Strategic Knowledge Agenda Lifestyle in Healthcare

april 2025

Coalitie
Leefstijl in de Zorg

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Foreword

The size of the group of patients in the Netherlands with lifestyle-related chronic conditions presents an increasing challenge in the face of the sparse capacity for healthcare and its rising costs. It is therefore crucial to focus on healthy lifestyle as an integral part of regular healthcare for people with a health complaint, disorder or disease in order to promote the overall health and wellbeing of the chronically ill, and to make healthcare sustainable and effective. The Lifestyle in Healthcare Coalition (Coalitie Leefstijl in de Zorg) follows up on the agreement in the Integral Healthcare Agreement (IZA)[1] to increase the commitment to healthy lifestyle by healthcare professionals and patients and to reduce (knowledge) fragmentation in the field.

We present in this document the Lifestyle in Healthcare Strategic Knowledge Agenda, prepared by the Research team of the Lifestyle Coalition in Healthcare comprising around 80 scientific experts spread across 28 Dutch knowledge institutions. The team's objective was to draw up a strategic knowledge agenda that identifies which knowledge is currently missing and which is essential for increasing and broadening the potential of lifestyle interventions in the treatment of lifestyle-related disorders (including cancer, obesity and dementia) in or through healthcare. The Strategic Knowledge Agenda therefore represents a broadly supported vision of themes in which investments should be made in the coming years to boost the integration of lifestyle in healthcare. An answer to the knowledge questions presented in this document will contribute to (1) better health and higher quality of life for patients, (2) support for policy aimed at the deployment of lifestyle in healthcare, (3) support for healthcare providers with regard to how to embed lifestyle to a greater degree and more effectively in their healthcare provision and (4) providing direction for new research programmes to improve the integration of lifestyle in healthcare.

The Strategic Knowledge Agenda is divided into four topics: sustainable behavioural change, implementation, biological mechanisms and health data infrastructure. Expert teams have been working on each of the topics and the results are presented in separate chapters. It is abundantly clear that the complexity of the challenges in the field calls for a pooling of knowledge and expertise that transcends the four topics. Commitment to answering these knowledge questions in the short term is crucial for further implementation of lifestyle in healthcare. We therefore call on parties to contribute to and co-invest in answering these knowledge questions.

Professor Stef Kremers, professor of Health Promotion and board member of Maastricht UMC+
Chairman of the Research Core Team of the Lifestyle in Healthcare Coalition

1 Integral Care Agreement: 'Samen werken aan gezonde zorg' | Report | Rijksoverheid.nl

Introduction

The Dutch healthcare system faces major challenges. The demand for healthcare is growing steadily and the number of people with chronic disorders is increasing, as are the socio-economic health disparities. The labour market is tight; healthcare spending is increasing. The societal mission to make healthcare people-centred and sustainable is increasingly high and urgent on the agenda.

Prevention and healthy living

Prevention through healthy lifestyles is a commonly cited solution to these healthcare challenges. 'Lifestyle' refers to behaviour for which a relationship with good health or with health problems has been established. It includes the totality of nutrition, exercise, relaxation, sleep, reduction of exposure to toxic substances (e.g. stimulants) and related psychosocial and environmental factors. There is growing evidence that lifestyle, influenced by our environment, plays a crucial role in the development and continuation of health problems. More than half of adults in the Netherlands, over 10 million people, have one or more mostly chronic diseases[2], many of which are lifestyle-related, and more than half of the adult population is overweight, putting them at increased risk of developing symptoms and diseases[3]. Many health issues can be traced back to deep-rooted social problems, such as poverty, inequality in education and income, loneliness and the design of our living environment. Although these problems arise outside the healthcare sector, they manifest themselves through health complaints, among other things, so the healthcare sector is expected to play a role in solving them.

Lifestyle in Healthcare Coalition

The Lifestyle in Healthcare Coalition is committed to increasing the commitment to healthy lifestyle by healthcare professionals and patients and reducing (knowledge) fragmentation in the field. The Lifestyle in Healthcare Coalition focuses on indicated and healthcare-related prevention within or from the healthcare system. Indicated prevention focuses specifically on people with incipient symptoms or with an increased risk of developing disorders (e.g. overweight people) to prevent them from worsening into a full-blown disorder. Indicated prevention can also serve as a form of primary prevention for other conditions. Also, these patients themselves can act as role models in their communities and thus

2 Source: Chronische aandoeningen en multimorbiditeit | Leeftijd en geslacht | Volksgezondheid en Zorg (vzinfo.nl)
3 Source: Overgewicht: volwassenen | De Staat van Volksgezondheid en Zorg (staatvenz.nl). Data are based on Health Survey/ Lifestyle Monitor, Statistics Nethetlands (Health survey from 2014 (cbs.nl) i.c.w. RIVM (Opbouw van de leefstijlmonitor | RIVM)

contribute to promoting primary prevention. Healthcare-related prevention focuses on people who are already experiencing illness or a condition and focuses on preventing complications, impairments, lower quality of life and mortality[4].

Research urgently needed

The agreements in the IZA and the high level of ambition of the Lifestyle in Healthcare Coalition show a high sense of urgency to keep healthcare humanised and affordable. Attention to lifestyle is in line with the shift in focus within healthcare towards health (rather than illness) and personal control.
Besides improving both physical and mental health, it is also important to pay attention to broad health indicators. Here, the focus is less on the absence of disease and more on promoting resilience, functioning and self-direction (participation). Patients themselves can give direction to their health by paying attention to exercise, healthy diet, relaxation and reducing the use of stimulants. There is ample evidence of health benefits, but there are also important knowledge gaps that need to be addressed with high priority in order to optimise lifestyle as an integral part of healthcare.

Strategic Knowledge Agenda ambition

The Strategic Knowledge Agenda 'Lifestyle in Healthcare' provides insight into current knowledge gaps and helps prioritise knowledge development. The agenda supports policy aimed at making healthy lifestyle an integral part of regular healthcare for people with a health complaint, disorder or disease and at making healthcare sustainable and effective. The Knowledge Agenda also gives direction to new research programmes and is an appeal to healthcare providers to give lifestyle (more) attention in practice.

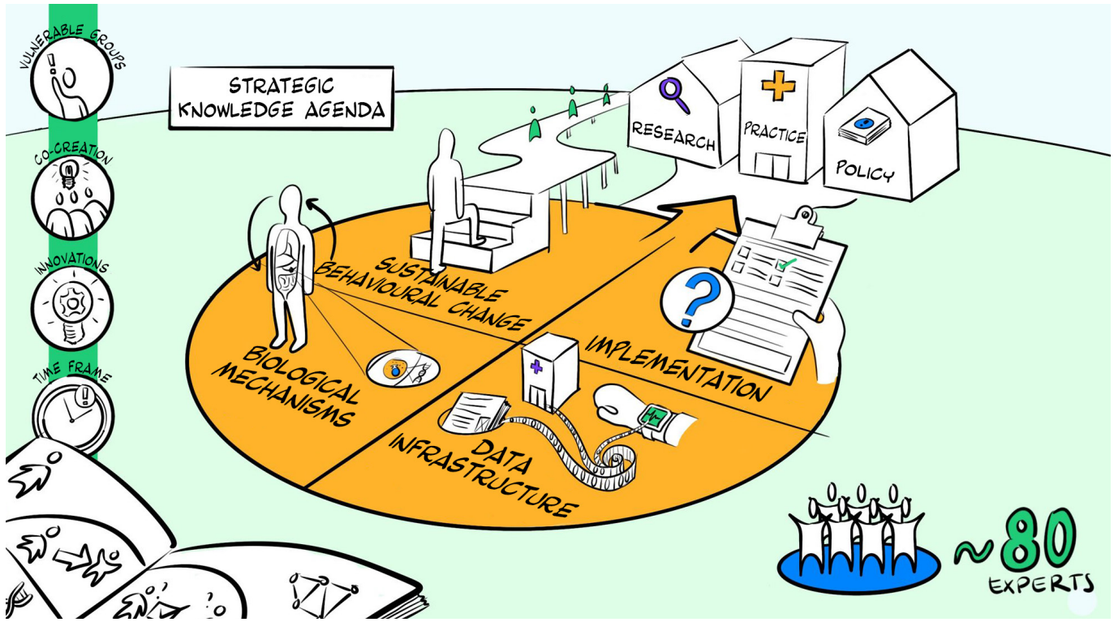
In line with the coalition agreement of the Rutte IV cabinet, the focus of this knowledge agenda is on chronic (physical and mental) diseases with a strong lifestyle component: cancer, obesity and dementia. Mindful of the discussions in the various expert sessions, the focus has been broadened to lifestyle-related comorbidities in these chronic diseases (e.g. cardiometabolic complications in obesity).

4 NFU paper preventie, wat is het?' June 2022

Creation of the Strategic Knowledge Agenda

This knowledge agenda was prepared by the Research team, one of the teams within the Lifestyle in Healthcare Coalition. In preparation for the Lifestyle in Healthcare Strategic Knowledge Agenda, knowledge questions and points of interest were inventoried from more than 100 existing knowledge agendas (period: 2015 - September 2023), selected for their focus on (aspects of) lifestyle. Parallel to the inventory of existing knowledge agendas, leading experts from the field were invited to the Research team as expert members to identify knowledge gaps from existing knowledge and already ongoing research. They made their contributions in several expert sessions per topic, in in-depth interviews, and in written feedback rounds (see appendix 1). The input obtained was processed into a set of knowledge questions related to **four topics**:

1) **Sustainable behavioural change**
   Promoting longer-term healthy behaviour.
2) **Implementation**
   Optimising the evaluation of implementation and effectiveness of lifestyle interventions.
3) **Biological mechanisms**
   Better understanding of the effects of lifestyle interventions on disease activity and quality of life.
4) **Health data infrastructure**
   Accessible data through an optimal health data infrastructure for citizens, healthcare professionals, researchers, municipalities and health insurers for monitoring and evaluation.



Topic – transcending issues

In addition to the knowledge questions per topic, topic-transcending issues and opportunities for improvement were formulated for future research in the field of lifestyle in healthcare in collaboration with the experts. In particular, this concerns the following issues:

(a) **Addressing vulnerable groups**
This knowledge agenda calls explicit attention to target group-specific research, focusing particularly on people in a socially vulnerable position (including people in a lower socio-economic position or people with a migration background). An important ambition of this knowledge agenda is to stimulate knowledge generation on what works among people in socially vulnerable positions and the development of interventions that reduce health inequalities.

(b) **Co-creation**
It is recommended to involve all end-users, including healthcare providers, patients and citizens, in the design process of a lifestyle intervention in healthcare, preferably in a form of co-creation. Such an approach helps ensure that the intervention is feasible for patients/citizens and matches their goals and priorities. Healthcare providers can properly assess whether the intervention can be implemented in current healthcare practice. It is desirable to properly document and, if possible, evaluate the method of approach to co-creation.

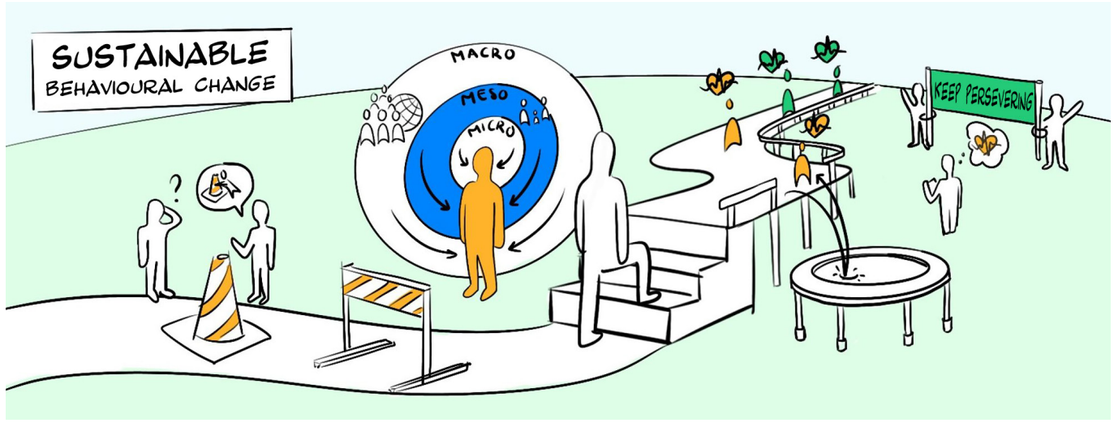
(c) **Strategic Knowledge Agenda timeframe**
This knowledge agenda highlights recommended research for the coming years. For the optimal application of lifestyle in healthcare, scientific research is also needed (e.g. intervention effects after five years).

(d) **Best practices outside the Netherlands**
It is important to learn from best practices and successful case studies from abroad regarding the use of lifestyle in the healthcare of people with physical or mental health complaints, conditions or diseases. When conducting research on knowledge questions in this agenda, one should look at (cooperation) strategies adopted abroad that have proved successful and how they can be implemented in the Dutch healthcare system.

(e) **Innovations**
Where feasible and appropriate, it is advisable to integrate innovative approaches such as artificial intelligence, integrative approaches to health, eHealth applications, blended healthcare, real world data use, etc. into future research. These approaches can contribute to the efficiency, accuracy and depth of lifestyle-related research.

Sustainable behavioural change

Behavioural change is key to effective lifestyle interventions in healthcare. This concerns not only behavioural change by the patient themselves, but also by people in their environment, healthcare providers, healthcare policymakers and professionals in the public domain who must provide the conditions and guidance to enable healthy behaviour. Although much is already known about effective strategies for the initiation of healthy behaviour and short-term behaviour change, investment in systematic research on sustainable behavioural change[5] is crucial. The three themes central to this are elaborated below.



5 Sustainable behaviour change refers to the process by which individuals or groups change their behaviour structurally and in the long term. Much of the existing research focuses on short-term (<1 year) changes.

Theme 1. Theoretical underpinnings of behaviour and behavioural interventions[6]

Behavioural science research has already produced a lot of knowledge about the factors that influence behaviour and behavioural change (so-called determinants). These lie both in the person themself and in their social and physical environment. In addition, much is already known about the effective elements of behavioural interventions in the short and medium term (e.g. Greaves et al., 2011[7]; Samdal et al., 2017[8]). Sustaining healthy behaviour for a long period of time requires abandoning existing behavioural patterns and forming new, healthy behavioural patterns. This may require a different approach, which acts on different determinants and uses different strategies. Knowledge about this is still limited. Systematic theory-driven research on determinants of and effective strategies for sustainable behavioural change, specifically in patients, is therefore crucial. In particular, this research should focus on answering the knowledge questions below.

A. Strategies to promote sustainable behavioural change

Knowledge questions:

1) What biopsychosocial[9] and contextual[10] factors increase the likelihood of sustained behavioural change?
2) What are the most effective interventions for sustainable behavioural change? And how do these differ from interventions aimed at short-term behavioural change?
3) To what extent are behavioural interventions effective for sustainable behavioural change in the general population also suitable for patients? What adaptations are needed to enable the application of effective interventions to patients?
4) How can the most effective interventions for sustainable behavioural change be integrated into practicable interventions in healthcare?

B. Monitoring and prevention of relapse

Knowledge questions:

5) What group-level biopsychosocial and contextual factors increase the likelihood of relapse into unhealthy behaviour?
6) How can the risk of relapse into unhealthy behaviour be reliably identified at the individual level so that proactive support can be provided to prevent relapse?
7) What interventions are effective in supporting the patient with (the risk of) relapse into unhealthy behaviour?

6 Behavioural interventions include interventions to promote healthy lifestyles and self-management.
7 Greaves, CJ, et al, BMC Public Health (2011). DOI: 10.1186/1471-2458-11-119.
8 Samdal GB, et al, Int J Behav Nutr Phys Act (2017). DOI: 10.1186/s12966-017-0494-y.
9 Biopsychosocial: consideration of biomedical, psychological and social factors.
10 Context: physical, sociocultural, economic and political (incl. laws and regulations) environment.

Theme 2. Strategies to promote the implementation of behavioural interventions

Several characteristics of the intervention, the user, the organisation and the environment influence the adoption, implementation and institutionalisation of behavioural interventions[11]. Examples include the extent to which patient and healthcare provider perceive that the intervention adds value compared to regular healthcare, the perceived workload of healthcare providers and their skills for implementation, and the funding of preventive behavioural interventions in healthcare. To promote the implementation of behavioural interventions in healthcare, it is important to remove barriers and design the healthcare system in such a way that it actually facilitates and encourages implementation. More knowledge is needed on how this should be organised. Knowledge questions at the patient and healthcare provider level are described below. The interactions between (characteristics of) the patient, healthcare provider, and the context in which implementation takes place are discussed under theme 3.

A. Patient

Knowledge questions:

8) What biopsychosocial and contextual characteristics of patients promote or hinder the use[12] of behavioural interventions?
9) What characteristics of behavioural interventions promote or hinder the use of the interventions by patients?
10) What strategies can be used to promote patients' use of behavioural interventions?

B. Healthcare provider

Knowledge questions:

11) What psychosocial and contextual characteristics of healthcare providers promote or hinder the use of behavioural interventions?
12) What characteristics of behavioural interventions promote or hinder the application of the interventions by healthcare providers?
13) What strategies can be employed to increase usage (adoption, implementation and institutionalisation) of behavioural interventions by healthcare providers?
14) What do healthcare providers and professionals in the public domain (prevention, social domain, education, sport, etc.) need to effectively collaborate on sustainable behavioural change in patients?

11 Fleuren MA, et al, Int J Qual Health Care (2014). DOI: 10.1093/intqhc/mzu060.
12 'Use' refers to patient acceptance and correct use of behavioural interventions.

Theme 3. A holistic view of behaviour and environment: the systems approach

In recent years, the need for a systems perspective has been increasingly advocated in both research, policy and practice around behavioural interventions. The premise is that the individual factors involved in sustainable behavioural change influence each other. To understand that behaviour, these factors need to be studied in context. And to change that behaviour, interventions should preferably focus on several of these factors simultaneously. Therefore, the individual should be studied in their whole context (so-called systems thinking). To successfully and sustainably implement behavioural interventions in healthcare, more insight is needed into the interactions between different factors at micro (individual), meso (groups of people) and macro (society) levels. For instance, behavioural change by patients may also require adjustments within the patients' family or social environment (e.g. the use of informal healthcare), and the use of interventions by healthcare providers influences the way of working within the organisation. Applying a systems approach in research on sustainable behavioural change aims to identify the complexity of this everyday reality, and to gain insight into how to change it. The knowledge questions below are central to this.

Knowledge questions:

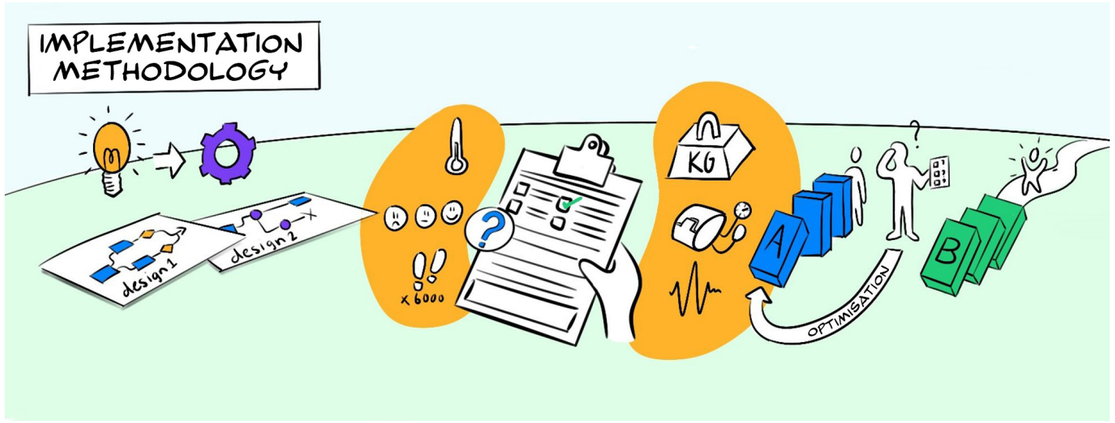
15) How do factors in the patient's physical, social, economic and political environment influence sustainable behavioural change, and how does that change affect the patient's environment?
16) What are the implications of the interactions mentioned in knowledge question 15 for the deployment of behavioural interventions in patients?
17) How can collaboration between the medical and social domains be encouraged and embedded for sustainable behavioural change?

Attention to target group differentiation and a personalised approach

When answering the knowledge questions, the importance of target group differentiation and a personalised approach should be kept in mind. Not everyone possesses the same level of capacities and capabilities to sustainably change their own health behaviour. Moreover, an approach that works for one person may not work as well for another. Personal and disease-related factors (e.g. the patient's health literacy, the type and stage of the condition), as well as contextual factors (such as a patient's home situation), help determine what is an appropriate intervention. Research on the efficacy of target group-specific and personalised strategies contributes to greater effectiveness of behavioural interventions in healthcare and is therefore strongly recommended.

Implementation

Research is important for the implementation of interventions[13] to lifestyle in healthcare in several ways. This topic focuses on which methods are most appropriate for evaluating the implementation or effectiveness of complex interventions to lifestyle in healthcare and which outcome measures should be investigated.



13 This includes all actions that contribute to the application of lifestyle in healthcare, from discussion in the consulting room to targeted referrals and various implementation strategies, including training healthcare professionals. The interventions referred to here are thus broader than just actively offering 'lifestyle interventions', such as a GLI.

In this knowledge agenda, the emphasis is on knowledge questions aimed at research into the implementation of lifestyle in healthcare and not on the practical implementation support needed to integrate lifestyle in healthcare. A distinction is made between research into the effectiveness of interventions to lifestyle in healthcare and implementation strategies for this (implementation research). Implementation research is understood as a process-oriented and planned evaluation of the introduction of innovations and/or improvements, with the aim of ensuring that they have a structural place in professional practice and/or the functioning of the organisation (Grol & Wensing, 2006[14]). Research into lifestyle interventions and their implementation almost always falls into the category of 'complex intervention research'. Appendix 2 contains the learning points for evaluating complex interventions.

Implementation takes time and, moreover, behavioural change is people work and requires constant adjustments, including in context. This makes it extra necessary to examine current practice. This may reveal why things that, for instance, are currently in guidelines still do not take place or succeed.
To answer these knowledge questions, the advice is to work with case studies so that new methods are directly applied to relevant questions in practice.

Theme 4. Designs for implementation research

Implementation research involves knowledge questions related to the implementation process and selected implementation strategy. Research can also be part of the implementation strategy, as in the stepped wedge design[15]. The implementation process is then explicitly aimed at generating knowledge as well. Different designs fit different forms of research. For example, it is quite possible to study an implementation strategy with a control group in which the lifestyle intervention is offered (e.g. in the form of a brochure), but without the accompanying implementation strategy. Implementation research can also focus on aspects of the implementation process, such as gauging change readiness in organisations and the value of such a concept.

Knowledge questions:

18) Which designs lend themselves best to guiding the implementation process towards lifestyle interventions in healthcare over a longer period, with short-cycle monitoring and possible adjustments in the interim?
19) Which designs lend themselves best to recruiting people in a socially vulnerable position (e.g. lower socio-economic position, migration background), and how do you prevent the informed-consent procedure from scaring people away?

14 Grol R, Wensing M (2006). Implementatie; effectieve verbetering van de patiëntenzorg . Maarssen, Elsevier, ISBN 9789035228528.
15 A special form of randomised trial in which a group-level intervention is introduced.

20) How can field labs play a role in (exploring) the implementation of lifestyle interventions? What context factors influence the effectiveness of an implementation programme and thus determine the generalisability of knowledge from implementation research?
21) How do you research the behaviour of healthcare professionals and other stakeholders in such a way that socially desirable answers are avoided and that the results provide real insight into the how and why of professional actions regarding the implementation of lifestyle in healthcare?

Theme 5. Designs for effectiveness research

The gold standard for demonstrating the effectiveness of an intervention in healthcare is a randomised controlled trial (RCT). The question is whether an RCT for lifestyle in healthcare is the most appropriate design. For interventions to promote lifestyle in healthcare, an RCT can also provide insight into effectiveness within a controlled setting. Using an RCT for lifestyle interventions has some specific challenges, such as: limited accessibility for people in a socially vulnerable position, limited generalisability to real-life settings due to differences in context, and heterogeneity in the control condition. There are alternatives and modifications to the RCT that reduce some of the above limitations of the RCT and contribute to better generalisability. Alternative designs[16] can also promote flexibility, as interventions or practices can be adjusted and improved during the study. It is recommended to include a process evaluation to gain early insight into why something does or does not work and the possibility to make adjustments. In addition, there is a need for suitable designs for research into complex conditions, including multimorbidity. This is because existing healthcare programmes for this target group often focus on a specific condition, while integrating multiple lifestyle and healthcare elements into the intervention could be considered.

Knowledge questions:

22) Which designs are suitable for evaluating the effectiveness of lifestyle interventions in healthcare and what are the strengths, weaknesses, opportunities and threats (SWOT) of a design in terms of methodological thoroughness, practical relevance to healthcare, and the feasibility of an intervention? How can these designs take into account complex conditions, such as the case of multimorbidity?
23) In the context of rapid implementation of lifestyle in healthcare, long-term studies are obviously not a useful tool. What are early indicators of the long-term effect of a lifestyle intervention and how can these be included as much as possible in effectiveness studies?

16 For example: trial within cohort study (TWICS) or quasi-RCT with, for example, historical controls. Alternative designs can also be drawn from other sciences (e.g. social sciences, health economics). Examples include a trial of intervention principles, leaving room for continuous quality improvement of the intervention (Mohr DC, et al., J Med Internet Res. (2015). DOI: 10.2196/jmir.4391).

Theme 6. Outcome measures for effectiveness and implementation research

When choosing a study design and outcome measures, consensus among involved parties (healthcare providers, policymakers, patients, insurers, etc.) should be sought. This happens in the Healthcare Evaluation and Appropriate Use (Zorg Evaluatie en Gepast Gebruik, ZE&GG) programme and in a Health Technology Assessment (HTA): people agree in advance on the evidence base of the subsequent outcomes of the study. In other words, it makes sense to ask what evidence the stakeholders, including insurers, need for broad implementation of an intervention.

The choice of an outcome measure depends on the purpose of the study. So, the question is really: for whom should the outcomes be relevant and what practical consequences do the outcomes have? In a specific context, this may itself be a knowledge question. For example, for the implementation of lifestyle interventions in healthcare, it can be particularly relevant to investigate what information healthcare providers need to do more with lifestyle, or what is the deciding factor for a patient to actively engage in a lifestyle intervention.

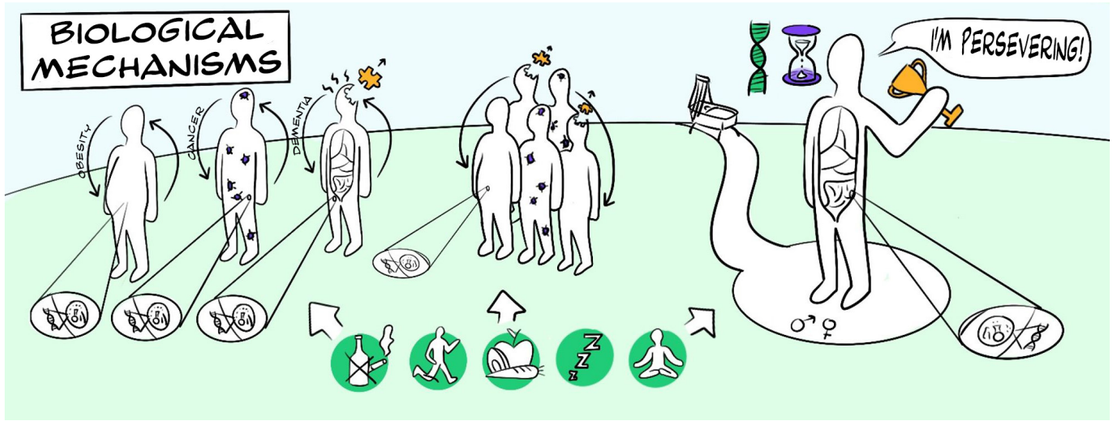
Knowledge questions:

24) What are the priorities of stakeholders (healthcare providers, policymakers, patients, insurers, etc.) when it comes to outcome measures for effectiveness and implementation?
25) How can the (direct) effects of implementation activities on professional actions or healthcare processes be validly measured (acceptance, usability, use, appreciation)?
26) What criteria apply to the price of a Quality-Adjusted Life Year (QALY) for lifestyle interventions?
27) Which meso- and macro-economic outcome measures are suitable for evaluating interventions to promote lifestyle in healthcare? And to what extent can this take into account the (future) demand for healthcare personnel?
28) How can we organise research on lifestyle interventions in the Netherlands in such a way that there is a degree of comparability in the outcome measures used, including in relation to PREMS and PROMS[17], and positive health?
29) Which (intermediate) clinical and medical/biological outcome measures are important for evaluating and implementing lifestyle interventions?
30) How do we choose outcome measures such that key target groups, such as people in a socially vulnerable position, can participate?

17 Patient Reported Outcome Measures (PROMs) measure patients' perceived health and quality of life and are often collected with repeated measures (to see progression over time). Patient Reported Experience Measures (PREMs) are questionnaires mainly about the care process and how patients experience it.

Biological mechanisms behind the effects of lifestyle interventions

Understanding the biological mechanisms underlying successful lifestyle interventions can contribute to more effective and personalised deployment of these lifestyle interventions in (curative) healthcare. The expert meetings revealed that the knowledge gaps regarding these biological mechanisms of lifestyle interventions are particularly associated with an integrated approach to lifestyle interventions in specific chronic conditions and in the context of multimorbidity. Knowledge gaps also exist because the synergy between different lifestyle interventions, the influence of contextual factors (e.g. socioeconomic position), and the effects of individual characteristics (e.g. age and gender) are not yet fully understood. Moreover, knowledge on the optimal timing, frequency and dosage of lifestyle interventions is still limited. Also, the biological mechanisms involved in sustainable behavioural change and personalised lifestyle advice (what works, when, for whom) require clarification and substantiation.



Many classical interventions used in healthcare, such as drugs, are known to work mechanistically. For a variety of lifestyle interventions (exercise, foods, dietary patterns, mental interventions, sleep hygiene, etc.), some mechanistic knowledge is available for primary prevention, but mechanistic knowledge in a curative setting is still often lacking. The focus of the themes below is on elucidating the biological mechanisms that underlie the effects of lifestyle interventions on disease activity and quality of life in patients. Knowledge of these can result in the accelerated implementation of lifestyle in healthcare.

Theme 7. Generic biological mechanisms

Chronic diseases (obesity, dementia, cancer and other population diseases) are often systemic diseases, affecting multiple tissues and organs. Lifestyle interventions intervene on multiple biological systems simultaneously, potentially having beneficial effects on several (chronic) diseases. This fact is a strong argument for the use of lifestyle interventions in healthcare. Currently, quite a lot of generic biological-mechanistic knowledge is already available on various lifestyle interventions, especially in the healthy population and those at risk of chronic disease. However, this knowledge is mostly lacking for deploying lifestyle in the curative setting. In addition, a growing number of patients in healthcare suffer from two or more chronic conditions (multimorbidity), where a combination of various lifestyle approaches could be considered. However, there tends to be a lack of mechanistic knowledge on how the components of various lifestyle interventions reinforce or perhaps weaken each other.

Knowledge questions:

31) What generic biological mechanisms underlie the effectiveness of lifestyle interventions in delaying/reversing chronic diseases?
32) What biological mechanisms underlie the effectiveness of lifestyle interventions delaying, reversing, and preventing multimorbidity?
33) What biological mechanisms are involved in the interaction between different components of lifestyle interventions (e.g. exercise and nutrition)? In other words, how do different components of lifestyle interventions reinforce or hinder each other's effects?
34) What biological mechanisms are involved in the interaction between lifestyle interventions and medication? In other words, how do different components of lifestyle interventions enhance or hinder the effect of medication?
35) How do intervention-specific factors (e.g. timing, duration, frequency and intensity) affect the effectiveness of an intervention in chronic diseases, and how can we make use of this knowledge in optimising the deployment of lifestyle interventions?

Theme 8. Disease-specific biological mechanisms

Besides broad generic mechanistic questions, the issue is also explicitly addressed of which disease-specific mechanisms underlie the relationship between lifestyle and chronic diseases with a strong lifestyle component: cancer, dementia and obesity. These disease-specific biological mechanisms can thus provide a point of leverage for lifestyle interventions.

Knowledge questions:

Cancer

36) To what extent can lifestyle interventions (specifically diet/fasting, exercise, sleep and stress management) affect the risk of tumour recurrence, improvement in quality of life and/or cancer-specific mortality? What biological mechanisms explain the effects found?
37) Which lifestyle-related interventions influence the effectiveness of regular cancer(-specific) medication, and what is the biological mechanism of this?

Dementia

38) Which lifestyle intervention is best used for which form of dementia? Which biological mechanisms are involved?
39) Which lifestyle intervention is best used in which stage of dementia? Which biological mechanisms are involved?
40) Which lifestyle interventions are most appropriate in early-onset dementia (<65 years) in comparison with dementia developed later in life? What biological mechanisms play a role in different age groups?

Obesity[18]

41) Which lifestyle interventions enhance or impede the effect of obesity medication and surgery (bariatrics) and how does this work mechanistically? This should take into account the timing of the use of the lifestyle intervention and/or medication in obesity treatment (before/during/after receiving obesity medication/bariatrics).
42) Which lifestyle interventions can promote fat loss and maintain muscle mass in the long term, thereby promoting metabolic health in obesity, and what mechanisms underlie this?

18 Obesity: in this knowledge agenda, the focus is broadened to children and adults with obesity or who are overweight in combination with overweight/obesity-related comorbidities (such as cardiometabolic complications, diabetes mellitus type 2, sleep apnoea, malignancies, psycho(social) problems, etc.). This broadening in terms of disease domain is in line with the new guideline for over-weightness and obesity in adults and children: Richtlijn Overgewicht en obesitas bij volwassenen en kinderen.

Theme 9. Role of individual and contextual factors on biological mechanisms

For lifestyle interventions, context factors such as (medical) history, socio-economic position, cultural and ethnic background and living environment, but also biological variables such as age, gender, phenotypic characteristics, microbiome and (epi)genetic differences, are very important for outcomes of the lifestyle intervention(s). Studying these differences provides starting points for mechanistic insights that can be used for a more personalised offer at the individual or subgroup level.

Knowledge questions:

43) What biological mechanisms explain why lifestyle improvement causes greater health gains in some people more than in others? How do contextual factors (such as socio-economic position, cultural background) affect biological mechanisms?
44) Which individual characteristics (e.g. age, disease onset age, gender, (epi)genetic traits, phenotypic traits, microbiome) and combinations of characteristics influence the effectiveness of lifestyle interventions on chronic diseases (favourable or unfavourable)? What biological mechanisms are involved?

Theme 10. Biological mechanisms of successful sustainable behavioural change

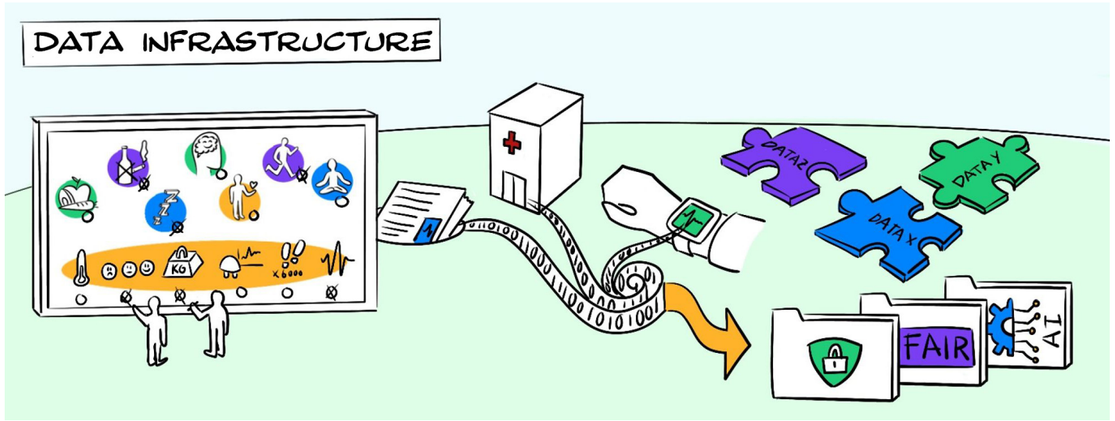
When deploying lifestyle interventions in healthcare, sustainable behavioural change is crucial (see the sustainable behavioural change topic). Much research has focused on the mechanisms behind intensive programmes (rapid weight loss, intensive training). However, for most patients, these cannot be for long. Currently, it is insufficiently known which biological mechanisms play an important role in sustainable lifestyle behavioural change. In addition, we do not yet sufficiently understand how mental lifestyle interventions (such as mindfulness and relaxation) and the classical pillars of ‘rest, cleanliness and regularity’ work and can contribute to slowing down/reversing chronic diseases. Indeed, structure in the day and a fixed rhythm of life work beneficially on a number of aspects, such as stress management, a healthy sleep rhythm and self-control for substance use. Further biological substantiation of such success factors will help to actively deploy them for lifestyle in healthcare.

Knowledge questions:

45) What is known about the biological mechanisms that enable sustainable behavioural change in lifestyle interventions?
46) In what way do different lifestyle interventions influence the (biological) reward system? And how can this reward system be effectively utilised to promote sustainable behavioural change?
47) What biological mechanisms underlie the effects of mental lifestyle interventions (such as mindfulness and relaxation)?
48) What biological mechanisms underlie the effects of lifestyle interventions aimed at bringing structure to the day?

Health data infrastructure

A good data infrastructure is the basis for (healthcare) monitoring and research into (the implementation of) lifestyle in healthcare. Besides healthcare data, data are also needed on the health, lifestyle, living environment and socio-economic conditions of diverse (target) groups. An extra effort is needed to build an infrastructure for the combined use of these diverse data and thus gain more insight into lifestyle and living environment factors. Given the many activities and rapid developments in the field of health data infrastructure, a roadmap should be drawn up to follow up on what is known about the knowledge questions, including the prioritisation and sequencing of the knowledge questions.



Stakeholders

The importance of a good data infrastructure is important for several target groups. For citizens, this is not only to make data more widely available and accessible, but also to gain insight and feedback into their own lifestyles. For healthcare professionals, this is to provide appropriate healthcare. Policymakers, the state, the province, municipalities and health insurers gain insight into the effect of policy, and researchers obtain knowledge that can in turn be translated into guidelines, advice and practice.

Existing initiatives

Data collection in the context of this Lifestyle in Healthcare Knowledge Agenda links up with various regional and national data collections and health data infrastructure initiatives. The collection and utilisation of health data is a high priority, both in healthcare and politics. Dutch initiatives such as Health-RI[19], the CumuluZ healthcare platform[20] and Population Health Data NL (PHDNL)[21] are working to collect as much reliable health data as possible and make it safely accessible for research. Organisations such as Statistics Netherlands, Nivel (primary healthcare data)[22], Dutch Hospital Data (DHD), Vektis (claims data) and various quality registration initiatives, such as the ELAN network[23], are pursuing similar goals.

Coherence and access

Lifestyle research requires (existing, already collected) healthcare data, supplemented by data collected by citizens themselves and data on the social, physical and economic environments in which citizens find themselves. eHealth, fitness apps and wearables are potential sources of additional lifestyle and health data, as are data from various prospective biobanks and cohort studies[24] (e.g. Lifelines, Helius, ERGO and the Maastricht study[25]). Self-collected data may be less reliable than biomedical data, but are of additional value due to continuous monitoring in one's own living environment. These data sources therefore represent new challenges in terms of standardisation, quality control, privacy protection and citizen trust when it comes to sharing these data. For lifestyle research in particular, it is important to be able to analyse data in context. Which data are relevant depends on the knowledge questions to be answered. The Electronic Health Data Exchange Act (Wegiz) and the European Health Data Space (EHDS) provide frameworks and create new opportunities[26]. We can learn from countries like Denmark, where a lot of health data from the Danish population is widely collected, linked and utilised for research and policy[27]. The knowledge questions below help answer the question of which health data infrastructure is desired in the Netherlands and what is needed for this.

19 www.health-ri.nl
20 www.nfu.nl/themas/data-infrastructuur/cumuluz-zorgplatform
21 www.populationhealthdata.nl
22 www.nivel.nl/zorgregistraties
23 www.live.lumc.nl/over-het-lumc/partners/partners-in-de-zorg/extramuraal-lumc-academisch-netwerk-elan
24 www.onderzoeksfaciliteiten.nl/facility/nederlands-cohort-consortium-ncc
25 www.lifelines.nl; www.heliusstudy.nl; www.ergo-onderzoek.nl; www.demaastrichtstudie.nl
26 Under the EHDS, a data licence will soon have to be applied to the Health Data Access Body (HDAB).
27 In Denmark, health data of all residents over the past 40 years are, in principle, accessible for research. The idea for the Netherlands has been articulated as 'Cohort-NL' in the Action Programme 'Nieuwe kansen voor Topsector Life Sciences & Health' and as a proposition. For the NWO GWI call, see e.g. https://www.rijksoverheid.nl/documenten/rapporten/2020/12/18/nieuwe-kansen-voor-topsector-life-sciences--health

Knowledge questions, challenges and obstacles

By analogy with the three major challenges for learning systems that Verheij identifies[28], we work here with three main themes:

1. What data are needed for scientific research on lifestyle in healthcare and monitoring of the implementation?
2. What preconditions must data and data infrastructures meet?
3. What is needed to make data suitable for research (processing, analysis, evaluation) and (healthcare) monitoring?

Theme 11. Data for scientific research on lifestyle in healthcare

Lifestyle factors are difficult to measure and are often still incompletely and selectively recorded in electronic patient records. Citizens are also increasingly collecting lifestyle data via wearables, among other things.

Knowledge questions:

49) Which lifestyle characteristics (including smoking, alcohol, drugs, exercise, sedentary behaviour, BMI, diet, sleep and stress) of patients can be monitored and compared with little effort?
50) How do we optimise the quality of these data? What methodological solutions are there to draw conclusions from incomplete datasets? How do we fund this kind of data sharing? How do we extract survey-specific data from text fields in patient records?
51) For lifestyle in particular, the context (e.g. living environment, socio-economic position and ethnicity) of patients and citizens is very important. What data (sets) are needed to acquire information on the context? And how can these best be processed and analysed?
52) What data are needed to conduct lifestyle research in a patient population in which many different conditions (multimorbidity) exist, so that the chosen intervention also does justice to this complexity?
53) What are the minimum data needed to make statements about implementation (uptake), adherence and effects of lifestyle interventions and the factors that influence them?
54) What data (and metadata[29]) for research on lifestyle and health and monitoring the implementation of lifestyle interventions in healthcare should, in principle, be available from every resident of the Netherlands regarding health, healthcare use, lifestyle, living environment, family situation and socio-economic conditions?
55) What data procedures (data sharing, question finding and shared data) are needed to use self-collected data from citizens to answer lifestyle questions, both by citizens themselves and by researchers and policymakers?

28 (1) Data are not there, (2) data should not be used, and (3) data are unsuitable for the purpose for which you want to use them. - www.tilburguniversity.edu/nl/actueel/agenda/inaugurele-rede-ra-verheij

29 Including how the data were collected and in what context.

Theme 12. Preconditions for data and data infrastructures

Preconditions are determined by the purpose of sharing data, the infrastructure and the target group. Different levels can be distinguished, such as the citizen, healthcare professional, government and population. In further developing a national data infrastructure for lifestyle in healthcare, it is important to make good agreements on data and data use from these goals and target groups. Preconditions such as privacy, reliability, coverage and the Findable, Accessible, Interoperable, Reusable (FAIR) principles contribute to data usability and public support for a data infrastructure.

Knowledge questions:

56) What minimum requirements (FAIR, ethical, legal, social, ELSI, metadata, AI readiness) must (national, regional and local) lifestyle data and infrastructures meet to be suitable for approaches such as federated learning? What adjustments in laws and regulations, governance, public trust and costs are desirable? What can we learn from both regional and national data infrastructures?
57) How do we promote trust[30] among citizens, professionals and governments in a regional and national health and lifestyle data infrastructure[31]?
58) How do we move from regional and/or thematic initiatives to a nationwide network of national health and lifestyle data infrastructure within which regional and/or thematic aspects remain secured?
59) What is needed for the actual implementation of the national (and regional) infrastructure in terms of hard infrastructure, soft infrastructure, interface/access to data, usability of data, education of healthcare professionals and education of citizens?
60) What does the process look like in terms of working with data in the field of lifestyle medicine? Different levels can be distinguished here: individual, the citizen and the healthcare provider; collective, the population. Related questions: who delivers, who benefits, how do you make it visible that working with data and registration works, what bottlenecks are there?
61) What are the strengths, weaknesses, opportunities and threats (SWOT) for a nationwide health data infrastructure (consider a concept like Cohort-NL, see footnote 27)?

30 See e.g.: www.nfu.nl/sites/default/files/2023-07/23.01421%20NFU-standpunten%20hoofdstuk%204%20EHDS%20verordening.pdf and file (patientsfederatie.nl); (https://www.patientenfederatie.nl/downloads/brieven-aan-de-kamer/1435-brief-commissiedebat-digitale-ontwikkelingen-in-de-zorg/file)

31 Health-RI and VWS are preparing a public campaign.

Theme 13. Steps to make data suitable for research

Specifically in the field of lifestyle, the availability and completeness of data are major bottlenecks. More generally, when reusing data, the context in which and the purpose for which data were originally recorded must always be taken into account. Besides completeness and correctness, the level of detail and timeliness of data are also relevant for data quality (Verheij, 2021[32], Van Veen and Verheij, 2022[33]).

Knowledge questions:

62) How do we make it easier to enable the capture, access, availability and searchability of data?
63) What methodologies (machine learning, epidemiological method, econometric method) are needed to enable data reuse and generate answers?
64) How do we motivate healthcare professionals in the first, second and third lines to carefully record all relevant data, and what aspects are important when doing so (trust, seeing benefits for own practice, technological support)?
65) How can we extract specific data for a study from self-reports and patients' own measurements (apps, devices) and what standardisation is possible/necessary for this?
66) How do we ensure that research approaches are applied to routine and self-acquired data that are sufficiently trusted, such that the results are also incorporated into guidelines?
67) How can synthetic data and digital twins be used to accelerate and enrich the research process?
68) What standardised solutions can be used to link Statistics Netherlands data, environmental data, healthcare data and other sources to answer questions about the health effects of lifestyle and living environment?
69) How do we present individual data in a way that gives the individual citizen/patient opportunities to take action (right presentation specific to the target group)? For example, how do you make the health gains visible if the individual stops smoking or starts exercising more? In other words, how do you translate the population level back to the individual level?

32 www.tilburguniversity.edu/nl/actueel/agenda/inaugurele-rede-ra-verheij
33 Van Veen EB, Verheij RA (2022). Further use of data and tissue for a learning health system: the rules and procedures in The Netherlands, compared to Denmark, England, Finland, France and Germany, MLCF/Nivel, Utrecht, ISBN 978-94-6122-816-1.

Appendix 1

Method used for creating the Strategic Knowledge Agenda

Inventory of existing knowledge agendas

In preparing the Lifestyle in Healthcare Strategic Knowledge Agenda, knowledge questions and focal points from more than 100 existing knowledge agendas (period: 2015 - September 2023) were inventoried, which were selected because of their focus on lifestyle (aspects). The knowledge agendas came predominantly, but not exclusively, from Dutch organisations. This inventory created a structured overview[34] [35] (in Dutch) that provided insight into the unanswered questions of relevant organisations. This information was used to supplement the experts' inventory of knowledge gaps (see below).

Expert consultation

In parallel with the inventory of existing knowledge agendas, over 80 leading experts from the field were invited as expert members to the Research team to identify knowledge gaps from existing knowledge and already ongoing research. They participated in several online expert sessions and feedback rounds by e-mail. In addition, a number of experts shared their views on the topics in individual interviews. For the topics Sustainable Behavioural Change, Implementation, and Health Data Infrastructure, three online expert sessions and three additional feedback rounds (by e-mail) were organised. For the topic Biological Mechanisms, two online expert sessions and three additional digital feedback rounds (by e-mail) reached consensus on the knowledge questions to be included in the knowledge agenda.

Format and results of expert session 1

The aim of the first expert session was to obtain an initial thematization of research topics and a corresponding list of relevant knowledge questions. Using two key questions (1. What is already known? 2. What knowledge is missing and is necessary to successfully implement lifestyle interventions?), existing knowledge and knowledge gaps within the main topic were discussed. Here, knowledge questions that arose from the inventory of existing knowledge agendas were also raised and discussed.

The input obtained from this expert session, supplemented by input from in-depth interviews, was processed into a first draft of knowledge questions for each topic. This first draft was shared for input with all experts within the theme, including those who could not attend the expert session. In addition, individual interviews were held with a number of experts to further deepen the themes and knowledge questions put forward.

Format and results of expert session 2

34 See https://leefstijlcoalitie.nl/publicatie/inventarisatie-van-bestaande-kennisagendas-leefstijl/
35 Okoli C, Pawlowski SD. Information & Management (2004). DOI: 10.1016/j.im.2003.11.002.

Prior to the second expert session, the knowledge questions for each topic were processed in an online questionnaire. Modelled on the so-called Delphi methodology[36], this questionnaire aimed to gauge the degree of consensus on the importance of the knowledge questions drawn up. All experts received an e-mail invitation and link to complete the questionnaire anonymously before the start of the expert session, for which use was made of the online survey tool Qualtrics (Provo, UT, USA). Experts were asked to rate all knowledge questions using six criteria (see criteria box).

The experts who had not yet completed the questionnaire at the start of the second expert session were given the opportunity to do so during the session. The data entered were then analysed and the results of this analysis were discussed in plenary. Here, the median and interquartile deviation of the assessment of the importance of the knowledge questions guided the discussion. Consensus on the importance of the knowledge questions was assumed at a high median (>= 4) and small interquartile deviation (<=1). Knowledge questions with a lower median and/or higher interquartile deviation were discussed in plenary, after which content or textual adjustments were made and/or a new rating was assigned to the knowledge questions in consultation.

Format and results of expert session 3

The input obtained from the second expert session was incorporated into a draft knowledge agenda for each topic. In addition, the core team checked for overlap between the various knowledge questions and, if necessary, knowledge questions were merged. Prior to the third expert session, the draft knowledge agenda per topic was submitted to the experts in a written feedback round.

Suggestions and adjustments were incorporated, after which the new version was discussed in the third and final expert session per topic. The aim of this session was to reach a general consensus on the content of the agenda; this concerned both the knowledge questions and the identified points of interest per topic. During this session, the final, mainly textual, changes to the agenda were discussed in plenary and general agreement on the content was obtained.

36 Linstone HA, Turoff M. (1975). The Delphi method: Techniques and applications. London, Addison-Wesley Publishing Company, ISBN 978-0201042931.

Criteria used for consensus on determining the knowledge questions:

1. **Social impact of the results of research on this knowledge question**
   (1 = very low; 5 = very high)
   In assessing this criterion, the experts were able to factor in the following aspects:
   a. The results of the research make an (in)direct concrete contribution to better patient healthcare.
   b. The results of the research make an (in)direct concrete contribution to a better quality of life for patients,
   c. Economic returns: reduces individual and social costs, promotes benefits (participation: labour, social).
2. **Urgency over time; to what extent research on this knowledge question has urgency; where to start?** (1 = very low; 5 = very high)
3. **Research success rate** (1 = very low; 5 = very high)
   In assessing this criterion, the experts were able to factor in the following aspects:
   a. Feasibility/researchability; (interim) results available < 3 years after start of research.
   b. Availability of research expertise; to what extent the research builds on existing knowledge.
4. **Implementation probability of research findings** (1 = very low; 5 = very high)
   In assessing this criterion, the experts were able to factor in the following aspects:
   a. Implementability of results
   b. Stakeholder engagement/support
5. **Scientific impact of results** (1 = very low; 5 = very high)

In addition to the above criteria, they were also asked to give an overall assessment of the importance of the knowledge question:

6. **How important do you think it is for this knowledge question to be included in the knowledge agenda?** (1 = not important; 5 = very important)

Appendix 2

Learning points from the MRC guideline on complex intervention research[37]

- Complex intervention research can take place from an effectiveness, theory and/or systems perspective, where the choice is determined by what is already known and what evidence would contribute most to the requisite knowledge.
- Complex intervention research goes beyond asking whether an intervention works in the sense of achieving the intended outcome. It is also about asking a wider range of questions (e.g. identifying what other effects the intervention has, assessing its value in relation to the resources needed to implement the intervention, theorising how the intervention works, considering the interaction with the context in which the intervention is implemented, how the intervention contributes to system change and how the evidence can be used to support real-world decision-making).
- There is a trade-off between accurate unbiased answers to limited questions and more uncertain answers to broader, more complex questions. Researchers should answer the questions that are most useful for decision-making, rather than those that can be answered with the greatest certainty.
- Complex intervention research can be seen in terms of phases, which incidentally are not necessarily sequential: development or identification of an intervention, assessment of intervention feasibility and evaluation design, evaluation of the intervention and effective implementation.
- Six key elements must be considered at each stage to be able to answer the following questions:

  (a) How does the intervention interact with the context?
  (b) What is the underlying programme theory?
  (c) How can different stakeholder perspectives be incorporated into the research?
  (d) What are the key uncertainties?
  (e) How can the intervention be refined?
  (f) From different interventions how do the required resources and outcomes compare?

The answers to these questions should be used to decide whether the study should proceed to the next phase, go back to an earlier phase, repeat a phase or stop.

37 K. Skivington et al, BMJ (2021). DOI: 10.1136/bmj.n2061

Colophon

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