseases, or even their unborn child. Despite their frequent use, only 5% of medications are adequately monitored, tested, and labelled with safety information for use during pregnancy and lactation. Many unanswered questions on safety, effectiveness, dosing, and transfer into breastmilk lead to undertreatment, uncertainty, and incorrect perceptions of the safety of medications during pregnancy and lactation. Similarly, medications used by children are often prescribed off-label due to a lack of pediatric studies.

37.1 Mission, vision and strategy

The program aims to develop a multidisciplinary platform to support and improve evidence-based pharmacotherapy in pregnancy, lactation, and pediatrics. The program's objectives are to develop, refine, and implement methodologies to study pharmacology, toxicology, and pharmacotherapy for these groups, to reduce the knowledge gap on pharmacology, toxicology, and pharmacotherapy for selected diseases and medications by adding evidence ranging from preclinical to post-marketing studies. Furthermore, the program aims to implement new dosing and treatment knowledge in clinical guidelines for pharmacotherapy, to facilitate and promote a normative framework for responsible innovation and implementation of pharmacotherapy in these groups, and to educate healthcare workers on pharmacological and safety issues in these special and vulnerable populations.

37.2 Research quality

This new research program aims to provide a multidisciplinary platform to support evidence-based drug use in pregnancy and in children. The program incorporates some excellent and high-profile research group leaders who are experts in their field, with research interests that all fall under the general areas of research covered by the program. Individual components of the program clearly contribute to the overarching objectives. However, there is less evidence of a clear overarching collaborative strategy which will support successful grant applications and execution of the work with successful grants. The high overall quality of the program is largely based on the individual quality of independent work of the RGLs.

The key aims and objectives of the group have been individually assessed, and a common denominator is that much is still in the planning phase, which is understandable for a new program. In the development and implementation of the mission to study pharmacology, toxicology and pharmacotherapy proposed approaches are the development of PB/PK models for pregnancy/lactation/pediatrics and the development of bioanalytical methods for drug quantification but nothing specific in terms of drug classes or areas of focus. The group has expertise in the right areas, but it is unclear what they are planning to do, partly reflecting the infancy of the newly formed program. In the aim to reduce the knowledge gap on pharmacology, toxicology and pharmacotherapy for selected diseases and medications by adding evidence ranging from pre-clinical to post-marketing studies, is the planned proof of concept PK trial with antiretrovirals in healthy breastfeeding subjects highly relevant, but additional proposals are still less well defined (e.g., studies with drugs to be selected from ongoing Gates Foundation project and pharmacoepidemiologic studies). The aim to implement new dosing and treatment knowledge in clinical guidelines for pharmacotherapy has interesting general ideas, but the approach seems generic in terms of investigating model informed dosing in pregnancy/lactation/pediatrics. Also, the aim to facilitate and promote a normative framework for responsible innovation and implementation in pharmacotherapy in these groups still has somewhat unfocused suggestions on the study of stakeholder perceptions of uncertainty and the risk of implementing pharmacotherapy in this setting. The aim to educate health care workers on pharmacological and safety issues in these special and vulnerable populations includes an interesting

proposal for joint PhDs and the development of modules and courses to engage stakeholders in pharmacotherapy.

Clinical trials have been carried out in areas like venous thrombosis in pregnancy, treatment of HIV both in pregnancy and in children, the treatment of children with tuberculosis and the use of antibiotics in critically ill children. The group has also been involved in post-marketing studies on safe drug use during pregnancy and improvements in perinatal pharmacoepidemiology. Senior RGLs have prominent positions in important groups and societies in this field, both at a national and international level. Some of the publications are in high impact specialty journals. Several RGLs in the program have a strong academic reputation.

37.3 Societal relevance

The activities of this program lend themselves well to providing an important societal impact, with research activities closely related to clinical care and patient treatment. Guidelines in pregnancy-related thrombosis, tuberculosis and HIV are good examples of societal relevance. The group has identified six themes around which societal impact is centered, with insufficient detail and clarity provided for any of these themes other than education, with useful proposals for a new master's course, a clinical pharmacology fellowship, modelling workshops and joint PhD appointments. Patient involvement can be improved. The program already has some good examples of successful educational activities, including annual PK and PK/PD summer schools, as well as global workshops on PK/PD modelling. The overall societal relevance of this program is therefore substantial, with research that has brought changes in practice at an international level. Media coverage, podcasts and partnerships with pharmacovigilance centers enhance the societal impact of the program in an area of clear unmet need.

37.4 Viability

While the individual themes and research activities of the RGLs are impressive, the viability of establishing 'obstetric and pediatric clinical pharmacology' as a new program of work is problematic. Many of the individual research themes are internationally competitive and have good visibility and a good standing within their respective fields, but the whole should be more than the sum of the parts. It remains unclear how the overarching program will be composed and how it will function.

The group is relatively small and consists largely of well-established RGLs, with no clearly identified younger upcoming theme leaders. There needs to be a commitment of both time and effort to take forward some of the general areas of interest and proposals put forward by the program. The program appears to have an active PhD pipeline, involvement in conference organization and mentoring activities.

37.5 Future outlook

The program is in its infancy but certainly has the potential to achieve its goals and submit competitive grant applications. The program is impressive in terms of clarity of the vision, mission, activities, outlooks and barriers of the program. However, this will rely on RGLs finding the time to work on these additional joint grant applications alongside current research interests and activities. For success in the long term, the program needs to think about succession planning and introducing promising young themes that lead into the overarching structure, both to strengthen the current activities and areas of expertise, but also to explore new project areas that will fit within the overall program.

Translating findings into routine practice nationally and internationally requires dedicated implementation of science and health-system partnerships. Similarly, changing prescriber behavior (off-label use in children, conservative prescribing in pregnancy, etc.) will fail without systematic dissemination and clinical decision support.

There are some potential risks and weaknesses, including the lack of a clear overarching collaborative strategy. Furthermore, the program depends on a small number of senior researchers and there is insufficient involvement of young upcoming researchers. Finally, fragmentation into the individual groups composing the program is a risk.

37.6 Conclusion

Obstetric and pediatric clinical pharmacology is a new program which focuses on an area of clear unmet need. The program is small and is clearly very much in its infancy, but has some experienced and well-established RGLs carrying out internationally competitive research. While the research quality and societal impact of individual constituents of the program are impressive, there is cause for serious concerns about the viability of the program. There is a lack of clear governance for the program, which is essential to be successful in a highly competitive field. Similarly, early career researchers with a focus in this area need to be identified and succession planning needs to be addressed urgently for this program to be successful.

37.7 Recommendations

- To implement a clear governance model for the program.
- To consider the most realistic and achievable way to support sustainable funding for the long-term infrastructure of the program.
- To consider capacity building and succession planning moving forwards.
- To continue transparent stakeholder engagement, co-design studies with patient representatives, and publish normative frameworks that justify ethically sound designs.

38 Sex and gender-sensitive health and reproduction

In the past few years, there has been a growing attention to sex and gender. This research program is committed to supporting Radboudumc in realizing a rigorous, cross-cutting approach to sex and gender-sensitive research.

38.1 Mission, vision and strategy

The program supports sex and gender-sensitive approaches by providing education to equip healthcare professionals, researchers, and policymakers with the knowledge and tools to integrate these approaches into their work. The program translates research across the translational spectrum, from fundamental to clinical to public health, to enable it to develop both clinical and public health interventions that improve health equity and outcomes for diverse patient populations, using sex and gender as an entry point for more precise and personalized analyses.

By advocating the translation of evidence into policies that incorporate findings on sex and gender differences, the program strives to ensure that healthcare systems, funding, and research agendas reflect these critical insights. The program strengthens patient and public engagement in research processes to ensure inclusivity, foster trust, and increase the societal relevance of scientific outcomes.

The program is dedicated to fostering collaboration among scientific research groups, creating an environment that advances precision and personalized medicine through exploration of sex- and gender-specific factors influencing health and disease in diagnostics, treatments, and care pathways.

38.2 Research quality

This is a relatively new research program. Overall, the quality of the research within this program is good. It draws upon a wide pool of interested researchers that have produced some high-quality outputs. The main context for this program is currently national with a focus on education for healthcare professionals in the Netherlands. There is potential to grow wider international networks due to its broad relevance in other countries where there is strong interest in gender differences.

The aims of this program of work are somewhat less focused than others. They partly relate to reproductive health in men and women, partly to identifying gender-specific elements across the breadth of healthcare, and partly to a broader agenda of improving health equity and outcomes for diverse patient populations. While this is not a drawback per se – perhaps even on the contrary – it will require attention to keep a balanced approach and maintain coherence.

The program also provides educational programs about gender differences for healthcare professionals. The stated focus is to ‘identify and address the unique ways sex and gender impact health conditions, diagnostics, treatments and care pathways’.

The research program’s strength is in driving interdisciplinary collaboration and innovation, and is less about an immediate increase in independent high-quality research with multiple publications. There are numerous relevant publications from the affiliated groups. The outputs from these groups are all relevant and interesting, but are listed in a way that risks missing alignment of the different outcomes. To be effective, this program needs to demonstrate that it is more than the sum of its parts, identifying strands that read across different clinical areas.

The interdisciplinary collaboration will help bolster leadership in this field, drawing on a wider field of expertise. Having a strategic team of spokespeople will help clarify leadership and demonstrate alignment of messages.

38.3 Societal relevance

Societal relevance of this program is excellent. The research has the potential to impact significantly on population and health systems' response to disease. There are opportunities to improve quality of life and to reduce inequalities in care. These changes could impact on all elements of the care pathway, including the patient's own understanding of the risks affecting them.

There is reference to educational and training initiatives, plus changes to guideline recommendations, which will undoubtedly help to drive change and improve care for patients. The promotion of personalized medicine is entirely correct, but the researchers may wish to consider the costs and benefits of promoting change at a population level, compared with individualized treatment pathways.

38.4 Viability

This is a recently founded program, and like all emerging programs, viability will depend on enthusiasm, strategic choices, and central support. The viability of related, specific areas within individual research groups is likely to be higher, but the focus here is on the wider research collaboration. The report states that there is a strategic team of four spokespeople that has partly developed from individual enthusiasm. Passionate people always make a difference, but there is a risk of ongoing viability if these individuals move elsewhere and leave a gap.

The online collaborative platform is an excellent initiative that will help cement joint working, but there remains a risk that the joint endeavor will fail if enthusiastic individuals are lost. Consideration should be given to ways of creating a sustainable program for the future, with dedicated funding sources that sets a strategic ambition.

38.5 Future outlook

This relatively new team is led with passion and dedication to their topic. Such leadership should be commended – it will catalyze and inspire others to contribute to this important area of research. In addition, there is public interest in women's health and issues of gender, which should add weight to the program and encourage future funding.

The main task facing this group is ensuring overall viability. As with any new initiatives, there is a risk that the initial enthusiasm wanes, that other core priorities reduce capacity for working across disciplines and the necessary infrastructure support is not put in place.

There are potential risks and weaknesses, which include the dependency of the program on a few individuals. For the short term this is fine, but for the medium- and long term this may be a risk. Furthermore, there is overlap with other programs, and the added value of the combination may not be sufficiently visible. Finally, the current program is very broad, which may carry the risk of lack of focus.

38.6 Conclusion

This is an inspiring and exciting new area of research, drawing in collaborators from various disciplines and specialties. It has an important focus on issues of relevance to society. The leaders of this new network are to be commended for their enthusiasm and vision for putting this in place.

Overall, the quality of research was good, with high societal importance. This is supported by good patient engagement. The main risk is one of sustainability, given that it is a new network without ongoing areas of financial support. The team is aware of this and is putting in place measures to bring people together to strengthen the network, pulling together a significant group of PhD candidates.

38.7 Recommendations

- The synergy of the program over its separate constituents should become visible.
- Strategic choices on focus may be in order. One to consider is whether sex differences between somatic disorders in symptomatology, diagnosis and treatment, that are present in virtually all diseases, should all be part of the program.
- An alternative name may be considered that provides greater focus and cohesion.
- The program may wish to consider the impact of new AI tools on society, including areas such as further education and employment, and whether there are any differential effects of AI by sex and gender.
- Another suggestion to be considered is to seek collaboration with those working in the field of genomics research to determine factors that may relate to perceived differences in outcomes by sex and gender.

39 Atherosclerosis and thrombosis

Cardiovascular diseases (CVD), including stroke, myocardial infarction, and peripheral arterial disease are the main cause of death worldwide. CVD is predominantly caused by atherosclerosis, a low-grade inflammatory disease of the arterial wall, with thrombosis ultimately causing vascular occlusive events. Risk factors for atherosclerosis include hypertension, dyslipidemia, obesity, diabetes, lack of exercise, unhealthy diet, and stress. Despite risk factor treatment, many patients suffer a high residual risk of developing CVD.

39.1 Mission, vision and strategy

The major challenges in the cardiovascular field are to improve individual CVD risk prediction, detection, prevention, and treatment. The mission of this research program is to contribute by further elucidating the pathophysiology of atherosclerotic and thrombotic diseases. This will reduce the burden of CVD, both for the patient as well as for society.

The goal of this research program is to elucidate the pathophysiology of atherosclerotic and thrombotic CVD, with a particular focus on inflammation, thereby improving personalized prevention, diagnosis, and treatment of atherosclerotic and thrombotic CVD. Clinical observational and intervention studies are performed in patients either at risk for or with CVD. These studies are based, at least in part, on the program's preclinical and translational pathophysiological studies. In addition, innovative diagnostic (imaging) tools and AI algorithms are developed and applied to facilitate risk prediction and early detection. Patients are recruited at Radboudumc Center for Cardiovascular Care and the Center for Brain and Senses. The program has strong connections with both clinical centers to ensure alignment of strategies in patient care and research.

39.2 Research quality

The mission for this program is to improve individual CVD disease risk prediction, detection, prevention and treatment. The specific aims of the research are to elucidate the pathophysiology of atherosclerotic and thrombotic diseases, to improve personalized prevention, diagnosis and treatment. To align the research portfolio across the individual groups, there are regular meetings to stimulate collaboration. This will be increasingly important as the field develops and care becomes more individualized. Overall, the quality of research within this program is excellent, and the program is world leading.

The research outputs are published in high quality international journals, and the team actively collaborates with research groups around the world. They are well-established and well-recognized for their contributions. The research programs reflect a shift from population-based studies to personalized care, which is aligned with the global trend in identification of risk and new treatment options. There is some inevitable overlap with the work programs on stroke and on diabetes, which requires active collaboration. There is also significant success in attracting funding.

In this context, the research into endogenous atherogenic factors is highly innovative, and further work into the practical application of these findings is to be encouraged. The world-renowned work into cohorts of patients with young stroke is also to be commended. In contrast, the role of exercise in prevention is extremely well-documented already and additional research may only generate marginal benefits. Research into behavior change strategies might lead to more effective strategies.

39.3 Societal relevance

This program has high societal relevance. The work is of great importance to the wider population, partly because atherosclerosis and thrombosis are among the most frequent contributors to morbidity and mortality, and because the team is actively ensuring the work reaches patients by driving change through guideline recommendations. There are positive links to patient organizations, whose input

will be essential to optimize research questions and determining appropriate outcome measures. In addition, the development of spin-off companies will help with ongoing sustainability. Ongoing attention to education and training initiatives also helps provide sustainability.

39.4 Viability

Viability of this program of work is excellent. It is supported by a team of researchers with established national and international collaborators, and funding from a range of different sources. These mixed funding streams offset risk of any one source of funding disappearing and render the program viable. Attention is also being paid to training younger researchers who will be able to develop and support the work in the future, as well as providing a focus on potential new developments. The program is one of the largest in RIMI, which implies that maintaining cohesion will require a constant effort.

To improve viability and to identify potential new areas of research, it might be valuable to consider additional horizon scanning. This could help pinpoint potentially important risk factors so far overlooked, perhaps including factors which were not present when much of the early epidemiological research was carried out into atherosclerosis.

39.5 Future outlook

This is a well-established research program with international and national recognition. There are important collaborations with other countries, significant ongoing funding streams and excellent engaged leadership. The future outlook is therefore highly positive.

There are potential risks and weaknesses. Most risks the program may face are likely to come from wider, global developments that impact on the research agenda or funding opportunities. Internally there are limitations to access to experimental facilities and departments, creating some barriers to improving ‘bench to bedside’ research. The group is large, and currently with good synergy, but this will require continuous attention. There is overlap with other programs, notably Cerebrovascular diseases.

39.6 Conclusion

The research program Atherosclerosis and thrombosis is well established, recognized nationally and internationally, with solid funding streams. A Patient Advisory Council helps ensure that the research areas are focused on important, relevant issues for patients.

It is a broad program reflecting the systemic nature of the disease and underpinning risk factors. There are advantages and disadvantages to expanding it further. The links to programs of research in diabetes, cerebrovascular disease and genomics are highly relevant, and for some there is some risk of too much overlap. Challenges for the future are largely external, relating to global changes in research funding and the potential for AI to act as a significant facilitator.

39.7 Recommendations

- To avoid overlapping with other programs, Cerebrovascular Disorders, either by shaping the overlapping area in one of integrated collaborations, or by agreeing on delineating which group is active in which area, i.e., primarily assign cerebrovascular research to the program Cerebrovascular disorders. A merger of the two programs is another option, which on the one hand is the most logical, but might also be inadvisable since the combination may become unwieldy large. RIMI is advised to thoughtfully assess which approach is best.
- Active engagement with the use of AI in research as this field is changing rapidly. The development of new tools has the potential to change the skills and activities carried out by the research team.
- Improve alignment of the overall research portfolio through the development of an overarching research plan, providing focus on core areas where there is likely to be the greatest impact.
- Facilitate access and connections between experimental and clinical departments to improve 'bench to bedside' research.
- Consider closer collaborations with those involved in genomics research, as this will impact both on algorithms for risk of atherosclerosis and on personalized treatments.

40 The impacts of (pre)diabetes

Diabetes is a highly prevalent, chronic condition. It has a strong negative impact on daily life, has substantial morbidity and mortality through its atherogenic effects on cardiovascular disease, and therefore comes with high individual and societal costs. Diabetes management relies heavily on self-care, a complex undertaking for patients, given the variety of factors underlying the disease. Despite these alarming facts, emerging technological solutions, the society-wide implementation of healthy lifestyle policies and interventions, as well as promising powerful pharmacological obesity treatment options offer hope to people with diabetes. This research program focuses on the impacts of (pre)diabetes.

40.1 Mission, vision and strategy

The evolving landscape in prediabetes and diabetes research provides excellent opportunities to apply novel technological and scientific advances that can halt or prevent disease consequences, thereby providing appropriate care for the individual. To date, individualized translation is uncommon and there is an urgent need for academic leadership to provide guidance in this field. This research program aims to characterize the underlying mechanisms that drive the development of (pre)diabetes and their complications, and to develop appropriate care by including technological innovations that result in a personalized approach to reverse the negative impact of (pre)diabetes.

Three specific aims of the program are based on existing and available forms of care, such as medical psychology and clinical technology, including a track with Radboudumc Health Innovations Lab, and on and research expertise, including clinical studies and experimental procedures in humans complemented with in-depth expertise in innate immunity. These choices and the complementary expertise of the program members in this field place the program in an unparalleled position to accomplish its goals.

40.2 Research quality

The program focusses on the reduction of the negative impacts of (pre)diabetes on people's lives. The group members are mainly active in the field of clinical experimental research, including imaging, advanced phenotyping and clamping experiments, to further understanding of insulin resistance and diabetes. For this research they also make use of AI. The research quality of the program is good. The program has an excellent position in running clinical trials in this field, has published several relevant publications in the field, and is acquiring sufficient funding from various sources. There are collaborations with other research groups in the Netherlands (for instance with researchers elsewhere that perform specific cohort studies and the group in Maastricht) and the RGLs are leading several European projects. There are public-private collaborations on the emerging field of GLP-1 inhibitors, but also on devices for monitoring patients.

The program is relatively small (three RGLs, two researchers in the Talent Track, four post-docs) compared with other programs. They are, however, interacting with several other programs where relevant, for instance, they share the laboratory with the immunity lab and work together with Exercise=Medicine, Atherosclerosis and Thrombosis and Innate Immunity. Still, the program could benefit from more intense collaborations with other programs, most importantly with the Exercise=Medicine program.

40.3 Societal relevance

Diabetes is a major health issue that influences health on a day-to-day basis. Technology plays an important role in the treatment of the disease and therefore studying the interaction between technique and the patient is highly relevant. One of the program's strengths is the connection to diabetes care. Understanding the mechanisms of insulin resistance and diabetes, and its association

with obesity and the effect of treatments is important to improve the (personalized) treatment of patients, which has direct societal relevance. The work on monitoring for and preventing hypoglycemia is highly relevant to patients.

The program has delivered some societal relevant products, for instance '*An updated national position statement regarding Do-It-Yourself (DIY) closed loop insulin treatment*' and the '*Let's DIY together*', which shows the societal relevance of this program. In addition, the program is active in publications for education in the clinic, policy and research. Shaping the program more intensively with the diabetes society may increase societal relevance further by increasing patient involvement.

40.4 Viability

Diabetes will not be resolved soon, and the number of patients will even grow, and so will the consequences of diabetes, that have major impact on patients' lives and society, in terms of morbidity, mortality, quality of life and costs. Also, the focus on newly developed medications (e.g. GLP-1 agonists), the use of technology and the subtyping of patients will remain relevant in the coming period. The program has some strong assets, for instance the multidisciplinary group. Therefore, viability can be positively assessed. There are some RGLs retiring soon, and funding is highly competitive.

40.5 Future outlook

The use of wearables and AI can benefit the lives of people with diabetes. The future here is the use of closed loops with continuous monitoring and pumps, including both insulin and glucagon. The program has the potential to perform the relevant clinical trials and has connection with relevant research groups and companies. These innovations are only effective if the patients and their families are involved in the development of these innovations. This program is well equipped for co-development. Inclusion of knowledge on epigenetics may further enrich the program, to fulfill the wish to become a program that strongly links the bedside to the lab.

There are some potential risks and weaknesses. Challenges include the costs of clinical trials, which are increasing, and the competition for funding is increasing – which is true for all research in the Netherlands. The pending retirement of some RGLs asks for a clear succession plan.

40.6 Conclusion

The (pre)diabetes program is a valuable program that innovates in an area that is relevant to a large health problem. The program aligns well with the other initiatives in the Netherlands and Europe. The scientific quality is good, and the program delivers innovation and important publications. The viability should get some attention, especially because the program depends on few people.

40.7 Recommendations

- To further strengthen the impacts of the program on (pre)diabetes, the organization of the program may be reconsidered, where approaches might be to merge with other programs (for instance with Exercise=Medicine).
- Related to this point is the question of whether it is fruitful to focus both on type 1 and type 2 diabetes.
- Consider changing the name to 'Impact of diabetes' as it is a better representation of the work done.
- The relationship between the 'data-driven approach in the Health Innovation Lab' and the 'Radboud Healthy data program' could be strengthened.

41 Kidney disorders

Chronic kidney disease is a leading cause of mortality and significantly increases the risk of cardiovascular complications. In addition to chronic kidney disease, there are over 400 different rare kidney diseases, and many of them ultimately also lead to chronic renal failure. This highlights an urgent need for innovative research and early interventions.

41.1 Mission, vision and strategy

The program's mission is to have a major impact on the future of clinical care for patients with kidney disease and to be at the forefront of the international field of nephrology research. The program's five goals are to gain a better understanding of the molecular mechanisms, physiology, and pathogenesis to develop treatments for 1) glomerular diseases, 2) tubular transport disorders, 3) vascular calcification, 4) kidney replacement therapy, and 5) ciliopathies.

To achieve these aims, the program will explore the molecular and immunological basis of these diseases, develop biomarkers for optimal prediction of disease prognosis and treatment efficacy, and study therapeutic strategies that emerge from these insights. The program's focus is on genetic, molecular, cellular, and immunological research to address both common and rare kidney disease, both of which can lead to chronic kidney disease (CKD).

The program builds on Radboudumc's expertise in patient care (Radboudumc Expertise Center for Rare Kidney Disorders) and the program's existing infrastructure and research in areas such as gene defects, transporters, and cellular functions, use of advanced culture systems models, transgenic animals, but also cohorts of patients and healthy volunteers. The program does this in international collaborations, including the existing integration into the European Rare Kidney Disease Reference Network (ERKNet). All research is driven by unmet clinical needs with a focus on innovating diagnosis, prognosis, and treatment strategies. The goal is to enhance patient quality of life, with an additional impact on scientific, societal and economic parameters.

41.2 Research quality

The Kidney Disorders program demonstrates impressive research quality, with a strategic focus on both mechanistic understanding and translational impact. Since 2018, program members have produced approximately 1,000 publications in high-impact journals, supported by prestigious grants including ERC, NWO-VIDI/VICI, Marie Curie Doctoral Networks, Health Holland, and NIH. Research spans glomerular diseases, tubulopathies, vascular calcification, kidney replacement therapy, and ciliopathies, integrating molecular, cellular, and immunological approaches.

The program's team structure integrates nephrologists, pediatric nephrologists, molecular biologists, physiologists, and clinical geneticists. The team has been successfully working together for many years, leaving a harmonic impression on the committee. RGLs balance research, clinical care, and education, fostering synergistic integration across disciplines. Collaborative networks, such as ERKNet and partnerships with TU Twente, enhance technological readiness, methodological innovation, and translational application. The program is further supported by the Radboudumc technology platforms, such as microscopic imaging and omics technologies.

41.3 Societal relevance

Kidney diseases affect more than 10% of the global population, with chronic kidney disease projected to become the fifth leading cause of death by 2040. The program addresses these urgent societal challenges by translating research into impactful clinical interventions.

Key societal contributions include development of treatments for glomerular diseases, tubulopathies, and ciliopathies. Other examples are the cost-effective use of eculizumab for acute hemolytic uremic

syndrome, innovative urine collection devices for neonates, AI-based transplant diagnostics, patient-derived organoid models, and advanced imaging technologies. The program actively engages patient organizations locally (NVR) and nationally (NVN), participates in World Kidney Day, hosts lab tours for patients, and disseminates knowledge through international societies.

41.4 Viability

The program has high viability, underpinned by a strong team, robust infrastructure, and a strategic funding portfolio. The program includes15 research groups, each with 5–15 members, that provide complementary expertise from basic molecular biology to clinical nephrology. Succession planning ensures sustainability, with identified internal talents and active recruitment strategies for new RGLs and junior investigators, which is important considering the nearing retirement of senior leaders. Individual and collaborative grants from EU, NWO, Health Holland, and private partners (e.g., CSL, Mercurna) provide stable resources. The strategic alignments with TU Twente and Maastricht UMC+, along with ERKNet integration, align research, education, and clinical care across Europe. Joint affiliations and annual scientific events stimulate collaboration, co-funding, and translational innovation.

41.5 Future outlook and challenges

The program is designed to become one of Europe's leading centers in translational nephrology. Its integration of cellular models, patient cohorts, and technological innovation provides a robust foundation for expansion of patient-derived organoid platforms and gene therapy initiatives (e.g., cystinosis cure), which will accelerate precision medicine in nephrology. Increasing adoption of AI tools for imaging and diagnostics will enhance prediction of disease progression and treatment response. Within 6–10 years, the program aims to deliver at least three new treatments for glomerular and tubular diseases and achieve a 25% reduction in pediatric kidney disease burden. Leadership in ERKNet and Europe will strengthen clinical data sharing, multi-center trials, and translational research networks to reinforce international visibility.

There are some potential risks and weaknesses, including talent recruitment, mentoring and retention. Increasing competition for European and national grants necessitates diversified funding. Bridging mechanistic discovery and clinical application remains difficult, especially in rare diseases. Developing interoperable data infrastructures across ERKNet and national centers is essential.

41.6 Conclusion

The program has established itself as an internationally visible and impactful initiative in the field of nephrology with a unique selling point. The program combines basic, translational, and clinical research across five key thematic areas. The program demonstrates impressive quality of research, international recognition, and has an excellent societal impact through improvements in patient care, public outreach, and innovative treatment strategies. Initiatives such as Kidnie and the Kidney Subsidy highlight commitment to pediatric kidney disease, aiming for a measurable reduction in disease burden over the next decade. The team shows synergy and funding and team structure form the basis for a long-lasting viability.

Since several senior leaders are approaching retirement, careful succession planning for team restructuring is required. Further, rapid growth and multiple research lines will require attention to coordination and integration. Mechanistic understanding, while strong experimentally, would benefit from enhanced systems biology and computational approaches. Additionally, maintaining leadership in predictive diagnostics and clinical translation requires expansion of AI-driven and data-sharing frameworks.

In conclusion, the Kidney Disorders program is a state-of-the-art, highly motivated initiative with major impact on nephrology research and patient care. Its strong foundation, societal relevance, and translational success position the program to reach a top status in the coming years, provided challenges in leadership transition, integration, and data-driven research are addressed.

41.7 Recommendations

- Implement a structured transition plan for senior researchers nearing retirement.
- Expand Talent Track opportunities to attract and retain early-career researchers, fostering the next generation of program leaders.
- Strengthen governance mechanisms to maintain cohesion across the five research themes.
- Promote crossline integration to enhance synergy between glomerular, tubular, ciliopathy, replacement therapy, and vascular calcification research.
- Integrate systems biology and computational modeling to complement experimental research and deepen mechanistic understanding.
- Expand data-driven nephrology, including AI, big data, and digital pathology, to maintain leadership in predictive diagnostics and personalized treatment.
- Focus on modeling drug-induced kidney injury and patient responder analyses to increase translational relevance.
- Continue development of innovative therapies, organoid models, and personalized interventions to improve patient quality of life and reduce healthcare costs.
- Maintain strong engagement with patient organizations to ensure research addresses unmet clinical needs.
- Monitor EU and NWO funding landscapes and align program initiatives with interdisciplinary, AI-driven, and translational priorities.
- Expand public-private partnerships to accelerate translation and commercialization of discoveries.
- Ensure strategic use of internal and external resources to maximize program cohesion and long-term impact.

42 Orofacial Health

The oral cavity or mouth is the entrance to the body and can be seen as a mirror of the general health of an individual. The worse the oral situation, the more chances for comorbidities and problems in general health of patients. This research program focuses on orofacial health, placing the well-being of patients at the center of our research on the mouth, face, jaws, and the underlying structures and mechanisms.

42.1 Mission, vision and strategy

The Orofacial Health program strives to create fertile ground for multidisciplinary collaboration for those who promote orofacial health, including basic and applied researchers, healthcare and public health professionals, and educators. The program aims to develop new solutions for orofacial health(care) problems, contributing to a future where everyone has optimal orofacial health. To achieve this goal, the main program objectives are to improve governance and financing of orofacial healthcare systems to make them more equitable, prevention-oriented, safe, efficient, sustainable, and integrated with general health. Further aims are to develop novel (pre)clinical diagnostic, preventive, and treatment strategies, and to monitor the quality of care to promote (supported by AI and 3D technology) person-centered orofacial healthcare based on scientifically justified and evidence-based practice guidelines. The program aims to develop minimally invasive reconstructive and biomaterial-based regenerative treatments and accelerate their clinical translation using advanced ex-vivo/in-vitro model systems, and equip new generations of orofacial health researchers and professionals with the skills necessary to shape and deliver the orofacial healthcare of the future.

The research program is committed to having a significant impact on orofacial health(care) by improving governance and financing of oral health systems, designing innovative (pre)clinical and public health strategies and decision-making tools, and developing new minimally invasive treatments.

42.2 Research quality

This is a very successful and comprehensive research program with, currently, 6 RGLs and ~15 associated researchers from, e.g., the Departments of Dentistry and Oral & Maxillofacial Surgery, as well as Gastroenterology and Hepatology of the Radboudumc. The team is highly multidisciplinary, and consists of material scientists, biologists, engineers, epidemiologists, clinical scientists (surgeons, dentists) and health economists working closely together in a stimulating environment, both with respect to the building and the people. This excellent research program encompasses fundamental, translational, and clinical research. It has had a large impact on the international field over the past six years, generated through several high-impact and highly cited publications, awards, acquisition of prestigious grants, organization of international conferences, initiatives in open science practices, participation in the boards of professional international organizations and advisory boards.

The aims are clearly defined and ambitious and range from fundamental science to clinical impact and educating new generations of researchers in the field. The connection between education and research is particularly well-developed. The program has a clear strategy to reach out to relevant partners outside the program including (technical) universities, insurance companies, orthodontists, policymakers etc. The program has an extensive and strong ability to acquire research funds, for a large amount of money over the past six years, including national and European grants, putting them at the top of national (and possibly international) orofacial health research. Recognition of the quality of the program is supported by prestigious individual grants, participation and leading role in various international consortia, board memberships, and secondary affiliations at prestigious international universities.

42.3 Societal relevance

The program has defined a comprehensive and ambitious impact pathway strategy, and its societal relevance is very good. It has contributed to the definition of multiple clinical guidelines. The program has started several investigator-initiated clinical trials. Its bachelor program Dentistry received the status of 'educational TOP program'. The program has yielded two spin-off companies. The program has a clear well-defined strategy to generate societal impact through the evidence-based initiation of clinical trials, by informing policy, and by stimulating valorization of research results to, ultimately, improve healthcare and educate research and clinical talent. Importantly, the research program is embedded in a highly intensive educational program for students of dentistry. The program has actively pursued public outreach including media appearances, and lectures at general audience science festivals. Currently, the engagement of patients or relevant patient organizations in helping to structure the program is largely absent.

42.4 Viability

The research over the past six years has been very successful. The specific goals for the coming six years and the research strategy have been clearly defined, and generic goals and aims have also been laid down in a structures and comprehensive manner. The program may further benefit from the definition of more specific research aims for each subgroup.

The RGLs in the program have different and complementary expertise and, since the start of the program, have clearly built a structure in which synergistic multidisciplinary collaborations are fostered. The program is currently in a transformative phase with several established researchers leaving the program and young talent starting. An apparent problem is the difficulty in recruiting enthusiastic individuals for research, despite the top-notch education program that is associated with the research program. This is not in any way the fault of the program and its members, who foster an open inclusive group and demonstrate a high level of enthusiasm and collaborative spirit, but due to the generally low-level interest of Dutch dentistry students for research. Despite these aspects, the viability of this research program is very good.

42.5 Future outlook

This is a program in which fundamental and clinical research are closely connected. The program has had a large scientific and societal impact over the past years, and their general aims are ambitious. The program could benefit from more specifically defined goals for the coming 4–6-year period.

There are potential risks and weaknesses. There are established researchers leaving, which could result in foreseeable difficulties to attract early career talented researchers. The specific goals can be defined in more detail.

42.6 Conclusion

Orofacial Health is a unique and very strong multidisciplinary research program within RIMI, linking fundamental, technological, clinical, epidemiological and health economic research. The research program is linked to an equally excellent education program. The program has an excellent track record in terms of scientific output and obtaining external research funding. It is expected that the program will continue to perform as such in the coming years.

42.7 Recommendations

- To develop a structured succession plan for senior researchers who will leave the group , including tenure-track recruitment and co-leadership models.

- To strengthen talent pipelines by expanding undergraduate research opportunities, creating clear academic career pathways for clinician-scientists
- To establish a Patient Advisory Board and systematically involve patient organizations in priority setting, grant preparation, and clinical trial design.
- To formulate subgroup-specific 4–6-year research plans with clear aims, milestones, and societal impact indicators.
- To further formalize collaborations with external partners and strengthen the valorization pipeline through innovation scans and business development support.
- To enhance communication and outreach through structured public engagement strategies.

43 Advanced imaging

Medical imaging is an essential factor in screening, diagnosis, treatment planning, image-guided therapies, and disease monitoring. Advances in MRI, CT, PET, ultrasound, AI, and molecular imaging have improved both imaging precision and personalization in healthcare. However, data interpretation, clinical translation, and computational analysis require further investigation.

43.1 Mission, vision and strategy

The mission of the program is to develop and implement innovative imaging technologies and strategies that enhance early and accurate diagnosis. Furthermore, the program aims to deepen the understanding of disease mechanisms, improve disease progression monitoring, and support the creation of personalized, effective treatment methods. Through interdisciplinary collaboration, technical innovation, and clinical translation, the program aims to create a sustainable, accessible healthcare system that improves patient outcomes and quality of life.

Specific goals of the program are deepening the understanding of organ structure, function, and disease processes to enhance knowledge of biological mechanisms, leading to improved early treatment, prevention, and improved patient outcomes; enabling earlier diagnosis, characterization, and staging of diseases to ensure more timely and effective treatment strategies; improving personalized treatment execution based on individual anatomy and pathology to enhance accuracy and reduce risks; accelerating the development and translation of imaging innovations in an accessible, cost-effective manner to ensure a sustainable and inclusive healthcare system; and, developing a functional whole-body 14T MRI system which will push material science boundaries forwards and drive fundamental breakthroughs in imaging sciences.

To achieve these goals, the program conducts fundamental and (pre)clinical research, with the aim of being both meaningful and impactful, to address healthcare needs, and to ensure the efficient translation of these innovations into clinical practice.

43.2 Research quality

The Advanced Imaging research group has produced work of excellent scientific quality, in line with its mission and its goals. Its strength lies in combining technical innovation (e.g., PET tracers, ultrasound-on-foil, AI for lung and prostate cancer detection) with clinical translation (e.g., image-guided bronchoscopy, MR-guided radiotherapy). The program's contribution to international imaging science is evidenced by leadership in developing new protocols (e.g., harmonized rodent fMRI), potential use of high-field 14T MRI, and consensus guidelines (PSMA-PET, GI radiotherapy contouring), which have the potential to influence practice beyond the Netherlands. Overall, the group has published in high impact journals of their field, including but not limited to Lancet Oncology, Radiology and Nature Neuroscience with significant citation counts. Their research is recognized as evidenced by the acquisition of competitive grants having received honors and awards.

43.3 Societal relevance

The research program shows strong societal relevance through contributions to international guidelines (PI-RADS AI, AAPM/EFOMP mammography dosimetry, Delphi consensus on liver ablation margins) and participation in policy initiatives such as EU4Health SOLACE for lung cancer screening. The BARICO study combines clinical, academic, and industry partners – however without naming any company names, and generating visible media attention around obesity and brain health. Public engagement is also evident in outreach on ethical issues of animal imaging. In addition, projects such as the Babychecker project indicate an orientation towards global health, with potential impact in low-resource settings. Involvement of four patient organizations shows patient involvement across disease

entities. There are relevant contributions to clinical care, including a less invasive, imaging-based approach for diagnosing pulmonary lesions that is now reimbursed in the Netherlands and being implemented internationally, as well as the ENFORCE project, which evaluates focal therapy as a potentially less harmful alternative in prostate cancer treatment.

While the 14T MRI project is cutting- edge, concrete steps of involvement remain unclear, and aspects such as costs, safety or regulatory-grade checkpoints remain as barriers for wider clinical adoption. The research group has published outstanding work on assessing AI-system's capability to assess prostate cancer imaging, leaving the question why no further concrete outlook for translation towards software as medical devices is being listed. There should be a forward look regarding next steps for translation (e.g., superiority studies, how to improve performance with AI in real world settings, compared with standard of care). For instance, AI for lung cancer screening and PSMA-PET are areas with multiple high-profile trials worldwide; the unique methodological or patient-cohort advantages of the Radboudumc work could be articulated more explicitly.

43.4 Viability

The research program includes 24 RGLs involved in 16 groups. Its large multidisciplinary team, numerous connections to other research programs at Radboudumc, supported by infrastructure such as MITeC, BioMR, and the MR-Linac, ensure that the program can pursue its mission of developing and potentially implementing advanced imaging and image-guided therapies. Financially, the program is sustained by a combination of institutional investments and a solid track record in competitive national and international funding. Input from a wide range of senior researchers and clinical scientists across departments underlines the robustness of its staffing. Risk management and regulatory compliance are not detailed program-specifically but are safeguarded through Radboudumc's institutional frameworks for ethical approvals, patient data security, and radiation safety, which are highly relevant to this field.

43.5 Future outlook

The program has a clear trajectory toward further integration of advanced imaging, AI, and personalized interventions, supported by strong infrastructure and interdisciplinary collaboration. Its ambitions—such as 14T MRI, image-guided minimally invasive therapies, and clinically embedded AI—position it well for international leadership. Strengthening clinical engagement to increase the pool of clinically active researchers, securing long-term financial stability, and clarifying the program's competitive role in global AI-imaging and 14-T imaging will be essential to maintain and extend strong international visibility.

Potential risks and weaknesses are the costs, safety and regulatory aspects that may limit clinical use of 14T-MRI. Furthermore, clinical researcher involvement is crucial for further development and applications.

43.6 Conclusion

The Advanced Imaging program demonstrates excellent research quality, with internationally visible contributions in imaging technology, protocol development, and clinical translation. Its strength lies in the integration of technical innovation and clinical applicability, reflected in high-impact publications, major competitive grants, and leadership in guideline development.

The program shows strong societal relevance, contributing to clinical guidelines, global health initiatives, and patient-centered innovations. Public engagement and collaborations with patient organizations further support impact. The program's viability is supported by its large interdisciplinary team, extensive infrastructure (MITeC, BioMR, MR-Linac), and strong funding record. The future outlook is promising, with clear ambitions in ultra-high-field MRI, image-guided interventions, and AI-driven diagnostics. To maintain international leadership, strategic attention is needed to expand

clinical researcher involvement, secure sustainable long-term funding, and clarify the program's differentiation and competitive advantage in AI and 14T innovation.

43.7 Recommendations

- Define the program's contribution and long-term strategy for 14T MRI, including scientific priorities, clinical pathways, and sustainability.
- Make a clearer attribution of scientific roles, to resolve inconsistencies between claimed contributions and cited evidence.
- Assess global competitive positioning in AI-based imaging and determine how program-specific strengths (datasets, clinical partnerships, infrastructure) can ensure differentiation.
- Expand the pool of clinically active researchers to support translational aims and strengthen cross-disciplinary integration.

44 Surgical innovations

Surgery is becoming increasingly less invasive and more tailored to the individual patient. These developments are enabled by technological advances in robotics, imaging, 3D technologies, AI, modelling, and data sciences. This research program studies several of these surgical innovations.

44.1 Mission, vision and strategy

The mission of this research program is to optimize the quality, safety, and outcomes of surgery, through the development, implementation and evaluation of innovative interventions. The program aims to facilitate these developments by providing a platform for collaboration across all domains involved, focusing on the full patient journey. The program follows the principles of "First time right", which entails that patient planning is optimized to minimize lead times, patients are optimally prepared for surgery, and the optimal surgical plan is defined, all to improve treatment quality and efficiency.

Specific goals of the program include identification of the right surgical treatment for the individual patient, including patient selection and the definition of the pre-operative plan, tailored to the individual patient, the optimization of the execution of the surgical plan, involving the development and implementation of technologies such as robotics and navigation, medical extended reality, and imaging techniques, and, finally, to evaluate the outcome of surgical interventions on the quality of life of the patient, providing crucial feedback for evaluation, further development, and improvement.

Over the last 50 years, nationally and internationally, surgery has changed beyond recognition. These developments have occurred across a range of specialties and diseases, with many procedures involving the use of robots. A research program in this area is therefore highly relevant.

44.2 Research quality

The mission of the program is to 'Optimize the quality, safety and outcomes of surgery through the development, implementation and evaluation of innovative interventions'. This makes the program very broad, since it also includes many types of surgeons and surgeries. The development of the program started late in the RIMI process and therefore the strategy is not fully developed. One of the main goals is to be the connecting program for surgeons and to stay well aligned with the clinic and build a program that is largely clinically oriented.

Research quality is good, as seen for instance by the high impact publications and several useful software packages that are frequently downloaded. Some prestigious research grants were secured in the program such as ERC Consolidator Grant, NWO Aspasia and Marie Curie Fellowships. There is coverage of an interesting range of topics, but it is not clear how these have been identified or how they fit together into a program. There is a clear need to further streamline the research strategy of this program.

Primary research methods are also unclear and, although there seems to be a feedback route into day-to-day practice, details on how this would work are lacking. Consistent definition of methods, as appropriate to answer the research question, is particularly important for collaborative work such as this in an area of rapid change and new developments. Several research group leaders within the program are leading important (inter)national projects including Horizon Europe grants, ZonMW and Health-Holland and ReumaNederland projects. The development of collaborations across several fields should be commended. The program aligns the surgical innovations in RIMI, and an annual science meeting is of benefit as stimulating interactions between the many PhD candidates.

44.3 Societal relevance

The large volume of surgical interventions performed each year in the Netherlands implies this is an area with obvious societal relevance. There are some excellent examples of how specific work has had an impact on treatment, both in the Netherlands and more widely. The concept of 'first-time-right' holds a promise to reduce the burden on health care. The program is not fully prepared for upcoming developments, such as the impact that AI and robotics are likely to have on the system. Within these there are questions about selection criteria for interventions, comparison of new with existing technology, healthcare resource use and outcomes.

A risk of the developments resulting from this program is that they may lead to a higher burden on the health care professional and lead to a more expensive health care system. HTA is therefore crucial to become integrated in the program. Examples of societal impact of the program are the hip implants pre-operative planning that is brought in practice at Radboud and is currently being scaled up. Other examples are AI for operative planning, and a cutting guide that is 3D printed. These technological advancements are prime examples of patient's benefit.

44.4 Viability

Viability of this program depends on the strength of the collaboration as well as on funding. For this program to become viable, each participating department or member should become convinced of the benefits from the collaboration, over and above their individual research outputs, to secure a long-term effective partnership. This would infuse enthusiasm in the group which currently seemed lacking. As in other programs, also in this program several RGLs are retiring in the coming years.

44.5 Future outlook

The fast development of AI and robotics generates a great opportunity for this program; however, the costs of these innovations may be high. Therefore, this program should focus on the innovations where the balance between costs and benefits is positive. With more focus in the research of the program and efforts to increase cohesion, the program can become more effective and have more impact.

There are several potential risks and weaknesses. The program has only recently come together, which implies it is largely unfocused. There is no interaction with non-clinical researchers, which will make it virtually impossible to keep this program afloat, given the clinical duties of all its members. Several RGLs are retiring. A further threat is the regulation of medical devices (MDR) and the overload of the demands by regulatory bodies, which makes research in this area administratively cumbersome and costly.

44.6 Conclusion

This program brings together some key aspects of RIMI. The program has good scientific quality as seen by the publication of some important scientific articles and the program managed to collect several (inter)national grants. Currently the program is still too much a collection of projects, and it needs to be structured regarding scope, focus, and cohesion, all to become a truly unified research program.

By strengthening the strategy, the current societal impact may be further increased. As many surgeries are performed annually in the Netherlands, a number which will increase with the aging population, the impact of innovations in this field has the potential to have a major societal impact. The broadness of this program makes its viability a concern

44.7 Recommendations

- To be viable, the program needs to connect with non-clinical researchers, as many other programs have integrated clinical research with either laboratory work, or economic and

health technology assessment (HTA) research, or psychological studies, or epidemiologists to jointly perform clinical research. There are prime examples of how this can be made to work, for non-surgical specialties in Radboudumc itself, and for surgery in other UMCs.

- The program should be more focused as there currently are many parallel tracks which may reduce efficacy. Strategic choices are in order.
- An intensive collaboration with the University of Twente may be useful.
- The EU directive on medical devices is perceived as a barrier for the program, which is not unique in the Netherlands. Europe is currently working on an adjustment of this regulation, and this program could be trial and involved in discussions with policy makers at the ministry of Health (VWS).
- Most impact can be made when benefits relative to costs of innovations are high. To monitor this balance, solid knowledge on HTA analysis should be part of this program.
- Cohesion should be built by organizing meetings and stimulating interactions at the junior staff level, which may also inform collaborative goals and focus of the program.

45 Healthcare-related Prevention

An unhealthy lifestyle is an increasing problem in the Western world. For example, only 29% of people meet the optimal food intake and 44% meet the guidelines for physical activity. Often lifestyle programs are not offered, not sufficiently personalized or designed in a medical model (intervention). Poor compliance and models that do not fit for specific population subgroups aggravate matters. The program wishes to tackle these problems.

45.1 Mission, vision and strategy

The mission of the program is to ensure that all patients are offered tailored, evidence-based, accessible, and cost-effective (indicated and healthcare-related) interventions that promote health and well-being. By investigating lifestyle factors and aspects of the living environment that contribute to chronic diseases, the program seeks to reduce the disease burden and enhance the quality of life for individuals and communities through research and education, and to promote citizens' health in the region Nijmegen / Oost Nederland.

Goals of the program include enhancing and optimizing (disease-specific) lifestyle interventions by utilizing and integrating innovative methodology, data-driven insights, and behavioral science, integrating scientifically valid, evidence-based generic, as well as disease-specific lifestyle-focused prevention into routine care by connecting the patient's living environment with healthcare, fostering collaboration and optimizing the role of care and social professionals, empowering individuals and communities through accessible, acceptable, personalized, and effective lifestyle interventions that align with their needs, values and abilities by means of citizen science, and ensuring equal access to these interventions for people of low socio-economic status or a non-Western demographic background.

45.2 Research quality

This two-year-old program, which fits the strategic prevention pillar within the institutional framework, integrates lifestyle and environmental interventions into routine patient care and aims to reduce the burden of chronic diseases, and improve the quality of life for individuals and communities in the Nijmegen region and beyond.

The program positions itself as an 'enabling program' that fosters interaction and synergy for healthcare-related prevention activities in the RIMI. It has successfully established a dedicated Prevention Hub, which facilitates collaboration across disease-specific research programs with lifestyle and prevention activities and involves high-profile RGLs and researchers who have harbored their activities partly in this program. Innovative methodologies are positioned as central to the program, including behavioral science, citizen science and field labs, complexity science, and system approaches. There is also a clear ambition to further develop data platforms. Research projects span a wide range of topics and approaches and focus amongst others on various tailored lifestyle interventions and adaptations, and accessibility to interventions. Furthermore, the impression is that the Prevention Hub has contributed to obtaining national and international collaborative grants.

The quality of the core research of this evolving program is considered good, with a clear potential to grow this further. This will depend critically, however, on strategic decisions and developments as detailed in the Future outlook paragraph. Part of the vision of the program, that it should enable 'the healthcare system to transition from hospital-based interventions and less medical to community-based programs' seems rather a leap and might require further discussion with the RIMI to better delineate to what extent this fits the RIMI strategy, and how feasible these plans are.

45.3 2.3 Societal relevance

The program aims to make impactful contributions to a more sustainable healthcare system by reducing costs and by alleviating pressure on healthcare. It also addresses health inequalities through targeted interventions and anticipates potential societal risks such as stigmatization. Radboudumc has established Field labs in Nijmegen neighborhoods, where researchers collaborate with citizens and professionals to co-create and implement health-promoting initiatives. The long-standing partnership with regional public health services (AMPHI) supports knowledge transfer and policy development. The societal relevance of the program is clearly relevant and may increase with time.

45.4 Viability

This 'enabling program' fits the Radboud strategic prevention pillar and has a viable structure with considerable interaction with many other programs. There are many opportunities to further create synergy as half of the current RGLs have prevention as one of the research topics. Importantly, the Sector Plan offers funding that further enhances collaboration and supports the preparation of future larger consortium applications. The program has also established a peer-community of PhDs fellows. The program involves a high number of high-profile researchers who have harbored their activities partly in this program, next to their activities in other programs. This is a strength, but poses also risks at the level of governance and involvement, and for developing a viable core research agenda. Overall, the viability of this evolving program is considered good, but dependent on the continuous commitment of the many individuals involved.

45.5 Future outlook

The vision of the program is that our healthcare system must transition from hospital-based interventions to community-based programs with personalized approaches. Key to this transition are lifestyle advice and cross-domain collaboration. Several unresolved questions remain, however, and the program aims to answer these with a solid evidence- based foundation. It will strengthen its infrastructure of disease-specific and generic programs and explore alternative methods of evidence generation next to randomized controlled trials. The program will be able to expand and increase both scientific and societal impact. It aligns with strategic priorities of the Radboudumc, engages stakeholders, and supports a shift from disease treatment to health promotion and community. As an evolving program, however, there are strategic questions that must be resolved.

There are potential risks and weaknesses, which include a thematic overlap with many other programs that require integration with disease-specific research. Furthermore, shifts in national policies may require adaptation.

45.6 Conclusion

The Healthcare-related Prevention program is a recently founded program that has positioned itself as a strategic 'enabling platform' within Radboudumc's prevention pillar. It integrates lifestyle and environmental interventions into patient care and could foster synergy across disease-specific programs through its Prevention Hub. Research quality is currently good and with clear potential, supported by innovative methodologies such as behavioral science, citizen science, and complex approaches. Societal relevance is very strong, already demonstrated by initiatives like Fieldlabs and partnerships with public health services, which promote co-creation and aim to address health inequalities. Viability is good, with institutional alignment, ample opportunities for collaboration, potential involvement of many relevant RGLs, and supportive services offered by the Sector Plan, but governance, ensuring involvement and thematic focus require attention.

45.7 Recommendations

- For this recently launched program that involves many RGLs from various domains, it is important to define a clear core research agenda to avoid too much thematic overlap and ensure coherence across diverse activities.
- Parts of the vision of the program might require further alignment with the overall strategy and vision of the RIMI.
- Governance structures should be more formalized and the long-term involvement of leading RGL should be secured to obtain program stability.
- Crucial to achieve the ambitious aims of the program is the development of robust data platforms and governance frameworks to support evidence generation and scalability.
- Although the program can probably rely on Sector Plan funding, it should also explore diversification of funding sources and increase participation in international networks and consortia to further elevate research quality and attract large-scale funding.

46 Exercise = medicine

This research program focuses on one of the world's leading detrimental lifestyles: physical inactivity. This is highly relevant as physical inactivity relates to morbidity and all-cause. Nonetheless, many clinically and societally relevant questions remain unanswered.

46.1 Mission, vision and strategy

The aim of the program is to improve the understanding of the health effects of physical (in)activity, from molecules, to human, to population, by studying the full range from sedentary behavior to high-intensity exercise. The program applies physical activity and exercise as a 'medicine' within the Radboudumc healthcare, work and home-environment. The main goals of the program are to prevent development and progression of non-communicable diseases, and to improve clinical and patient-related outcomes. Furthermore, the program aims to optimize the health benefits of exercise and physical activity in primary, secondary and tertiary prevention and treatment of disease.

This requires a strong interdisciplinary approach. A mixture of various types of studies allows the program to understand mechanisms and translate innovative interventions to clinic and society. To achieve its ambitions, the program identified four focus areas: to improve guidance by the production of: evidence-based reports on sedentary behavior, optimal physical activity 'dose', and volumes of exercise for public and disease-specific guidelines, to understand the mechanisms by which physical activity affects health and by improving the benefits and use of exercise protocols, to optimize through multidisciplinary work the content, use, and implementation of exercise-/physical activity-based interventions, and, finally, to understand differences in effects of exercise and physical activity between groups and individuals, leading to precision exercise medicine, optimizing its effects for all populations.

46.2 Research quality

The scientific relevance of the program's research is good, as shown by the publications, prestigious (consortia, personal and research) grants, high citation scores, participation in clinical guidelines and consortia, and focus on co-creation and implementation. The ambition for the near future is to make datasets available to others, to have their own research data appear in guideline papers, and to establish board memberships of scientific societies or councils. This offers further opportunities for strengthening scientific relevance and impact. There is some concern that the research has more aspects of replication than being truly innovative, and that it is more aimed at solving remaining aspects in well-established concepts than trying to break new ground.

The program has a strong regional connection through projects such as *Build4Health* and the *Regio-deal Gelderland*, which link research to local health and environmental issues. Nationally, the Radboudumc group distinguishes itself for its clear "molecule-to-man-to-population" approach and its focus on translating research into practice through implementation science.

The group's work fits within international priorities, such as the WHO Global Action Plan on Physical Activity, and has contributed to several international guidelines, for example through the American Heart Association's Scientific Statement and the POLARIS project in oncology. However, the group's main activities and collaborations are national and regional, and its international research network and visibility could be stronger. Although interdisciplinarity is a strength of the program, given this breadth, there is some risk of fragmentation or insufficient integration across sub-disciplines.

46.3 Societal relevance

The societal relevance of the exercise = medicine program is evident not only from the well-known health effects of inactivity, but also by products from the program such as guidelines and project grants with various stakeholder groups. The program translates state-of-the-art insights when implementing innovations in clinical practice and has strong links with clinical departments and patient organizations (e.g. Harteraad, PHAROS). They also work together with industry and government policy partners to target society.

Public engagement is a strong element: the annual 4Day Marches study attracts media coverage and public interest, while researchers appear in television, radio, and podcast interviews to communicate findings to lay audiences. The program has a strategic approach for transforming results from the research to clinical practice and it also has a wide variety of collaborators ensuring a multidisciplinary approach and a breeding ground for impact.

46.4 Viability

A good infrastructure, prestigious and adequate funding, collaboration with a wide variety of stakeholders, and involvement in scientific and clinical societies makes the program viable for the future. The ambitions for the next six years are clear and relevant. Data science expertise is lacking in the program.

The program seems to have state-of-the-art infrastructure for assessing physical activity and exercise, including fully equipped research labs on motion analysis, cardiorespiratory responses, and pulmonary/muscle/vascular function, but also on innovative monitoring of home-based evaluations. This allows the program to continue to focus on understanding physical activity and its effects. Leadership currently seems to rest on a few individuals. To ensure resilience and succession, it will be important to nurture collective leadership and visibility among emerging mid-career researchers. It also seems the international leadership is mainly present in the cardiovascular and oncology domains.

46.5 Future outlook

Generally, the outlook is good, since the program builds on a solid track record, has sufficient funding and has societal relevance. The limited involvement of clinicians is problematic to further expand the societal relevance. Strengthening collaboration both with other research programs and with other actors both in the region and internationally will be an important aspect for the future of this program.

There are some risks and weaknesses. First, the focus of the program seems to be mainly on the regional and national context. It is unclear whether the program has a strategy for international collaboration in consortia or for international impact of their research. Furthermore, the research is not truly innovative, nor has it a strategy to become so. This may be inherent to have a lifestyle, i.e., an exposure, as the focus of the program, rather than a (group of) disorders. The program depends on a few senior individuals, and the involvement of junior researchers in strategy and planning is absent.

46.6 Conclusion

The research quality is good, and so is the academic reputation of the group, as shown by several output parameters. The societal relevance of the program is high, since the program successfully implements innovations in clinical practice and has strong links with patient organizations, policy makers and private partners. Viability does not give cause for concern. The ambitions for the next six years are clear and relevant, but lack the ambition to be truly ground-breaking.

46.7 Recommendations

- While the program is convinced it should be connected to every clinical department, it is not. Developing a strategy to strengthen the connection with clinical departments seems essential to maximize the impact of the program's research, although it may be overambitious to wish to connect to all.
- Obvious partners are the programs on psychology and other programs in which prevention is a major aspect (e.g., the program on (pre)diabetes). In fact, a merger with the program on (pre)diabetes may benefit both.
- Developing a strategy for dealing with the threats of limited career opportunities for young talent seems essential for long-term stability of the program. Involvement of young staff (PhD candidates and post-docs) in the program's planning could be improved.
- The program needs to find a balance between its regional and national collaborations and try to become more visible and active in international research networks. The group's broad disciplinary composition is a strength, At the same time, this diversity requires careful coordination to ensure that scientific quality remains high and consistent across all domains and integration between disciplines is reached.
- It should be clearer how the different disciplines are integrated.
- An inherent weakness may be the focus on a single lifestyle factor, and mainly from a physiological standpoint. It may be advisable to broaden the approach to more aspects of lifestyle, or consequences of it.

47 3D biology and disease mechanisms

The step from experimental research in the lab to clinical application in the patient fails often. The reasons are diverse, including unexpected lack of efficacy in patient subsets, or adverse effects. This research program develops three-dimensional cultures which predict cell behavior at the tissue level but also at the organ level, so interventions can be found that are less prone to failure.

47.1 Mission, vision and strategy

The program aims to enhance the fundamental understanding of single-cell function and multicellular integration in health and disease. Rather than focusing on a specific disease, the program uses an orthogonal approach and connects mechanisms with relevant disease models, with overarching aims to build and integrate advanced imaging and reporter technologies for monitoring cell function in 3D tissues. These aims include identification of molecular mechanisms of cell and tissue organization under homeostatic and pathological conditions, with state-of-the-art 3D model systems, and interrogation of these models by testing clinically relevant mechanisms and targets, with molecular and genetic interference technologies across disease types in vitro and in vivo.

The program integrates 3D organotypic culture systems and preclinical animal models as well as mines databases from human samples to identify molecular targets and develop approaches for intervention and strategies of drug delivery. Examples of disease types include cancer and tumor immunology, organ fibrosis, kidney failure, muscular dystrophy, malaria and other infections, and ocular disorders.

47.2 Research quality

The program presents well-defined scientific aims and a clear overarching goal: to advance the fundamental understanding of single-cell function and multicellular integration in health and disease. Rather than focusing on a specific disease area, the program develops and applies an innovative technological and conceptual platform that integrates advanced 3D biology models with cutting-edge imaging, molecular, and single-cell analysis technologies.

The program has produced internationally highly recognized and scientifically influential work, positioning itself among the global leaders in integrative cell and tissue biology. Its distinctive strength lies in the convergence of advanced imaging innovation and disease-relevant multicellular models, establishing mechanistic links between fundamental cell behavior and translational outcomes. Over the past six years, the unit has achieved major conceptual and methodological advances, integrating 3D model systems, advanced microscopy, molecular reporters, and single-cell omics to elucidate mechanisms underlying cell behavior, tissue dynamics, and disease progression. Key discoveries include identification of sublethal damage as a mechanism for cytotoxic T-cell efficacy; insights into collective cancer invasion and therapy resistance; discovery of mitochondrial-derived vesicles governing cell fate; elucidation of mechanochemical principles of calcification; and new understanding of renal ion transport and epigenetic regulation during aging and disease.

These findings have led to high-impact publications in leading journals, confirming the program's scientific quality, originality, and influence. The program is a powerhouse of advanced 3D biology, uniting organotypic culture systems, multi-photon and cryo-correlative microscopy, single-cell omics, and in silico modeling. Breakthroughs in three- and four-photon microscopy, cryo-correlative electron microscopy, and bioengineered hydrogel systems illustrate technological leadership. The translation into a commercial spin-off (SBMatrices BV) exemplifies effective bench-to-product innovation.

Members have received ERC Advanced and Starting Grants, NWO-Zwaartekracht grants, and NIH-U54 collaborations, highlighting sustained success in highly competitive funding environments. Program

members contribute to international methodological standards and have been recognized with prestigious awards.
The program exemplifies collaborative interdisciplinarity, merging expertise from physics, chemistry, biology, clinical medicine, and computational sciences. Dual appointments between Radboud Science and Radboudumc facilitate close integration of basic and clinical research.

47.3 Societal relevance

The program demonstrates excellent societal relevance by translating fundamental discoveries in cell and tissue biology into clinical, industrial, and educational impact. Its research addresses pressing biomedical challenges across cancer, fibrosis, kidney and muscle disease, ocular disorders, and infection, bridging fundamental science with therapeutic innovation. The program has delivered concrete applications with direct societal benefit, such as the development of tumoroid-based approaches for salivary gland cancer and drug repositioning of anti-malarial and anti-diabetic compounds, as well as alternatives to animal models (synthetic PIC hydrogels).

The program strengthens the Netherlands' biomedical infrastructure through partnerships with SB Matrices BV, Genmab, Zeiss, Thermo Fisher, Evonik, and MDxHealth, and through contributions to national platforms such as NL-BioImaging and NEMI. By bridging fundamental biology and industrial application, the program generates economic value while fostering technology transfer and knowledge-based innovation.

Education and training are deeply embedded within the program. Leaders coordinate interdisciplinary teaching across bachelor, master, and PhD programs, covering molecular imaging, tissue culture, and translational biology. The program interacts with patient organizations (e.g., Hematon, Hipofam, NVN), participates in public science communication, and conducts outreach through museum exhibitions and educational platforms such as the ERC-funded EyeFun program.

The program's focus on predictive, human-relevant models addresses a core bottleneck in medicine: why promising interventions in vitro or in animal models often fail in patients. This positions the program to complement human challenge model initiatives, providing platforms to test the translational validity of mechanistic insights and improve predictive power in biomedical research.

47.4 Viability

The program demonstrates high viability for the next six years, underpinned by a robust strategy that aligns with evolving scientific and societal needs. Its forward-looking aims remain highly relevant as biomedical research increasingly emphasizes personalized and translational approaches. Program leadership exhibits strong foresight, integrating emerging technologies such as artificial intelligence, advanced biomaterials, and collaborative clinical research into core methodologies. This strategic orientation is complemented by consistent success in securing external funding Continuous investment in talent development, structured strategic retreats, and cross-institutional collaborations reflect proactive management and adaptability to evolving scientific, technological, and societal challenges.

The program includes multidisciplinary teams encompassing biology, chemistry, physics, medicine, and AI supported by state-of-the-art platforms such as NL-BioImaging, NEMI, and RTC Microscopy. These infrastructures provide continuity, technical excellence, and access to advanced imaging and analysis capabilities.

The unit maintains a critical mass of expertise, with 10+ research groups comprising 5–15 members each, fostering a rich intellectual ecosystem and strong collaborative culture. Regular cross-program seminars, joint supervision, and shared PhD training enhance cohesion and knowledge exchange.

47.5 Future outlook and challenges

The future outlook for the 3D Biology and Disease Mechanisms program is highly promising, built on a robust strategy that integrates advanced 3D culture models, high-resolution imaging, multi-omics approaches, and interdisciplinary collaboration. Its mission is to bridge fundamental discovery with clinically relevant interventions positions the program to address evolving biomedical challenges in various disorders and advancing mechanistic understanding and innovative modeling.

There are also some potential risks and weaknesses. First, questions remain regarding the strategic prioritization of collaborations, particularly how resources and expertise are allocated when supporting other disease-focused programs. Balancing individual projects with cross-programmatic initiatives and ensuring adequate budgetary support for shared efforts will be key for maintaining focus and impact. Furthermore, the program is heavily dependent on critical infrastructure.

47.6 Conclusion

The program is exceptionally well-positioned to remain a driver of high-impact biomedical research with strong translational and societal value its interdisciplinary, collaborative ethos**,** combined with technological innovation and educational leadership**,** ensures continued relevance in evolving biomedical landscapes. Further opportunities are afforded by close collaboration with the highly complementary initiative in the science faculty.

47.7 Recommendations

- Validating predictive models and interventions in heterogeneous patient populations is a focal area for future improvement.
- Broad disease coverage risks diluting focus and creating overlaps with other research programs, and therefore this topic requires constant attention, and strategic planning to prevent fragmentation.
- Accelerating high-throughput imaging and single-cell omics generates massive datasets, requiring sustained investment in computational infrastructure, data integration, and responsible AI frameworks.
- Succession planning and support for early- and mid-career researchers are essential.
- Ensuring that core facilities, imaging platforms, and funding streams remain flexible, resilient, and up to date in dynamic national and international contexts is critical for ongoing viability.

48 Molecular and cellular mechanisms of development and disease

The intricate and highly regulated interactions of molecules mediate normal development and support the continued good health of individuals. Understanding the molecular processes involved is pivotal for understanding what can go wrong and how diseases develop.

48.1 Mission, vision and strategy

Radboud Institute of Molecular Life Sciences (RIMLS) was originally founded as an interfaculty institute with researchers from both Radboudumc and the Radboud University Faculty of Science (RU FNWI). In recent years, all Radboudumc research has been re-centered in the Radboudumc Institute of Medical Innovation (RIMI). RIMLS is now an institute of the Faculty of Science (RU FNWI) and contributes to Radboudumc's research mission, and for that reason, is scientifically affiliated with the RIMI. The mission of the RIMLS is to discover and explore the molecular and cellular mechanisms of development and disease. This important scientific field lies at the intersection of basic and translational research.

RIMLS is a nucleus of molecular systems biology expertise: RIMLS researchers develop and apply their technical capabilities and 'omics' infrastructure (Radboud Single-Cell Centre, advanced proteomics, next generation sequencing) in combination with computational approaches, with a view to further understanding of the molecular processes of gene regulation in medically relevant contexts. This has led to foundational insights into molecular mechanisms and to new sophisticated experimental and computational methods. Moreover, in collaboration with clinical researchers, this has contributed to new and better disease models and to improving the understanding of the molecular basis of disease.

48.2 Research quality

RIMLS does provide basic research along three pillars: molecular mechanisms in development and disease, key enabling molecular technologies and computational approaches

As RIMLS is part of the science faculty, it is an independent program that has developed independently and most likely will continue to develop independently. RIMLS is particularly interested in systems biology, addressing fundamental questions on cellular processes and gene regulation, and developing novel technologies (omics) at high depth level. RIMLS hosts 14 RGLs. The program is closely linked to the RIMI program '3D biology and disease mechanisms' and there are established collaborations between the two. The track record is impressive, with publications and highly competitive personal grants, and has shown strong technological innovation capacity, yielding insights and expertise that is of clear benefit to RIMI, such as from the single cell center. An estimated 40% of publications is done in collaboration with Radboudumc scientists. The research pillars show deep integration between experimental and computational biology, ranging from fundamental epigenetic mechanisms and single-cell proteomics to high-impact tool development (e.g. ANANSE**,** DEP**,** Seq2Science**,** UniverSC**),** which are widely adopted internationally.

48.3 Societal relevance

Discoveries in stem cell differentiation, chromatin regulation, and gene expression mechanisms have made significant contributions to our understanding of aging, cancer, immune responses, and infection. Notably, the corneal stem cell reprogramming system developed stands out for its translational relevance, offering promising therapeutic applications for vision restoration. In addition, the identification of inflammatory regulatory circuits and chromatin-based leukemia subtypes represent advances that may inform future drug development, and thereby contribute significantly to society.

RIMLS research has resulted in tangible commercial outcomes, including the establishment of two spin-off biotech companies, Lemba Therapeutics and sCellgen. Additionally, a patented proximity-labeling technology originating from RIMLS has already been licensed for commercialization. Active collaborations with industry partners such as Janssen Pharmaceuticals, 10X Genomics, and StemSights help ensure that fundamental scientific findings are effectively translated into clinical and commercial applications.

RIMLS has an important role in training the next generation of biomedical scientists, as evidenced by its coordination of two master's specializations and contributions to multiple bachelor and master programs, including Medical Biology, Molecular Life Sciences, and Molecular Mechanisms of Disease. The institute's commitment to public engagement is demonstrated through its collaborations with the NEMO Science Platform and participation in public events and charity initiatives, fostering broader societal understanding of biomedical science.

48.4 Viability

RIMLS benefits from a diverse and competitive funding base, including NWO, ZonMW, KWF, EU, CZI, NIH, and the National Growth Fund, ERC Synergy, Oncode Accelerator Growth Fund, providing a solid basis for further investments in spatial transcriptomics, single-cell proteomics, and data science. Income also is generated through provision of core facility services (proteomics, sequencing, RSCC). These high-profile grants also make the RIMLS attractive to talent.

As in several programs, concern was expressed about the ability to develop a critical mass in computational biology and the infrastructure costs and investments needed to deal with the fast-evolving high density data landscape. It was not clear whether there is sufficient core funding for these aspects, that are difficult to secure through competitive funding. An interesting and strategic move is the expansion of computational biology (via the Sector Plan Biology) and the strengthening of AI/data science links with the new Medical Data Science Master's program.

48.5 Future outlook

RIMLS sees great potential in strategic collaboration with RIMI, along with its own fundamental research agenda, which view seems fully justified. It aims to seek further strengthening with computational biology and AI integration. It has the ambition to become more visible within the Radboudumc to further cement its role as a strategic partner in translational health research. As a relatively small institute, RIMLS must actively promote its identity and impact within the larger Radboudumc and national research landscape.

The collaboration between RIMI-RIMLS is clearly beneficial for both RIMI and the Faculty of Science. The program is uniquely positioned as a bridge between basic and clinical research, fostering truly integrative biomedical discovery. There is also overlap, for instance where both RIMLS and the 3D biology research line list 2D and 3D models as assets. However, the research leaders in both programs seem aware of this and express the wish to work on complementarity.

There are some potential risks and weaknesses. First, the program needs to become more visible within Radboudumc to solidify its role as a strategic partner in translational health research. Faculties and RIMI and RIMLS should remove some current barriers that make the current collaboration sometimes administratively cumbersome. Finally, there may be too much overlap with other programs.

48.6 Conclusion

The committee considers the research quality and societal impact both as of high standard. The balance between core facility works and individual research topics is difficult to assess. Societal impact is highlighted with two start-ups and substantial teaching responsibilities. Viability is also very good, especially with two recent younger researchers joining the group. There is a clear ambition to collaborate with RIMI, particularly the 3D program.

48.7 Recommendations

- RIMLS offers basic research of high quality that offers national and international visibility. Both institutes should be keen to go on supporting the valuable collaboration. It is important to continue to strive for strong complementary activities.
- RIMLS and RIMI work on complementary topics, which is not always clear. Both institutes could try to increase visibility of RIMLS. The educational activities of RIMLS are of great interest for RIMI researchers, and the more translational aspects of RIMI could benefit from engaging with RIMLS. There is a need for more advocacy in basic research work.
- A merged program of a university faculty and a university medical center unavoidably lead to some administrative and financial hurdles. The institute's leadership should strive to minimize these.

Appendix I. Site visit – program

Research Program evaluation			
Day 1: Monday 10 November 2025			
12:15	Arrival at Huize Heyendael		
12:30	**Welcome lunch** Welcome & introduction by dean Radboudumc		
13:30	Internal Committee meeting		
14:15	**Generating insight with impact** Introduction to research programs by scientific director RIMI		
14:30	Move to program evaluation session A		
	Program evaluation parallel sessions A1, A2 and A3		
Subcom	*Alpha 1*	*Alpha 2*	*Alpha 3*
Subject	***A1: Immunity***	***A2: Imaging / Oncology***[1]	***A3: Healthcare 1***
Room	*Start: Building L, route 960, room De Wilg (M367.00.090)*	*Start: Building D, -1, NM waiting area* *End: Building C, route 738, MiTeC*	*Huize Heyendael, Cals Room*
14:40	Cellular adaptive immunity	Breast cancer	Contextual, personalized communication and care
15:30	Innate immunity in health and diseases	Thoracic oncology	Quality of life of vulnerable patients
16:20	Break	Move to next program	Break
16:40	Chronic inflammatory diseases (CID)	Non-/minimally invasive oncology	Sex -and gender-sensitive health and reproduction
17:30	Human challenge models	Advanced imaging	Value-based networked healthcare
18:20	Move to Huize Heyendael		
18:30	Internal Committee meeting		
19:00	**Walking Dinner** Welcome by Rector magnificus Radboud University		

20:30	End of dinner
20:35	Taxi to hotel

Day 2: Tuesday 11 November 2025			
8:00	Taxi to Radboudumc		
8:30	Arrival at Experience Center, *Ground Floor Entrance* & move to program evaluation session B meeting point		
	Program evaluation parallel sessions B1, B2 and B3		
Subcom	*Alpha 1*	*Alpha 2*	*Alpha 3*
Subject	***B1: Infectious diseases***	***B2: Oncology***	***B3: Healthcare 2***
Room	*Start: CDL, Onderwijsruimte (r.231-M220.01.023)* *End: Building P, Route 983, Atlas room (M604.-1.100)*	*Experience Center, Route 5, De Oversteek (M260.-1.216)*	*Experience Center, Route 5, Keizer Traianus (M260.-1.128)*
8:45	Vector-borne diseases and zoonoses	Prostate, bladder and kidney cancer	Sustainable health systems
9:35	Fungal disease	SANITY: Synergistic combinations of ablation and immunotherapy in cancer	Stimulating appropriate care and reducing low-value care
10:25	Break	Break	Break
10:55	Optimal infectious disease care and outbreak response	Cancer immunotherapy, a pan-cancer program (CI-app)	Psychology, behavior & health
11:45	Treatment optimization for mycobacterial diseases	Precision medicine in patients with solid cancer	Healthcare-related prevention
12:35	Move to Huize Heyendael		
12:50	Lunch in Huize Heyendael (committee only)		
13:45	Move to program evaluation session C		

	Program evaluation parallel sessions C1, C2 and C3		
Subcom	*Beta 1*	*Beta 2*	*Beta 3*

Subject	***C1: Rare and genetic diseases***[2]	***C2: Biomedical science***	***C3: Cardio-vascular diseases***[3]
Room	*Start: Building E, Route 828, Conference Room 2 (M320.03.042)* *End: Genome lab, route 898 -1*	*Research Tower, route 260, Zetta room (M850.00.046)*	*Start: Building A, route 644, De Waterhoen (M480.00.040)* *End: Building N, Route 968, Margarheta Vasalis (M368.01.122*
13:55	Parkinson & other movement disorders	Biomarkers for health(care)	The impacts of (pre)diabetes
14:45	Hereditary cancer	Kidney disorders	Atherosclerosis & Thrombosis
15:35	Break	Break	Break
15:55	Genomics for rare diseases	3D biology and disease mechanisms	Exercise=Medicine
16:45	Hearing & Vision for all	Molecular and cellular mechanisms of development and disease	Cerebrovascular disorders
17:35	Move to Experience center, *Ground Floor Entrance*		
17:50	Taxi to hotel		
18:45	Dinner (committee only)		

Day 3: Wednesday 12 November 2025			
8:00	Taxi to Radboudumc		
8:30	Arrival at Experience center, *Ground Floor Entrance* & move to program evaluation session D		
	Program evaluation parallel sessions D1, D2 and D3		
Subcom	*Beta 1*	*Beta 2*	*Beta 3*
Subject	***D1: Neuroscience***	***D2: Drug development***[4]	***D3: Clinical innovation***
Room	*Trigon, Kapittelweg 29, Oval Office Room (0.073)*	*Start: F Building (Amalia ziekenhuis) Route 819, pantry.* *End: F building, Route 835, De Wilde Kat (M325.04.104)*	*Dentistry building, Route 309, De Ardennen (M362.00.078A)*

8:45	The brain across development in health and disease	Treatment improvement for severe hematological diseases	Gynecologic oncology
9:35	Dementia	Therapy development for rare disorders of the brain	Supportive cancer care
10:25	Break	Break	Break
10:55	Neuromuscular disorders	Academic drug therapy development	Orofacial health
11:45	Stress and mental health	Obstetric and pediatric clinical pharmacology	Surgical innovations
12:35	Move to lunch		
12:50	Lunch at Huize Heyendael (committee only)		
13:50	Internal Committee meeting		
14:45	**Q&A Session with RIMI Directors** Opportunity for the committee to address remaining questions on the Research Programs		
15:15	Work on program reports (committee only)		
17:00	Taxi for committee members “program only”		
17:00	Core committee: preparation for institute program; align focus and questions		
18:00	Taxi to hotel for core committee		
19:00	Dinner (committee only)		

Day 4 – Thursday 13 November 2025	
8:00	Taxi to Radboudumc
8:30	Arrival at Huize Heyendael
8:30	**Introduction by Dean Radboudumc**
8:45	**Research Institute for Medical Innovation (RIMI)** Presentations on RIMI and committee interview
9:35	Short break
9:45	**Continuation: committee interview RIMI**
10:25	Internal Committee meeting
10:55	**Introduction by Dean Faculty of Science (FNWI)**

11:05	**Radboud Institute for Molecular Life Sciences (RIMLS-FNWI)** Presentation on RIMLS-FNWI and committee interview
11:45	Internal Committee meeting
12:30	**Lunch with research support staff in 5 groups:** Grant support, Clinical Research Support, Open Science, Data/IT/AI, Science communication
13:30	**Scientific Career Path** • Brief presentation on Scientific Career Path • Committee interview on Scientific Career Path • Interview with researchers in 3 groups: 2 postdocs, 2 researchers in TT1, 2 researchers in TT2, 2 research group leaders
14:30	Internal Committee meeting
14:45	**Tour of Radboudumc Technology Centers** Committee tour showcasing selected core facilities
15:45	**Graduate School and PhD Training** • Brief presentation by Graduate School management • Interview with PhD candidates in 3 groups • Internal committee meeting to formulate questions • Interview Graduate School management
17:00	Internal Committee meeting
18:00	Taxi to hotel
19:00	Dinner (committee only)

Day 5 – Friday 14 November 2025 – Institute evaluation	
8:00	Taxi to Radboudumc
8:30	Arrival at Huize Heyendael
8:30	**Research and Innovation Council** Interactive discussions with R&I Council members at 5 tables
9:15	**Patient representation in research** Dialogue with patient representatives who contributed to research in 5 groups
9:45	Break

10:00	**Research integrity** Brief presentation on research integrity and committee interview
10:30	**Q&A Session with RIBO** Final opportunity for the committee to address remaining questions
11:00	Break
11:15	Internal Committee meeting
12:30	Lunch (committee only)
13:30	Internal Committee meeting
14:00	Move to Oranjezaal (route 607)
14:15	**Concluding assembly** A gathering of the research community, featuring a presentation of the committee's interim findings, followed by informal drinks.
15:00	End of program
15:05	Taxi to hotel/train station

Appendix II. Composition of the evaluation subcommittees

In the table below, the subcommittee members of each program evaluation are shown.

TABLE 1: COMPOSITION OF EVALUATION SUBCOMMITTEES

Research group	Research program	Subcommittee members
Alpha 1: Infection & Immunity	18. Cellular Adaptive Immunity	Janna Saarela Gabriele Pradel
	19. Innate immunity in health and diseases	Janna Saarela Gabriele Pradel
	20. Chronic inflammatory diseases (CID)	Janna Saarela Jildau Bouwman
	21. Optimal infectious disease care and outbreak response	Marion Koopmans Matthijs Brouwer Coen van Hasselt
	22. Human challenge models	Matthijs Brouwer Marion Koopmans Coen van Hasselt Jildau Bouwman
	23. Vector-borne diseases and zoonoses	Gabriele Pradel Marion Koopmans Matthijs Brouwer Coen van Hasselt
	24. Fungal disease	Marion Koopmans Coen van Hasselt Jildau Bouwman
	25. Treatment optimization for mycobacterial diseases	Coen van Hasselt Matthijs Brouwer Jildau Bouwman
Alpha 2: Oncology	10. Breast Cancer	Irene Hernandez Giron Jacques Neefjes Susann Schweiger
	11. Prostate, Bladder and Kidney Cancer	Onno Kranenburg Susann Schweiger Julian Varghese
	12. Thoracic Oncology	Janne Lehtio Irene Hernandez Giron Onno Kranenburg Julian Varghese
	14. Precision Medicine in patients with solid cancer	Janne Lehtio Susann Schweiger Julian Varghese
	15. Non-, Minimally Invasive Oncology	Irene Hernandez Giron Jacques Neefjes
	16. Cancer Immunotherapy, a pan-cancer program (CI-app)	Jacques Neefjes Onno Kranenburg Susann Schweiger
	17. SANITY, Synergistic combinations of Ablation and Immunotherapy	Jacques Neefjes Onno Kranenburg Janne Lehtio
	43. Advanced Imaging	Julian Varghese Irene Hernandez Giron Jacques Neefjes
Alpha 3: Healthcare	1. Sustainable health Systems	Maurits van Tulder Gillian Leng Gareth Veal
	2. Stimulating appropriate care and reducing low-value care	Isabelle Fabbricotti Gillian Leng

		Maurits van Tulder
	3. Value-based networked healthcare	Maurits van Tulder Isabelle Fabbricotti Gillian Leng
	4. Contextual, Personalized Communication and Care	Isabelle Fabbricotti Gareth Veal Nic van der Wee
	5. Psychology, Behaviour & Health	Nic van der Wee Frits Rosendaal Maurits van Tulder
	6. Quality of Life of Vulnerable Patients	Isabelle Fabbricotti Frits Rosendaal Gareth Veal
	38. Sex and gender-sensitive health and reproduction	Gillian Leng Frits Rosendaal Nic van der Wee
	45. Healthcare-related prevention	Nic van der Wee Frits Rosendaal Gareth Veal
Bèta 1: Genetics & neuroscience	8. Hereditary Cancer	Jacques Neefjes Irene Hernandez Giron
	27. Dementia	Julian Varghese Mathijs Brouwer Nic van der Wee
	28. Parkinson & Other Movement Disorders	Julian Varghese Mathijs Brouwer Jacques Neefjes
	29. Neuromuscular disorders	Mathijs Brouwer Irene Hernandez Giron Jacques Neefjes
	30. Stress and Mental Health	Nic van der Wee Susann Schweiger Julian Varghese
	31. The Brain across Development in Health and Disease	Susann Schweiger Mathijs Brouwer Julian Varghese Nic van der Wee
	33. Hearing & vision for all, from diagnosis to treatment	Irene Hernandez Giron Susann Schweiger
	36. Genomics for rare disease	Susann Schweiger Jacques Neefjes
Bèta 2: Fundamental & drug development	13. Treatment improvement for severe hematological diseases	Gareth Veal Janne Lehtiö Janna Saarela
	32. Therapy development for rare disorders of the brain	Coen van Hasselt Gareth Veal Gabriele Pradel
	34. Academic drug therapy development	Coen van Hasselt Gareth Veal Janne Lehtiö
	35. Biomarkers for health(care)	Janne Lehtiö Gareth Veal Janna Saarela Marion Koopmans
	37. Obstetric and pediatric clinical pharmacology	Gareth Veal Coen van Hasselt Gabriele Pradel Marion Koopmans
	41. Kidney disorders	Gabriele Pradel Coen van Hasselt Janna Saarela

	47. 3D biology and disease mechanisms	Janna Saarela Gabriele Pradel Marion Koopmans
	48. Molecular and cellular mechanisms of development and disease	Marion Koopmans Janne Lehtiö Gabriele Pradel Janna Saarela
Bèta 3: Cardiovascular & clinical innovation	7. Supportive Cancer Care Research	Maurits van Tulder Isabelle Fabbricotti Gillian Leng
	9. Gynecologic Oncology	Onno Kranenburg Jildau Bouwman Frits Rosendaal
	26. Cerebrovascular disorders	Gillian Leng Isabelle Fabbricotti Frits Rosendaal
	39. Atherosclerosis & Thrombosis	Gillian Leng Frits Rosendaal Maurits van Tulder
	40. The impacts of (pre)diabetes	Jildau Bouwman Frits Rosendaal Maurits van Tulder
	42. Orofacial Health	Onno Kranenburg Isabelle Fabbricotti Maurits van Tulder
	44. Surgical Innovations	Jildau Bouwman Onno Kranenburg Gillian Leng
	46. Exercise = Medicine	Maurits van Tulder Isabelle Fabbricotti Onno Kranenburg

Appendix III. Proposed selection criteria for top-programs

To identify the top programs, the committee evaluates their quality based on the following criteria. Given that the programs have only just begun to operate, the committee is asked to focus on forward-looking plans (strategy), but to consider also past performance as an important predictor of future success. Assessing grant proposals for a large-scale project may require a similar perspective and approach.

1. **Research quality (33% weight):** The research quality of the program is assessed in its international and national context. The evaluation committee does this by assessing a research program in the light of its own goals and strategy. Contributions to the body of scientific knowledge are central to this evaluation. The evaluation committee considers the quality of the research and the academic reputation and leadership in the field. The committee's evaluation is based on a narrative argument and is supported by evidence of the program's scientific achievements in the context of the national or international research field. The protocol explicitly follows the guidelines of the San Francisco Declaration on Research Assessment (DORA).
    - The research program includes researchers with a strong international reputation. These influential and innovative researchers can make very important and innovative contributions to the development of their discipline or disciplines.
    - The composition of the program at the group and individual level and the expertise present are well suited to carry out the proposed research program.
    - The program leaders (RGLs) have demonstrated their ability to lead and inspire teams and partnerships and together form a well-balanced team.
    - The members of the program devote a great deal of attention to developing a new generation of research leaders who can keep excellent and innovative lines of research at the forefront., The members of the program form an optimally composed consortium that is focused on the content and implementation of the proposed research strategy.
    - The research program is highly challenging and urgent and focuses on specific innovations and challenges in the scientific field concerned. It is excellent, well positioned internationally and clearly visible. It belongs to the world elite or has the clear potential to do so.
    - The research program is focused, has optimal scientific coherence, and integrates all perspectives relevant to the main research questions. The scientific potential of the entire program clearly exceeds the sum of its parts.
    - The program is outstanding in terms of theoretical and methodological soundness, planning, and execution. It will be assessed whether the scientific objectives of the program and the required size of the program are appropriate in relation to the intrinsic needs of these objectives.
2. **Societal impact (33% weight):** The societal relevance of the program's research is assessed in terms of its impact on health and healthcare. This impact often takes time to become apparent. Thus, an impact that has become apparent in the last six years may well be due to research conducted by program members long before that time. The evaluation committee reflects on societal relevance by evaluating the achievements and plans (strategy, impact pathway) of a research program in the light of its own goals and strategy. The assessment is based on a narrative argument that describes the major research findings while also providing evidence of societal relevance in terms of impact on health and health care. Societal impact can be broadly defined as any change in health and healthcare that is (partly) the result of the knowledge, products and skills generated by the proposed research program. Impact can be

caused by innovative products or services, but it can also be instrumental (e.g. changes to guidelines, policies, behavior etc.), conceptual (changes to knowledge, awareness, attitude etc.), and capacity building (changes to skills and expertise).

- The research program includes researchers with a strong track record in knowledge transfer in health and healthcare. These influential and innovative researchers can make a very important and innovative contribution to the development of public health, healthcare or both.
- The composition of the program at the group and individual level and the expertise present are well suited to realize the impact pathway.
- The program leaders have demonstrated their ability to lead and inspire teams and partnerships towards societal impact.
- The members of the program devote a great deal of attention to developing a new generation of research leaders, academic clinicians or entrepreneurs who can keep excellent and innovative lines of knowledge transfer.
- The research program is highly challenging and urgent and focuses on specific innovations and challenges in health and/or healthcare. It is excellent, well positioned internationally and clearly visible. It belongs to the world elite or has the clear potential to do so.
- The research program is focused, has optimal scientific coherence, and integrates all perspectives relevant to the main impact targets. The potential of the entire program clearly exceeds the sum of its parts.
- The program is outstanding in terms of knowledge transfer, planning, and execution. It will be assessed whether the impact pathways of the program and the required size of the program are appropriate in relation to the intrinsic needs of these objectives., The program has the potential to result in a paradigm shift that has (or will likely have) consequences to health and healthcare.
- The research program has an optimal involvement of (non-academic) stakeholders at various stages to reach optimal societal impact. These stakeholders likely include patients but may involve other stakeholder groups.
- The research program has shown to be able to build public support for research and innovation or has a clear and feasible pathway how to address this as part of the impact pathway.

3. **Viability (33% weight):** The extent to which the objectives of the research program remain scientifically and societally relevant for the coming six-year period will be assessed. It is also assessed whether the goals and strategy of the program, as well as the foresight of its members, are optimal for achieving these goals. Finally, it assesses whether the plans and resources are adequate to implement this strategy. The evaluation committee also considers the viability of the research program in relation to expected developments in the field and in society, as well as the broader institutional context.
    - The research program has set ambitious and distinctive goals that appear feasible given the quality of researchers and infrastructure.
    - The strategy of the research program is clearly and logically structured and provides an excellent framework for achieving the described goal(s).
    - The impact pathway and the funding strategy have an optimal balance between ambition and feasibility, realistically reflecting the quality of researchers and research.
    - The research program provides indicators for adequate monitoring of progress and has clear ideas to adjust the program if necessary.
    - The program has adequate scientific interaction that strengthens mutual collaboration within their program, crossing borders within and beyond the Radboudumc and the academic environment in general.

Appendix IV. Provisional indicators to assess and monitor the results of the RIMI Institute

SEP utilizes indicators to gauge research performance, offering evidence-based evaluations of quality, relevance, and viability. These indicators enable continuous monitoring, support strategic planning, and enhance accountability. By providing objective measures, they help identify areas for improvement and ensure effective use of resources.

Table 1 provides an overview of the indicators the RIMI institute has identified to assess and monitor the results of the RIMI activities (Part A). **The indicators for the research programs (part B) will be less elaborated, and will not be comprehensive and quantitative, but rather encompass relevant examples supporting the narrative of the research program.** The indices in table 1 are listed in accordance with the categories of evidence suggested by the SEP:

- Research Quality: products (output, activities)
- Research Quality: use of products (outcome)
- Research Quality: marks of recognition ((short term) impact)
- Societal Relevance: products (output, activities)
- Societal Relevance: use of products (outcome)
- Societal Relevance: marks of recognition ((short term) impact)

Table 1: Examples of indicators for part A per assessment criterium.

	SEP criterium Research quality SEP aspect open	**SEP criterium Relevance to Society**	**SEP criterium Viability**	**SEP aspect academic culture SEP aspect HR policies SEP aspect PhD policy and training**
Research products: activities/ output	• Total number of a. (open access) journal articles b. Theses c. Duration of PhD projects	• Investigator-initiated clinical trials • Publications reporting new evidence improving health and healthcare • Prototypes/patents of new products or services	• Finances • Input of research staff (#/FTE) • Infrastructure and services • Risk management (ethical, security and regulatory compliance) • Environment (CO2, animals, waste) • Funding (FTE/%)	• Narratives and case studies

Use of products: outcomes of activities/ outputs	• Research citations a. Category normalized citation impact b. Percentile indicators c. Proportion of papers that remain uncited within 2 years • Careers of PhD/postdocs	• Health recommendations by public bodies • Formal clinical guidelines • Products and services on the market		• Outcomes well-being survey • Enrolment and success rate of PhD candidates
Marks of recognition: (short term)	• Peer-reviewed grants • Honors and Awards • Role in scientific panels and review board	• Societal awards and honors • Public expert role • Scaling up of health recommendations, clinical guidelines, products, and services • Exits of spin-off companies		• Narratives and case studies