mind the gap!

MULTI-STAKEHOLDER DIALOGUE FOR PRIORITY SETTING IN HEALTH RESEARCH

King Baudouin Foundation
Working together for a better society

mind the gap!

MULTI-STAKEHOLDER DIALOGUE FOR PRIORITY SETTING IN HEALTH RESEARCH

SHARING EXPERIENCES FROM 3 PILOT PROJECTS

Tuberous sclerosis complex
Return to work after long-term disability
Non-Alcoholic Steatohepatitis (fatty liver disease - NASH) and the contribution of biobanks

PREFACE

Health research agendas do not always match the needs and health priorities of patients and their relatives, or of their doctors and other caregivers. Today, researchers, academia, industry and research funders largely determine health research priorities. The specific knowledge and expertise of patients, relatives, carers and other stakeholders remain largely undervalued and underused. It is meaningful and enriching to also involve the expertise of these parties in determining the priorities for biomedical and health research: it widens the range of research themes, allows the identification of unmet needs, key uncertainties will emerge and precious research funds will be better allocated.

The practice of exchanging ideas and experiences on priorities in health research has not yet become widespread in Belgium. In a number of countries, such as the UK, France, The Netherlands, Canada, Australia/New Zealand, USA and the Scandinavian countries, this exercise has been successfully carried out on a number of occasions already[1].

The King Baudouin Foundation (KBF) organized in November 2015 a workshop for researchers, patient organizations, care providers, pharmaceutical companies and research funding bodies on the involvement of less traditional stakeholders in setting health research priorities. Various examples from other countries were presented and discussed[2].

Following this two-day workshop, KBF invited participants to propose projects on multi-stakeholder dialogues for priority setting in health research. Three pilot projects were approved for support:

- '**Research in tuberous sclerosis complex (TSC)**', initiated by Prof. Anna Jansen, UZ Brussel, and Eva Schoeters, be-TSC (see annex 1);
- '**Return to work after long-term disability**', initiated by Saskia Decuman and François Perl, RIZIV-INAMI[3] (see annex 2);
- '**Research in Non-Alcoholic Steatohepatitis (fatty liver disease-NASH) and the contribution of biobanks**', initiated by Profs. Sofie Bekaert and Hans Van Vlierberghe, UZ Gent (see annex 3).

In the three pilot dialogues, 'health research' was defined broadly: besides research on the effectiveness of medical treatments, it also includes fundamental and strategic basic research focusing on cause of disease as well as on interventions such as care, family support, diagnosis or even research on healthcare organization.

This publication sets out experiences drawn from these three pilot projects, which were very different in their content, field of research, methodological approach and results. On the other hand, they have much in common. Not only did they use a dialogue approach to search for health research priorities, they also dealt with a number of fundamental questions: who are the obvious stakeholders to be involved? What is the most appropriate way to involve them? How to make sure that the process remains inclusive so that all relevant voices are heard and their opinions are considered? How to build a comprehensive research agenda and how to prioritize this agenda?

However, it was clear from the onset that there is no standard all-embracing model to structure multi-stakeholder dialogues. Every context and every stakeholder group requires a tailor-made approach in order to achieve an optimal harvest of information and to create a wide support base for the created research agenda.

The concrete results and methodologies of each of the three pilots have been published separately (see annexes 1 to 3). Each pilot project, although being in a very different context, successfully brought together a diversity of stakeholders in search of joint uncertainties and needs, and resulted in completely new insights. In all three cases, the dialogues culminated into an encouraging, novel and widely supported research agenda.

This guide is intended, above all, to encourage readers to step aside for a moment from the well-trodden tracks of traditional research agendas and take a new and open-minded look at the opportunities and priorities that exist in biomedical and health research. Because one thing is sure: dialogue works!

WHY MULTI-STAKEHOLDER DIALOGUES IN PRIORITIZING RESEARCH AGENDAS ?

GIVING A VOICE TO SILENT PARTIES

THE USER PERSPECTIVE – Researchers, academia and industry most often determine research agendas for health and biomedical research. But to what extent do these agendas match the demands in society and the needs of the users of the research results? These users (patients, their relatives, taxpaying citizens, but also caregivers, health professionals, governmental administrations, insurers etc.) are seldom involved in setting research agendas. In the case of patients and their informal carers, however, many become experts in their health condition, as well as technical experts in self-care and in monitoring symptoms. Thus, the research system would be stronger if these hidden mines of expertise were tapped more effectively[4].

RESTORE BALANCE IN POWER DYNAMICS – Several problems underlie the current inability to make research more relevant to patients and the wider public. Most importantly, research is a power rich and hierarchical environment in which successful researchers are at the top and patients, carers, and the public are viewed as passive beneficiaries at the bottom. These power dynamics make it difficult for research ideas brought forward by patients to gain acceptance, even when they may offer greater benefit to patients' life quality and wellbeing. Secondly, research questions prioritized by patients often seem unexciting to researchers and research funders. This is further enhanced when the proposed interventions have a more generic nature, are in a context of health care organisation and/or are considered unprofitable for industry[4].

A NOVEL 'UPSTREAM' COLLABORATION – Multi-stakeholder involvement in the programming of research is one way of allowing silent but concerned parties to have a voice. It is an iterative, inclusive, participatory, multi-actor process in which stakeholders work together to prioritize research priorities. Multi-stakeholder dialogues tackle the very 'upstream' element of research, whereas many patient participation initiatives and other stakeholder engagement initiatives tend to focus on later stages[5]. The main idea of stakeholder dialogues for setting research priorities is that research should be conducted *with* the end users of the research results (i.e. the patients, carers ...) and not solely *on* them.

BENEFITS FOR ALL!

FROM EMPOWERING TO INCREASING RELEVANCE – The aims of these multi-stakeholder dialogues are to increase benefits for people and society, to enhance the efficient use of limited resources, to improve accountability and governance of public expenditure, and to harmonize applied health and fundamental biomedical research. During the November 2015 KBF workshop, the many potential benefits for different stakeholder groups were spelled out (see table 1).

INCLUSIVE AND OBJECTIVE – A recent evaluation of four highly structured public and patient engagement processes in planning research activities – the James Lind Alliance Priority Setting Partnerships (UK), Dialogue Method (Netherlands), Global Evidence Mapping (Australia), and the Deep Inclusion Method/CHoosing All Together (US) – showed they were highly successful in setting research priorities that were inclusive and objectively based, specific to the priorities of stakeholders engaged in the process. The processes were robust, strategic and successful in promoting equity in patient voices[1].

TABLE 1. POTENTIAL BENEFITS OF MULTI-STAKEHOLDER DIALOGUES FOR PRIORITIZING RESEARCH AGENDAS[2]

FOR RESEARCHERS AND THE SCIENTIFIC COMMUNITY

- increase the relevance of research
- give researchers access to new knowledge, new data, new perspectives and new horizons
- generate new research questions and research themes
- make it easier to implement findings in clinical practice
- improve the quality of research with less waste, greater feasibility, better outcomes and higher cost-effectiveness
- obtain results which are easier to communicate
- foster multi-disciplinary approaches to research
- harmonize applied clinical research and fundamental biomedical research

FOR PATIENTS, INFORMAL AND PROFESSIONAL CAREGIVERS (AND OTHER END USERS OF THE RESEARCH)

- empowerment
- meaningful inclusion and engagement
- unmet needs being identified and addressed
- inclusion of user perspectives and experiential information from the outset in research, design and development of health practices
- outcome parameters and criteria which are adapted to needs
- balance realism and hope, avoid creating false hope

FOR RESEARCH FUNDERS (GOVERNMENTAL, INDUSTRIAL, PHILANTHROPIC AND OTHERS, AS WELL AS TAXPAYING CITIZENS)

- identify unmet needs in society
- avoid mismatches between what is being researched and what should be researched for the benefit of patients and society
- increase accountability and transparency
- balance scientific excellence with societal relevance
- increase the efficiency of research and cost-effectiveness of healthcare
- increase the sustainability of the research and development system and of the healthcare system
- provide opportunities to combine collective outcomes (evidence-based observations) with individual-based experience
- increase economic benefits from research through better technology transfer
- create opportunities through funding of shared research priorities to really make a difference in the lives of patients

A STRUCTURED, WELL PLANNED AND MULTISTEP PROCESS

Experiences from the three KBF pilot projects learn that, in order to meet expectations, careful planning of a stakeholder dialogue and prioritization activity is important. During the planning of the dialogue, many of the issues in all phases should be considered and decided upon. On the other hand, flexibility is key to the process. It is important to approach unexpected results or challenges with an open mind and to be prepared to make adjustments during the course of the dialogue. No two dialogues are copies of each other. In each dialogue, the content, the stakeholders involved, the context and/or the aims might be different.

This was also the case for the three KBF pilot projects (see table 2 and for details annexes 1 to 3). Although the projects were carried out under the same heading – 'Mind the Gap: Multistakeholder Dialogue for Priority Setting in Health Research' they were different in content, dialogue processes and types of stakeholder involvement. Each project has a particular focus and scope and works in a specific context of stakeholders and problem complexity.

FUNDAMENTAL BUT FLEXIBLE BUILDING BLOCKS...

Nevertheless, there are many ingredients and building blocks in common between all three projects because they were based on two well-established dialogue models that have been described in the literature, i.e. the James Lind Alliance Priority Setting Partnership[6] and the Dutch Dialogue Model[7]. These methodologies provide structured, detailed, step-by-step guidance for the entire priority setting process and have a proven track record[1/8].

EACH KBF MULTI-STAKEHOLDER DIALOGUE CONSISTED OF FOUR DISTINCT PHASES (SEE FIGURE 1)

1. Preparatory phase
2. Consultation phase
3. Consensus and prioritization phase
4. Dissemination/implementation phase

Sometimes, if parallel trajectories were set up with different stakeholder groups during the consultation phase, there was also an interim prioritization before the consensus phase. This interim prioritization was carried out in each stakeholder group separately.

The three KBF dialogues are essentially exercises in the co-production of knowledge between stakeholders and experts. This shared knowledge forms the basis of broadly supported priorities for future research. In the remainder of this chapter, we focus on the approaches and methodologies to co-produce this knowledge, with a specific focus on the integration of stakeholder perspectives and their translation into options for research. The aim is to give the reader – and potential future organizer of similar stakeholder dialogues – insight in the choice of appropriate approaches and to highlight some critical choices of which the reader should be aware of for future dialogues (see figures 1 and 2). These insights are the result of a post hoc evaluation workshop with all members of the steering committees of the three pilot projects.

A total of twelve attention points or core elements were identified: eight relate to specific phases within the dialogue, three are more overarching and one alludes to an opportunity for improving such dialogues in the future.

FIGURE 1 – FOUR PHASES WITH EIGHT PHASE-SPECIFIC CORE ELEMENTS FOR A SUCCESSFUL DIALOGUE

PHASE 1

PLANNING AND PREPARATION

During this phase, the project team is established, key stakeholders are identified, an initial list of issues, perspectives and ideas of patients and other stakeholders is drawn up, and the social conditions for collaboration are created[7].

1. COMBINE FOCUS AND SCOPE WITH PROBLEM OWNERSHIP

- define, characterize, and demarcate the problem area
- identify problem ownership among stakeholders

⚠ Avoid top down initiatives - dialogues are likely to have a higher participation rate if the problem owners are involved in the problem definition.

⚠ Owners can be patient organisations, researchers, clinicians, funders, but also societal or governmental organisations.

⚠ Problem ownership must be recognised by peers and other stakeholders. Participating problem owners should be prepared to serve the general interest.

⚠ If appropriate, draft a 'status quaestionis' on the topic.

2. SET UP A REPRESENTATIVE AND ACTIVE STEERING COMMITTEE

⚠ The steering group shall be composed of committed persons with expertise in the problem area but with a willingness to go beyond their own stakeholder's interests.

3. RECRUIT AND ENGAGE A WELL-BALANCED GROUP OF STAKEHOLDERS

⚠ Proper stakeholder mapping is key to every multi-stakeholder dialogue. It is important that all organisations with a potential stake in the research prioritization are invited to become involved.

PHASE 2

CONSULTATION PHASE

The different stakeholder groups are consulted separately to develop a list of research topics from the perspective of each stakeholder group. In some projects, the stakeholders also 'interim prioritize' their research topics.

4. ADAPT AND MIX CONSULTATION METHODS

⚠ A mix of methods is used during the consultation phase (including exploratory and in-depth interviews, focus groups, workshops, questionnaires or Delphi-type consultations), tailored to what is most adapted to a specific stakeholder group.

5. FORMULATE TOPICS AS RESEARCHABLE QUESTIONS (BUT ALSO ARCHIVE NEEDS AND CONCERNS)

⚠ Reviewing, sorting out and turning the outcomes of the consultation phase into a list of indicative researchable questions is one of the most complex, tedious and time-consuming parts of the process, requiring data management and critical appraisal skills combined with intrinsic content knowledge into the subject.

⚠ Moreover, researchable questions should pass through various filters and meet a diversity of criteria (they should not be solved by already conducted research, the question should be researchable, (partially) duplicated questions should be sorted out, ...).

PHASE 3

CONSENSUS AND PRIORITIZATION PHASE

The various stakeholders take note of each other's researchable questions and priorities. They strive towards consensus through dialogue and finally prioritize a common research agenda.

6. CREATE A SHARED MINIMAL KNOWLEDGE BASE AND A COMMON LANGUAGE

⚠ There are many ways to make the dialogue well informed for all stakeholders involved. Choices have to be made on which type of information is needed and what the minimal information base is that needs to be shared in order for the group to have a meaningful conversation.

7. STIMULATE MUTUAL LEARNING AND GO FOR CONSENSUS BUILDING

⚠ A core component throughout the whole trajectory is to clarify the perspectives and agendas of the various stakeholders, in order to allow mutual learning during the dialogue. An external facilitator creates the conditions for dialogue, stimulates mutual learning and, if necessary, acts as a mediator.

PHASE 4

DISSEMINATION, IMPLEMENTATION AND PROGRAMMING

The priorities are disseminated among stakeholders, the research community and possible funders. The research agenda is translated into a funding plan and the agenda is actively used to take research action.

8. CREATE PERSPECTIVES FOR IMPLEMENTATION

⚠ The results of the priority exercise are published in order to increase exposure to researchers, funders and other stakeholders (including politicians) and augment credibility of the dialogue results.

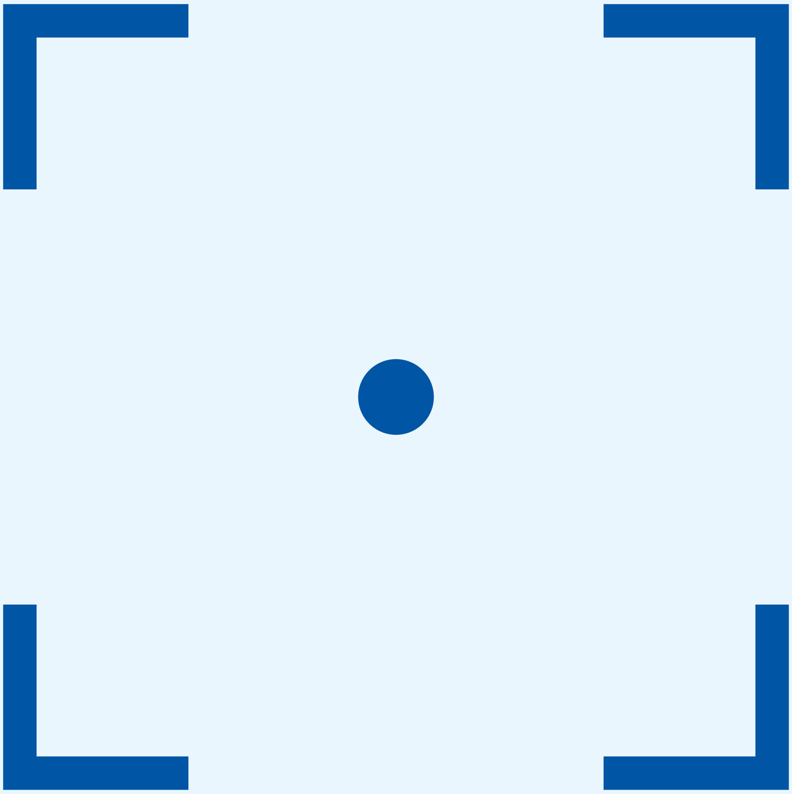
⚠ At the same time, potential opportunities for getting the research funded and to execute research programs are being explored.

TABLE 2. SUMMARY ‘MIND THE GAP PILOT PROJECTS’ FOR DETAILS SEE ANNEX 1 - 3

This table summarizes the critical choices that were made for each of the core elements in each of the three pilot projects, highlighting again the fact that each successful multi-stakeholder dialogue should be the result of a tailor-made process.

TSC	WORK DISABILITY	NASH/BIOBANKS
CONTEXT		
Rare disease with many unmet needs	Prominent societal problem	Disease with challenging future impact on health and society. Wicked ethical, legal, societal issues related to biobanks
1A. FOCUS AND SCOPE		
All uncertainties related to a specific rare disease	All researchable uncertainties related to returning to work after long term work disability, but within the competence area of the Belgian Federal Minister of Public Health and focussed on 2 conditions: musculoskeletal and psychological disorders (including burn out)	Initially very broad (all liver diseases), had to be narrowed down to a more specific disease field. Further confinement by superimposing the requirement of biobank contribution on the research questions. Second objective on challenges for biobanks
1B. OWNERSHIP OF THE PROBLEM AREA		
be-TSC as patient organisation, group of researchers/clinicians, KBF as potential funder	RIZIV/INAMI	BBMRI (and biobanks), hepatologists The topic NASH was not (yet) on the radar of patient organisations, therefore a problem ‘owner’ on the users’ side could not be identified
2. STEERING COMMITTEE		
See annex 1	See annex 2	See annex 3
3. STAKEHOLDERS		
Active patient organisation, but few patients are known, so access to patients was limited. Small but highly committed research community. Large number of medical and non-medical disciplines involved in the care of TSC patients and relatives	No dedicated patient organisation. Many stakeholders, some professionally organised	No NASH patient organisation, other relevant patient organisations do not have NASH on their radar yet. NASH research community is small and relatively fragmented. Biobank community is in full (re) organisation and tries to (re)define its societal role

TSC	WORK DISABILITY	NASH/BIOBANKS
4. CONSULTATION METHODS		
Focus groups, in-depth interviews, Delphi-like method	Focus groups	Focus groups, questionnaire
5. RESEARCHABLE QUESTIONS		
Initial proposal by data manager, revised /validated by steering committee and final revision by stakeholders (consensus workshop)	Idem	Idem
6. SHARED KNOWLEDGE BASE AND COMMON LANGUAGE		
Project started in parallel trajectories (patients vs experts) and each trajectory started from own knowledge, experience, and expertise. Exchanging and sharing information between the two groups was reserved for the consensus meeting	Project started in parallel trajectories (8 focus groups) and each trajectory started from own knowledge, experience, and expertise. Exchanging and sharing information between the different groups was reserved for the consensus meeting	Intensive information provision on liver function and liver diseases, NASH and the functioning of biobanks during all phases and in all focus groups/workshops
7. STIMULATE MUTUAL LEARNING		
During consensus workshop, alternation of small discussion groups and plenary deliberation.	Idem	Idem
8. IMPLEMENTATION RESEARCH PROGRAMMING		
KBF call for research projects	RIZIV/INAMI has set up a research agenda	Continued dialogue and advocacy



1. COMBINE FOCUS AND SCOPE WITH PROBLEM OWNERSHIP

Surely, the single most critical factor in all prioritizations lies in the precision of defining the problem area, followed as a close second by the assignment of problem ownership.

Without a clear definition, understanding and articulation of the problem and the problem area, the aims and focus of the dialogue remain blurred and obscured for the stakeholders. Therefore, expectations and contributions of participating stakeholders will never get aligned properly.

Besides defining the project focus, an initial scoping exercise is also required, not only to mark the boundaries of the project, but also to ensure there is sufficient time, resources and commitment from stakeholders to conduct the process. The scope is defined by the population of interest (e.g. adults and or/children), the breadth of the problem area and its unique issues, the competence and capacity of the problem owners/project initiators, and the size of the evidence base against which the intermediate outcomes of the dialogues need to be checked.

It is certainly important to consider the resource implications of scope. Dialogues with a broad scope may take longer, require greater resources, incur more costs, but touch on the interests of more stakeholders.

With the definition and scoping of the problem also comes the requirement to assign levels of problem ownership: who owns various aspects of the problem area? Imperatively, the major owner should be among the prominent stakeholders organising the dialogue. Often the main problem owner is the organization that initiated the priority setting exercise, but ownership can be expanded to include other committed stakeholders who might provide resources, expertise, funding and/or staff to support and execute the dialogue.

In the case of the TSC-project, the focus was on a specific rare disease, but the scope was very broadly defined: the contributing stakeholders could bring to the dialogue all types of uncertainties related to the disease. In this project, ownership was divided over three parties, all represented in the steering committee: be-TSC (the Belgian TSC patient association), a Belgian hospital organising a multidisciplinary consult for TSC patients, and KBF.

KBF not only provided the resources and coordinated the dialogue, but, depending on the outcome of the dialogue, also showed interest to launch a call for research projects in TSC, however without committing itself from the onset or during the course of the dialogue.

An extended 'status quaestionis' was drafted in order to get a grip on the disease and the associated clinical and biomedical problems, to get an overview on the status of current research, to map out the possible stakeholders (nationally and internationally) and to become informed on existing research agendas and current funder's research priorities.

The project on work disability encompasses a broad topic, with medical and social aspects and with a high impact on individuals, society and economy. Therefore, the theme is currently very prominently present on the political agenda. It was decided upfront by the steering committee to limit the scope of the dialogue to the medical aspects[9] for two diseases that cause the majority of long-term sick leaf: psychiatric problems and skeletomuscular diseases. The owner of the problem area was the Centre of Expertise on Work Disability of the Benefits Division of the Belgian RIZIV/INAMI. KBF representatives coordinated the dialogue, provided the resources for the dialogue and engaged a consultant for data-management, facilitation and reporting.

The focus of the third pilot project was originally on liver diseases and biobanks. It was felt very early on by the steering committee that this focus was too broad, as liver diseases encompass a broad range of diseases with very different aetiology and associated researchable questions. Therefore, an initial multi-stakeholder workshop was organised to define criteria for properly setting the focus and the scope of this project. To this workshop, different groups of relevant stakeholders were invited. Based on the results of this workshop, supplemented with additional literature review by members of the steering committee, it was decided to focus the dialogue on NASH (non-alcoholic fatty liver disease). The ownership of this project was divided between a select group of biobank managers and biobank organisations and a group of hepatologists. All parties were represented in the steering committee, as well as representatives of the KBF who coordinated the dialogue. Representatives of patients/patient organisations could not be included in the steering committee as NASH was not yet on the radar of these organisations.

2. SET UP A REPRESENTATIVE AND ACTIVE STEERING COMMITTEE

The steering committee is a small group that organises, oversees, coordinates and implements the dialogue. It will be made up of a representative mix of delegates of the major stakeholders/problem owners, possibly supplemented with experts in the problem field and the persons executing the dialogue (data/content manager, process manager/facilitator, coordinator).

Members of the steering committee will bring with them knowledge (theoretic/academic, medical, but also experience knowledge) of the problem field and access to networks and individuals within their own stakeholder group. They should be prepared to approach and utilise their networks and contacts before, during and after the course of the dialogue.

Members are able to listen to, respect and incorporate into the dialogue the perspectives of other parties. Steering committee members with direct relevant experience such as patients, carers, healthcare professionals, researchers, … are invited to participate themselves in the priority setting exercise.

During the various phases of the dialogue, information needs to be managed and adapted, and information exchange processes need to be designed. This is the work that will turn the raw information into researchable questions and verify that those questions are true uncertainties. A large amount of qualitative data needs to be managed, but also presented and shared among the stakeholders. Usually an information or content manager and/or a methodological specialist / facilitator are part of the steering committee.

Lastly, the dialogue requires good leadership and a considerable time commitment from a general coordinator who has the overall responsibility for successfully completing the dialogue.

In the TSC project the steering committee consisted of Eva Schoeters (representative of be-TSC, the Belgian TSC patient association), paediatric neurologist Anna Jansen (coordinator of the multidisciplinary TSC consult at the Universitair Ziekenhuis Brussel), and Annemie T'Seyen and Bénédicte Gombault from KBF as coordinators of the dialogue. KBF engaged Peter Raeymaekers (LyRaGen) as content manager and Alain Wouters (Whole Systems) as methodological and process specialist and workshop facilitator.

In the project on work disability, Saskia Decuman, head of the Centre of Expertise on Work Disability at RIZIV/INAMI, formed the steering committee together with Bénédicte Gombault and Yves Dario from KBF as coordinators of the dialogue. Stefan Gijssels (Seboio) executed the dialogue and was also responsible for the data and process management.

Sofie Bekaert, from Bimetra and the biobank of UZ Gent, and her colleague Hans Van Vlierberghe, hepatologist-gastroenterologist at UZ Gent, initiated the project on liver diseases and biobanks. In order to enlarge the support base and to include perspectives from other Belgian biobanks and a larger group of liver specialists (BASL), the steering committee was enlarged with hepatologist Peter Stärkel (Saint-Luc, UCL), Laurent Dollé (Biothèque Wallonie-Bruxelles) and Annelies Debucquoy (BBMRI.be). KBF representatives Bénédicte Gombault and Annemie T'Seyen coordinated the dialogue; Peter Raeymaekers (LyRaGen) and Alain Wouters (Whole Systems) were engaged for project execution.

The steering committee is a small group that organises, oversees, coordinates and implements the dialogue.

3. RECRUIT AND ENGAGE A WELL-BALANCED GROUP OF STAKEHOLDERS

Proper stakeholder mapping is key to every multi-stakeholder dialogue. It is important that all organisations with a potential stake in the research prioritization are invited to become involved. This is a prerequisite for safeguarding transparency, guaranteeing inclusiveness and demonstrating that the priority setting took place in a fair manner.

Stakeholders should be selected and balanced on the basis of the diversity of their perspectives and backgrounds. Broad stakeholder involvement based on multidisciplinary and multi-sectorial backgrounds minimizes the likelihood of research topics being overlooked and maximizes the support base for the outcomes of the dialogue.

Stakeholders to involve are people who have had experience in the problem area, carers and relatives of those affected, practitioners, allied health professionals, researchers and experts in the field. Also potential sponsors, representatives of organisations involved in the care of people with the specific health problems or organisations doing research in the topic, delegates from industry, and in some cases even unions, insurers, employers etc. can be included.

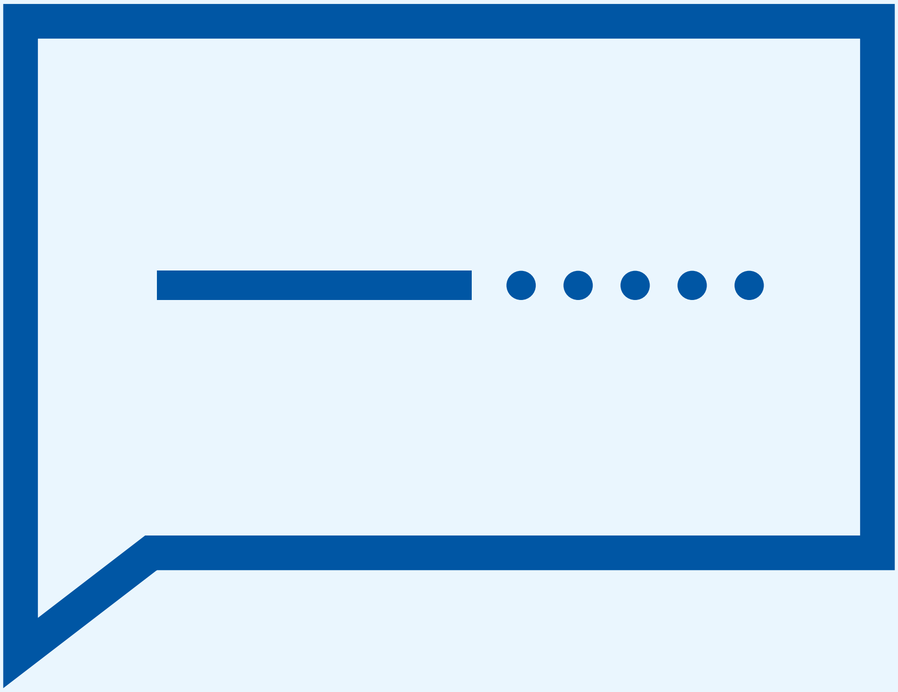
For TSC, two separate approaches were followed for mapping the stakeholder field. At first, a group of clinicians from various disciplines, all involved in caring for TSC patients, were brought together with a representative of the Belgian patient organisation and members of the King Baudouin Foundation. The aim of this meeting was to identify and name all stakeholders concerned. Secondly, a 'status quaestionis' was drafted based on the published scientific and medical literature. This provided an inventory of the past and current research efforts, but also of the involved experts/scientists/clinicians, the funders and the industry partners. This helped in identifying the profiles and experts who needed to be interviewed. Supplementary experts were allowed to take part in a second round of interviews and in two subsequent Delphi rounds.

It should also be noted that the recruitment of stakeholder representatives is sometimes cumbersome: very often stakeholder organisations delegate their 'expert' to the dialogue, while it might be more useful to have representatives who experience the problem area on a daily basis. In the project on work disability, for example, employers had the tendency to delegate members of their human resource department or the occupational physician, while the real 'experience expertise' is on the work floor with the managers, the foreman and the colleagues.

Also the question about patient and citizen representation is imminent. Who represents the patient with a rare disease, a person on long-term sick leaf, a citizen interested in research? Are they properly represented by patient organisations, unions, mutualities, consumer organisations, ...? In all three projects, the explicit choice was made to involve witnesses with hands-on experience. They were not only involved in the information gathering phases but also invited to take part in the dialogues, alongside their classical representatives and other obvious stakeholders.

In the NASH & Biobanks project, no NASH patient organisation could be identified. Moreover, NASH was not yet on the agenda of other patient organisations, which could/should have an interest in this upcoming disorder (diabetes, obesity, heart disease, other liver diseases patient organisations, ...). The topic is (for the moment) probably too forward-looking. It was therefore difficult to involve patients and relatives. Of the three pilot projects, this was also the project that implicated most explicitly citizens who did not have an immediate stake in the subject, apart from being a member of society.

Proper stakeholder mapping is key to every multi-stakeholder dialogue.



4. ADAPT AND MIX CONSULTATION METHODS

During the consultation phase, broader stakeholder views on matters related to research, needs and uncertainties are gathered. These come from the stakeholders themselves and from the people they represent. Gathering these opinions is most often done through in-depth interviews (face-to-face or by telephone or Skype) and focus groups.

These consultations are performed separately for the different stakeholder groups and use whichever method is best suited to the stakeholders' members, resources and infrastructure. An example: for some diseases, it is no good practice to bring patients together because of infection risks. In other cases, the consultation facilities and methods should be adapted in accordance with stakeholders' restrictions (mobility, language, availability).

Uncertainties can also be gathered via surveys (online and/or on paper). Patient organisations can often use existing communication mechanisms, including newsletters, meetings, email networks and online message boards to help communicate this survey or foster participation to focus groups or allow for interviews.

Clinicians are invited to identify uncertainties that they find relevant when treating patients with the specific health problem, but also to recall areas where research is lacking. Face-to-face interviews or focus groups can be applied here too, but also Delphi-like consultations[10] via e-mail or any other form of moderated internet interface can be applied.

The initial gathering phase is characterized by divergence and consolidation phases within each stakeholder group. After broadening the scope by harvesting information from personal experiences, the defining of researchable questions, weighing and semi-prioritization of these questions within each stakeholder group often constitutes a phase of refocusing.

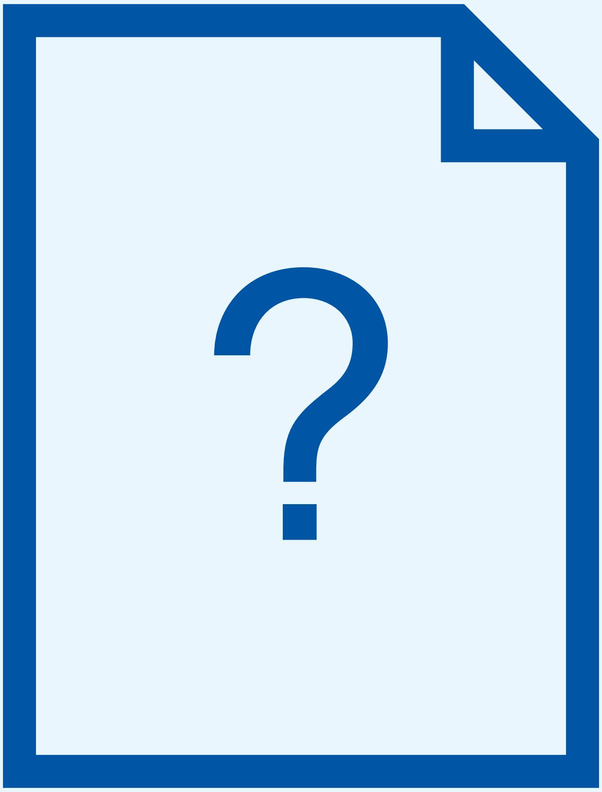
Semi-prioritization can be done by using surveys (quantitative phase often including some kind of voting). Another possibility is to use a Delphi methodology within a stakeholder group to define priorities by mutual agreement or organize priority workshops within a stakeholder group.

The Dutch Dialogue Model tends to use methodologies based on dialogue to arrive at intra-stakeholder priorities. Additional validation meetings and/or Delphi methods are often deployed to reach a concerted agreement among the homogeneous stakeholder group. In Priority Setting Partnerships by The James Lind Alliance, the interim priority setting process, usually leading to a shortlist of 25 to 30 researchable questions, may be carried out by the whole Partnership or by the representative steering group. The JLA does not impose a strict method for this stage.

Two separate consultation tracks were followed in the TSC project: a patient and patient's relatives' track and an expert's, practitioner's, researcher's track. Because of the rarity of TSC and the relative young existence of the Belgian TSC patient organisation (be-TSC), only a limited number of Belgian patients and relatives were known at the beginning of the project. Therefore, it was decided to gather researchable questions in the patient's track by means of one focus group and supplementary individual interviews with patients, parents of patients and spouses. During a workshop with representatives from 6 European TSC patient organisations, researchable questions were redefined, validated and interim prioritized.
In the expert track, 17 Belgian and international clinical experts and researchers were initially interviewed. The gathered researchable questions were presented by e-mail to a panel of 25 international TSC experts for validation, deepening and broadening. In a second Delphi round the researchable questions were interim-prioritized by voting by the same group of experts.

The project on work disability used focus groups and individual interviews with 1) patients and people with previous work disability; 2) psychiatrists and those supporting people with psychological disorders; 3) rheumatologists and specialists in musculoskeletal disorders; 4) personnel managers and human resources specialists; 5) general practitioners; 6) representatives of organizations representing employers, employees, self-employed people and insurers; 7) researchers; and 8) experts and doctors from RIZIV/INAMI. No interim-prioritization was done in this project.

For the NASH/Biobank project, separate focus groups were organized with biobank managers and representatives from the pharmaceutical and biotech industry. A full day bilingual workshop was also organized with patients and citizens, and logistically supported by expert members of the steering committee. Liver specialists, gastroenterologists and researchers were surveyed with a questionnaire with open questions. No interim-prioritization was done either for this project.



5. FORMULATE TOPICS AS RESEARCHABLE QUESTIONS (BUT ALSO ARCHIVE NEEDS AND CONCERNS)

The output of focus groups, in depth interviews or open questionnaires is often a mixture of personal stories, broad themes and issues, unmet needs, fears and hopes, uncertainties and assumptions. Reviewing, sorting out and turning this diverse, but inevitably rich treasure trove of data into a list of indicative or researchable questions is one of the most complex, tedious and time-consuming parts of the process.

It requires data management and critical appraisal skills, combined with intrinsic knowledge of the subject. This is surely beyond the competences and capabilities of one person, and therefore requires the contribution and engagement from members of the steering committee.

The option was taken to formulate 'researchable questions', which are different from 'research questions' in that they are usually broader in scope and less well specified. On the other hand they are concrete enough to allow researchers and funders to set up a research program based on the formulated question. For example, in clinical research, a true 'research question' is most often defined as a 'PICO' question: it includes specific information about the studied population (Patients with disease X, between the age of Y and Z, …), the Intervention (drug A, intervention B), the Comparator (best current practice, placebo …) and the Outcome (survival, quality of life, side effects, …). A 'researchable question' would be formulated as 'What is the best current treatment for symptom Q in patients with disease R?'

Along the process, other types of information may arise to the surface. Examples are unmet needs or policy matters for which no supplementary research is needed, but which need the implementation of specific measures to solve the issue. Retaining, documenting and publishing this information is certainly added value to most projects.

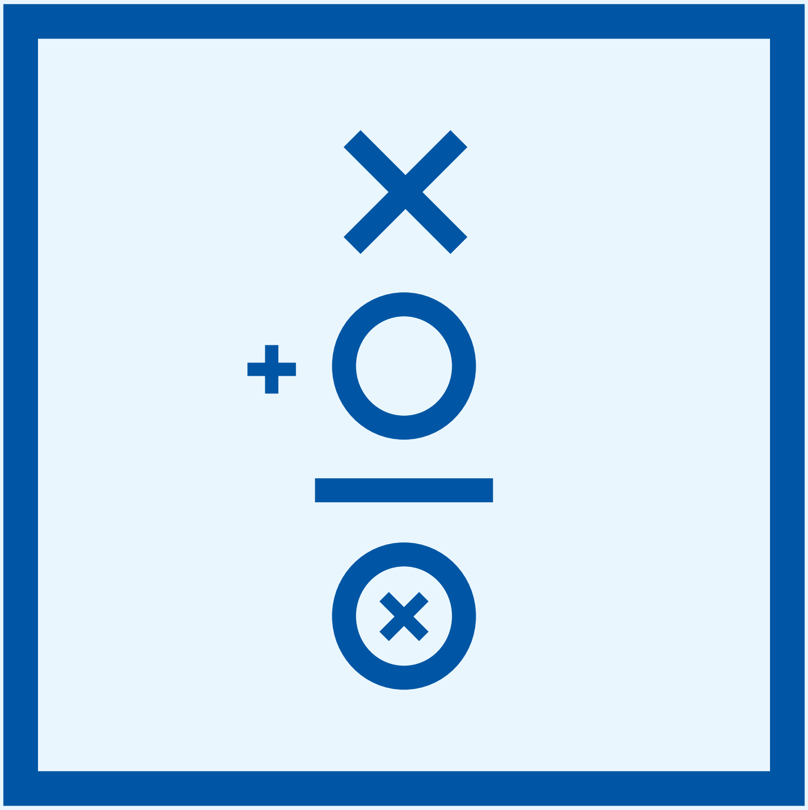
In all three projects, the option was taken to push the outcomes from the consultations maximally towards 'researchable questions' and not to leave them as ill defined 'research areas' or 'broad research topics'. Researchable questions demand for a materialised problem definition, push towards clarity and force stakeholders into concrete thinking.

In reality this seemed to be working for nearly every mentioned uncertainty, whether defined by researchers, clinicians, patients or patients' relatives. Even for less obvious research topics in the areas of care provision, health system organisation, family and social support etc., this was feasible.

Attention should be paid to the language used: questions should be accessible to a lay or non-medical audience but also accurate enough to engage clinicians and specialists. As indicated by the James Lind Alliance, the question defining part of the process is highly interpretative and subjective. During the three pilot projects, it was felt that this phase went beyond the competence of one individual, but at the same time, it was unfeasible to execute this phase with all the stakeholders involved. It is therefore vital that steering committee members contribute to and comment on the outcomes of this process to ensure fairness, neutrality and completeness. Their experiences as patients, carers or clinicians will help ensure that the submissions of those groups are interpreted and captured appropriately in the formatted questions.

During this phase, duplicate questions need to be removed, as well as topics that have already been solved by research or which cannot be subjected to research. Also, decisions need to be made about the extent to which questions are combined: too many very specific questions will be very difficult to prioritize. Conversely, questions that are too broad may be difficult for researchers to interpret or may contain too many elements with no sense of priority between them.

Lastly, during some of the pilot projects, information surfaced that in itself could not be transformed into researchable questions, but that was nevertheless considered by one or more stakeholders to be vital for the life quality of patients. For example, the TSC project identified 10 unmet and urgent needs, requiring policy attention, without the need for additional research. These needs were included in the final report. In the project on NASH/Biobanks, 28 issues and 10 big challenges on biobanks were defined which could potentially hamper an optimal contribution of biobanks to NASH and other biomedical research. These issues and grand challenges can form the basis for future dialogues.



6. CREATE A SHARED MINIMAL KNOWLEDGE BASE AND A COMMON LANGUAGE

Every participant to the dialogue has a vested interest in being well informed. There are many ways to bring and share information among stakeholders. Choices have to be made on which type of information is needed and what the minimal information base is that must be shared in order for the group to have a meaningful conversation.

Therefore, a balance has to be found between the amount of information given and the information that stakeholders bring themselves to the table during the process.

Discussion and information exchange should be kept in plain language; the content should be accessible to all stakeholders; and high-level technical discussions should be avoided, if possible. If profound technical knowledge is a necessity to come to concluding researchable questions, time has to be invested to sufficiently explain these aspects to all stakeholder groups.

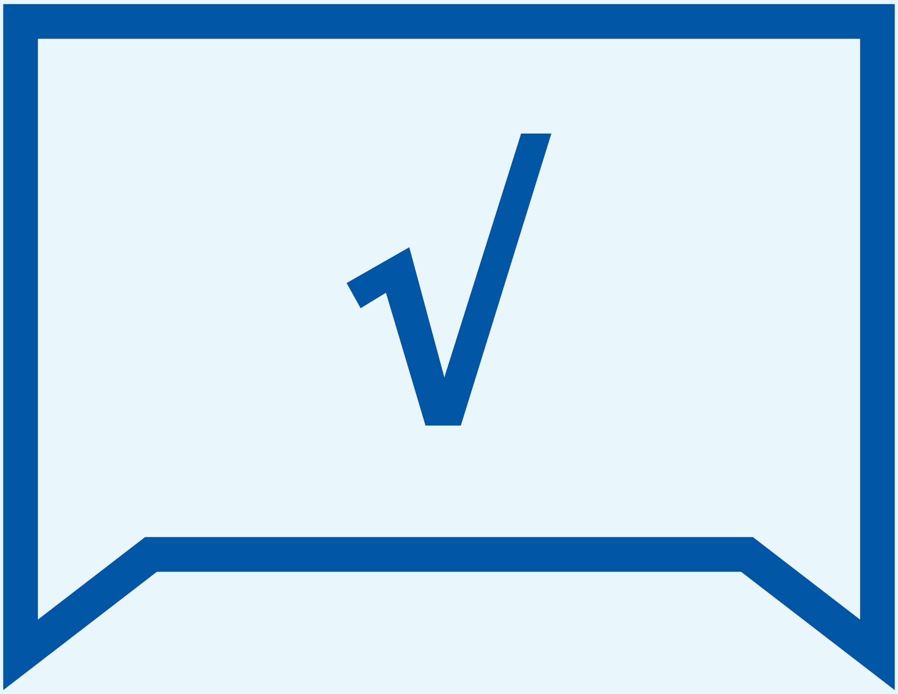
In the NASH & Biobank project, a lot of upfront information had to be given to stakeholders during the various focus groups and workshops. The type, level and content of information was adapted to the background of the participants. Biobank managers needed to be informed about NASH; patients, citizens and industry representatives about the function of the liver, about NASH and about biobanks; hepatologists about biobanks, etc.

On the other hand, the TSC project showed that the knowledge of patients should never be underestimated. They are the ones who are skilled in the science of what it means to live with a specific disorder on a daily basis. They are the experts on their own diagnostic and therapeutic experiences, on their contacts with the medical and non-medical care providers, on how their relations with the outside world are influenced by their disorder, and on their own feelings, uncertainties, hopes, worries and desires. Moreover, patients with a rare disease have often become experts in the clinical matters of their disorder as, for many of them, searching for a correct diagnosis, an accurate prognosis and proper treatment has taken many years.

Also the representative organisations of patients, and especially the umbrella organisations at pan-national level, follow the scientific progress closely. They are often present at medical and scientific conferences. In the TSC project, some doctor-specialists and researchers even testified that they were challenged by the patients and their relatives on their knowledge about the many different clinical and non-clinical aspects of the disease. These specialists had to admit that they are not experts in all aspects of TSC, certainly not in the issues outside their field of expertise, and that was confronting for some of them. The patients and their representatives often had a better overall view compared to many of the professional experts.
Therefore, the choice was deliberately made in the TSC project to keep the trajectories of patients and relatives separated from the trajectory of the experts for as long as possible, in order to avoid 'mutual contamination'. Only at the time of the consensus meeting were both groups confronted with each other's priority lists (which overlapped by approximately 30%).

A similar observation was made during the project on work disability. Often, professionals are experts within their own subdomain, while being unaware of many of the issues, views or even opportunities in adjacent fields. Becoming aware of one's own limitations adds to solving the raised problems.

Every participant to the dialogue has a vested interest in being well informed.



7. STIMULATE MUTUAL LEARNING AND GO FOR CONSENSUS BUILDING

During the conversation within mixed stakeholder groups, there is a lot of non-directed learning going on, at least if sufficient time is allowed to get to know each other's points of view, perspectives and practices. Moreover, in the exchange of ideas, all stakeholders should be considered as equal partners.

Therefore, a core component of the consensus and final prioritization phase is to maximise the synergy between process and content, in order to sufficiently clarify the perspectives and agendas of the various stakeholders and allow mutual learning during the deliberations. Process considerations have ramifications on the possible consensus building and acknowledgment of raised mutual knowledge has implications on the ensuing dialogue processes.

Being adaptive for both process and content throughout every phase of the dialogue requires intensive work of the core project team and the steering committee. The members of the project team facilitating the various phases of the dialogue should create the conditions for dialogue, stimulate mutual learning and, if necessary, act as a mediator.

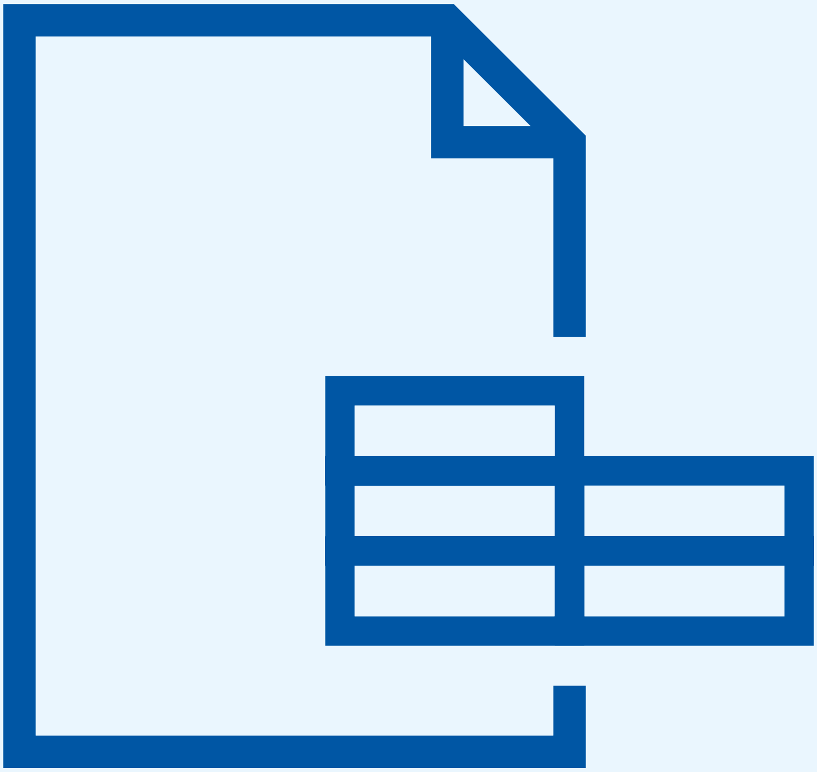
Especially the consensus phase is about mutual learning through dialogue. As the aim of this phase is to integrate the agendas of different stakeholders via a workshop with representatives of the relevant parties, participants have to understand and assimilate the content of and the rationale behind those different agendas and relate them to one's own agenda. It is all about thinking more broadly: beyond one's own stake, but at the same time, participants should be aware of the impact of novel proposals on their own situation.

The consensus workshops in all three pilot projects included sequential steps of consensus building and alternating phases of personal reflection and choice. Discussion and deliberation took place in small, usually mixed stakeholder groups, alternated with plenary feedback, argumentation and discussion. Finally, a transparent, shared ranking or voting exercise was carried out and the results were further discussed in plenum.

In the TSC project and the project about returning to work, the group and plenary discussions during the consensus workshop led to a substantiated pre-selection of well-defined research questions and a final individual voting process to lists of respectively 15 and 10 research priorities.

In the NASH/Biobank project, two separate rounds of prioritization took place. In a first round, the members of the steering committee prioritized the NASH researchable questions according to the possible contribution of biobanks. Only those researchable NASH questions, to which biobanks can effectively contribute, were brought to the consensus workshop with other stakeholders. During this workshop, NASH research topics were prioritized from a societal perspective. However, after final voting in the NASH/Biobank project, a plenary discussion led to the conclusion that both groups of researchable questions were actually of equal importance, but that one group could be more easily put into practice because they could capitalize on the current functioning of biobanks. The other group of research questions calls for a thorough redesign of biobanks, but in the long run, research on these questions would yield in at least as much benefit for patients and society compared to the higher ranked group (see annex 3)

During the conversation within mixed stakeholder groups, there is a lot of non-directed learning going on, at least if sufficient time is allowed to get to know each other's points of view, perspectives and practices.



8. CREATE PERSPECTIVES FOR IMPLEMENTATION

Agreeing to a top 10 or top 15 research priorities is not the end of the dialogue. It is important that the results of the priority exercise are disseminated and published in order to increase exposure to researchers, funders and other stakeholders (including politicians) and augment credibility of the dialogue results.

At the same time, members of the steering committee and other involved stakeholders should take responsibility for finding ways to identify potential opportunities for getting the research funded and research programs executed. If potential funders have not been involved in the dialogue, a process to influence the research community needs to be elaborated and executed. It is therefore important to ensure that a mobilization plan is integrated from the planning phase of the dialogue on. The implementation phase should be an integral part of the dialogue too.

The research institute on work disability of the RIZIV/INAMI is using the results of the multi-stakeholder dialogue as input for its new research and study program. The outcomes of the dialogue also guide the proper allocation of research budgets to this program.

KBF participated in the TSC dialogue mainly as resource provider to support the dialogue and as coordinator. Throughout the dialogue, however, KBF discovered the obvious research gaps in TSC and the burning need for TSC research support in Belgium and beyond. Therefore, the Foundation launched in 2018 a call for research projects focussing on TSC Associated Neuropsychiatric Disorders (TAND) (Research priority number 1) with the aim to better understand the processes (causes and mechanisms) underpinning the neuropsychiatric disorders associated with TSC and/or to translate and implement fundamental discoveries into better prevention, diagnosis, treatment or quality of care for patients with TSC and their relatives.

Rather than emerging into a research programming and implementation phase, the NASH/Biobanks project aims to be the start of a continued dialogue between the various stakeholder groups in order to promote and advocate the use of biobanks as a precious common good for supporting and advancing research in liver diseases, but also in other biomedical research fields, for the benefit of patients, citizens and society.

Agreeing to a top 10 or top 15 research priorities is not the end of the dialogue.

FOUR OVERARCHING CORE ELEMENTS FOR A SUCCESSFUL DIALOGUE

FIGURE 2 – OVERARCHING CORE ELEMENTS FOR A SUCCESSFUL DIALOGUE

The following four attention points are applicable to all four phases of the dialogue.

9. BE VIGILANT ABOUT TIMING AND RESOURCES

⚠ A properly executed multi-stakeholder dialogue for research priority setting takes time and resources, depending on the scope and nature of the topic and the number of stakeholders involved. As a rule of thumb, one should take a time schedule of 12 to 18 months into account. And this is without the dissemination, implementation and programming phase.

10. USE PRIORITIZATION AS A DRIVING FORCE

⚠ The imperative of ultimately reaching a list of collective priorities – which is made public by the organiser – obliges all stakeholders not only to understand and immerse themselves into the perspectives and agendas of others, but also to give in on their own positions and agendas.

11. INCORPORATE VALUES AND ETHICS

⚠ Diverging values and principles between different stakeholders or disciplines are likely and should be resolved in a fair and legitimate way. During the dialogue, nobody should feel marginalised or perceive that his/her views are less valid than others. Everyone should have equal opportunities to share their particular concerns.

Inclusiveness, openness, transparency and trust are prerequisites for a successful and productive dialogue.

12. USE ‘SYSTEMS THINKING’ TO UNDERPIN PRIORITIZATION

⚠ Many of the raised researchable questions are interrelated, some of them being dependent on other questions. Applying rules and techniques of systems thinking to tease out the interdependence of the questions, together with the barriers that hamper the irresolution, allows the identification of questions with the biggest leverage effect.

9. BE VIGILANT ABOUT TIMING AND RESOURCES

The amount of time and resources that are absorbed by a properly executed multi-stakeholder dialogue for research priority setting should not be underestimated. The amount of time to run a dialogue depends on the scope and nature of the topic, the number of stakeholders involved and the available resources. As a rule of thumb, the Priority Setting Partnerships organised by the James Lind Alliance and the Research Priority Dialogues of the University of Amsterdam take between 12 and 18 months to complete. And this is without the dissemination, implementation and programming phase.

Considerable labour goes into the practical planning and management of the consultations and the harvesting, analysis and representation of the intermediate results. On top of that, building up relationships within the research and stakeholder community; recruiting representatives of stakeholders; giving training and education to certain groups; dispersing and publishing results; and advocating for proper research follow up are hidden efforts that are often under-recognized.

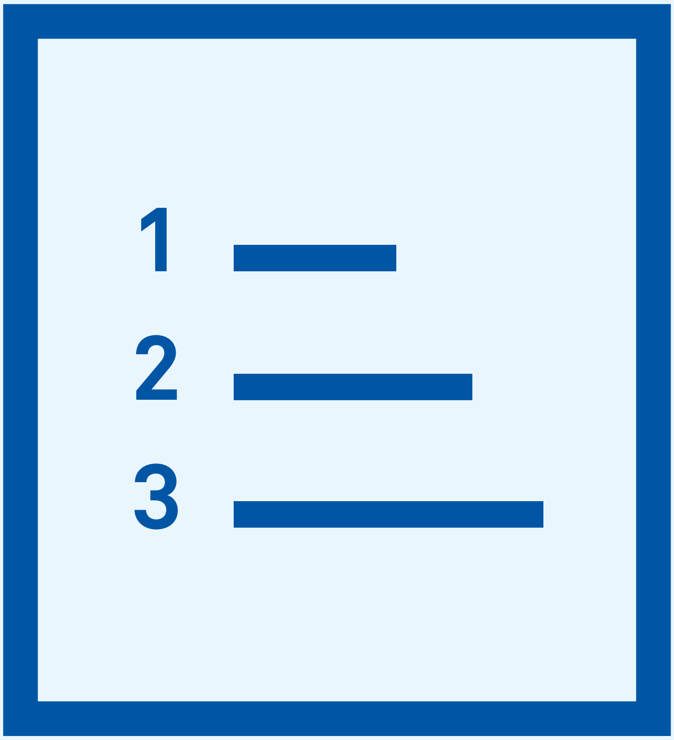
Key costs in multi-stakeholder dialogues are coordinating staff costs, data and process management, venue hire, refreshments, alimentation, reimbursement of travel costs, communication and publication costs, etc.

Nearly every decision – process or content wise – during the course of the dialogue has an impact on the resources and the timing. Therefore, during the planning phase of the dialogue, careful and prudent considerations should be made about the use of resources and the timing, while providing for the necessary margins to deal with unforeseen circumstances during the process.

The three pilot projects also took each between 12 and 18 months to be completed and published in reports. Each of the projects was coordinated by a duo of KBF representatives and included the engagement of (part time) consultants for data and process management, interviewing, and workshop facilitation.

Most of the 'smaller' meetings – focus groups, limited workshops – took place at the premises of the KBF in Brussels or of one of the stakeholders. More extended workshops took place in rented meeting venues elsewhere.

The amount of time and resources that are absorbed by a properly executed multi-stakeholder dialogue for research priority setting should not be underestimated.



10. USE PRIORITIZATION AS A DRIVING FORCE

Emphasising, during the entire process, that the end product will be a published, consensual but prioritized list of researchable questions brings a positive dynamic to the dialogue. It at least prevents that the dialogues lapse towards noncommittal talk exercises in which arguments are exchanged back and forward, but without true consensus building and a perspective to come to a shared end result that is beneficial to all.

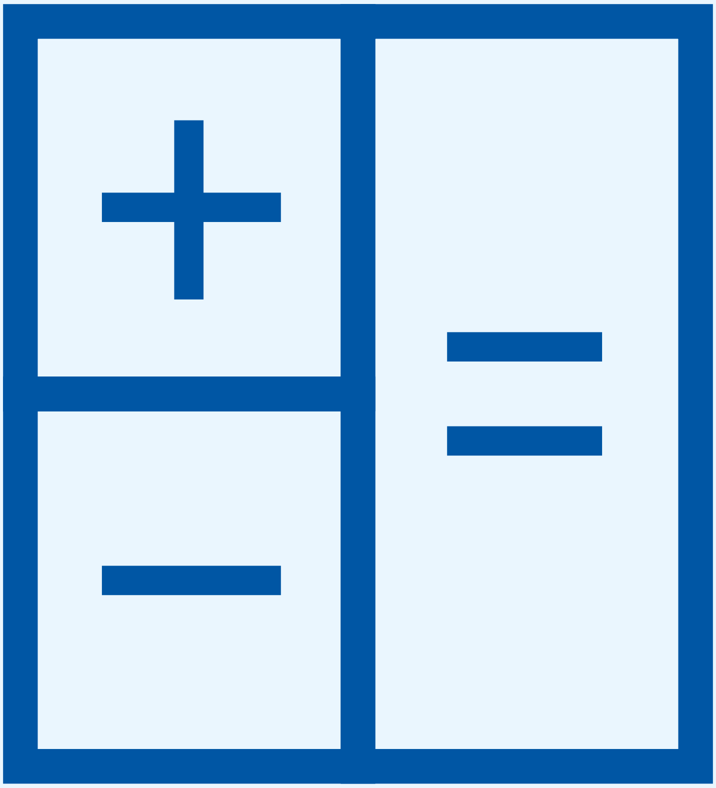
It forces participants on the one hand to look beyond their own agenda and to get insight into the perspectives of other stakeholders. On the other hand, they are obliged to distinguish main issues from side issues.

It might be worthwhile to explicitly define criteria for identifying and prioritizing research topics with all stakeholders, in order to facilitate the prioritization process. Clear and consensual criteria are informative about the objectives and goals that participants want to achieve and provide an alternative outlook and objective filter for evaluating and reconsidering one's own priorities and those of others. It furthermore increases transparency and helps in explaining the results obtained to representatives or people coming into the process at a later stage.

In the case of NASH/Biobanks, a full day workshop with a mixture of stakeholders, including patients and citizens, was devoted at the very beginning of the dialogue to identify criteria for focusing and scoping the topic and the problem field.

In the case of TSC, along the various phases of the dialogue, a growing list of criteria was established to help participants to prioritize researchable questions.

Emphasising, during the entire process, that the end product will be a published, consensual but prioritized list of researchable questions brings a positive dynamic to the dialogue.



11. INCORPORATE VALUES AND ETHICS

Diverging values and principles between different stakeholders or disciplines are likely and should be resolved in a fair and legitimate way. But at the same time, it is important to state and encourage understanding of the different perspectives, since this forms the basis for collective learning, mutual understanding and concerted priority setting.

However, during the process, nobody should feel marginalised or perceive that his/her views are less valid than others. Everyone should have equal opportunities to contribute their particular concerns. Inclusiveness, openness, transparency and trust are prerequisites for a successful and productive dialogue. When it comes to priority setting, the participants have to set aside their personal agendas and work with priorities that will deliver maximal benefits to all.

Be aware of tokenism! Tokenism is the practice of making only a perfunctory or symbolic effort to be inclusive, especially by recruiting a small number of people from normally underrepresented groups.

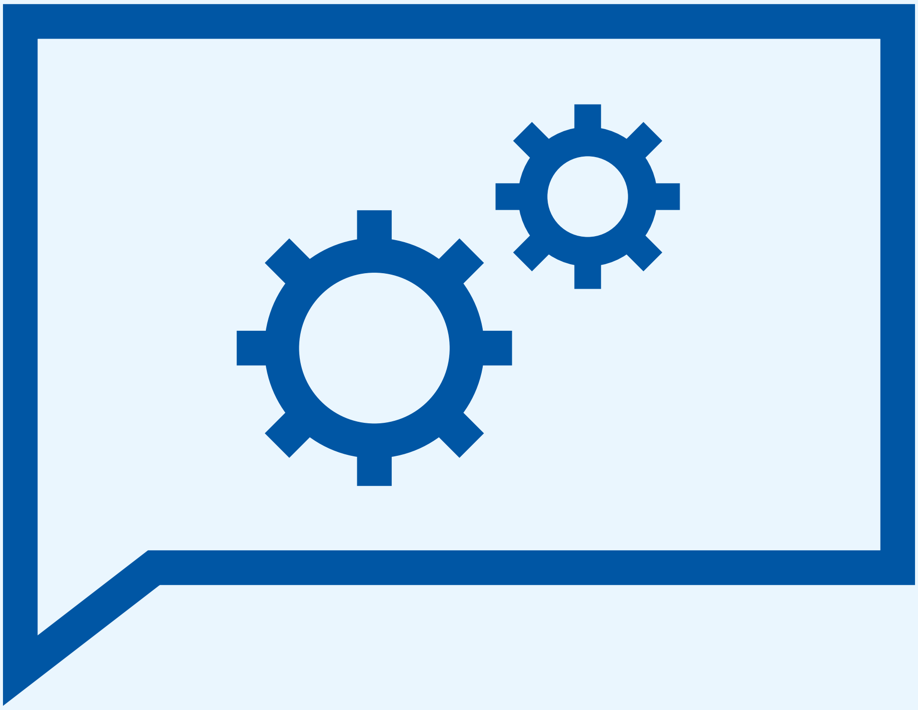
To make sure that every voice was heard, it was necessary in all three pilot projects to go through a carefully considered, inclusive process. Therefore, from the start, the pilot projects were designed to be wide-ranging, whilst respecting the focus and scope of the project, and ensured that the perspectives and points of difficulty faced by all the stakeholders were included. This is necessary to give the participants a feeling of ownership over the content and over the issues raised. This approach is important and necessary in order to gather as much information as possible in complete openness. It also increases the participants' identification with their specific uncertainties, concerns and preoccupations.

Possible feelings of tokenism were addressed, in each of the three pilot projects, by inviting in consensus workshops at least an equal number of patients/citizens compared to the total number of other stakeholders. Also, during every phase of the project, diversity (sex, ethnic- cultural background, language, discipline, disease symptoms…) and social inclusiveness were points of attention.

All members of the steering committees of the three pilot projects felt that inclusiveness and transparency was more easily achieved when the organiser can offer an independent dialogue platform. In all projects, at some point in the trajectory, participants indicated that the results were only achieved because the KBF, as independent organisation, provided such a sovereign platform.

And lastly, although the formats of the different phases are usually rigorous and well planned beforehand, the process should be flexible enough to allow people to change their minds, raise concerns or allow new perspectives to emerge during the dialogue. An experienced support team, seasoned in participatory methodologies but without previous involvement in the topic, and thus independent from other stakeholders, may be a welcome addition to the other members of the steering committee.

Diverging values and principles between different stakeholders or disciplines are likely and should be resolved in a fair and legitimate way.



12. USE ‘SYSTEMS THINKING’ TO UNDERPIN PRIORITIZATION

Many of the raised researchable questions are interrelated, some of them being dependent on the solving of other questions. Applying rules and techniques of systems thinking to tease out the interdependence of the questions, together with the barriers that hamper their resolution, would allow the identification of questions with the biggest leverage effect.

In systems theory, a system can be defined as a group of items that regularly interact with each other or are interdependent, forming a unified whole. Looking in a reductionist way to such systems – i.e. looking only at the level of the parts or elements – does not enable to fully depict or deeply understand the complex nature and dynamism of the problem field and identify the most appropriate solutions.

Systems thinking and systems theory could be helpful here. It is a set of synergistic analytical skills used to identify and understand systems and their elements, predicting their behaviors, and devising modifications to them in order to produce desired effects[11].

In none of the three projects, systems theory has been applied, or at least not in a systematic or dedicated way. In retrospect, all of the three pilot projects could have benefitted from such an approach. Not only to identify the measures with the biggest leverage effect, but also to understand the problem area in its many refinements and as a contribution to the mutual understanding of the problem field and its possible solutions.

An example of a systems thinking approach in the TSC field could have been the following: one of the priorities with the biggest leveraging effect could be the financing and setting up of in-depth and sustainable registries with patient information and intervention outcomes (priority 8). Such registries form an absolute prerequisite to solve many of the other questions in the TSC field, especially if these registries would be linked or coupled to a biobank or biorepository with patient bodily material (blood samples, tumor samples…). Properly constructed, sufficiently financed and well maintained, registries would tremendously support and advance our knowledge on the most common and most troubling symptoms of the disease, it would allow to study the natural course of the disorder, give insight in factors worsening or soothing symptoms, and get a grasp on interventions and treatments that benefit patients and their relatives the most. In short, setting up such an infrastructure would be helpful to answer at least 6 of the 7 preceding research priorities in TSC.

Systematically bringing to light the position of each of the researchable questions within the 'system' governing the problem field would have informed each of the dialogues at a higher level, without any doubt. It would not only have given insight into the interdependencies and relations of the various questions, but would also have allowed to explicitly identify the intrinsic goals of doing research on the individual questions and on the goals of TSC research in general. Whether introducing systems theory and systems thinking into the dialogues would have changed the priority list is uncertain. But it would have further supported the consensus building and led to even more mutual learning and common insight into the problem field. On the other hand, it would, undoubtedly, have added an extra phase to the dialogue.

> *Many of the raised researchable questions are interrelated, some of them being dependent on the solving of other questions.*

CONCLUDING OBSERVATIONS

THE DIALOGUE MODEL WORKS

Multi-stakeholder dialogues for setting research priorities combine a transactional process (working towards research priorities) with a relational process (leading to commitment, support and ownership). The dialogue model was successfully applied to three very different subjects: (1) research into a rare disease (tuberous sclerosis complex); (2) research into a combined medical-social problem, which is high on the policy agenda (returning to work after long-term disability); (3) research into a future disorder with high impact on patients and society (NASH), and how a commodity like biobanks might help turning the tide. All three dialogues have led to a list of research priorities that are not only shared and supported by all involved actors, but that have led (in two of the three cases) to a concrete implementation of a research agenda.

MUTUAL LEARNING IS AT THE CORE OF THE DIALOGUE PROCESS

A multi-stakeholder dialogue is in essence a social learning exercise. Participants learn from each other's experiences, perspectives and viewpoints. The dialogues combine theoretical knowledge with experience knowledge. Paradigm shifts occur: patients and relatives become *the* experts of their own disease because they have knowledge in fields that the traditional experts miss. Actors who have been in antagonist positions for many years suddenly discover common ground. Policy and decision-makers are confronted with how their policies are experienced in daily life by various impacted groups.

IN COLLABORATIVE STRATEGIES, THE CONTRIBUTION OF UNHEARD PATIENTS AND CITIZENS ADDS MOMENTOUS VALUE

If stakeholders are invited to health policy and research priority setting exercises, the people that are most confronted with these problems – patients, informal caregivers, citizens – are seldom invited. Usually they are 'represented' by one or more stakeholder around the table. Many claim to speak with the voice of 'the patient' or 'the citizen', or at least pertaining that 'they know what is best for these groups'.

The experience within these pilot projects constitutes evidence of the value of the voices of unrepresented patients and citizens, i.e. people who represent themselves and who testify from their own experiences. However, these voices can only contribute if a number of preconditions are met:

- These people are being surveyed employing the most optimal methods and procedures adapted to their capabilities and limitations;
- If upfront information is required, this is provided in a neutral, objective, understandable and transparent way;
- They are coached non-directively during the dialogue;
- Their contribution is valued equally to that of experts and other stakeholders.

Increasing the societal relevance in research by listening to *all* relevant stakeholders, also the voices that are usually silent, is an outcome that has clearly been achieved by all three projects.

A HIGH-PERFORMING MODEL FOR REAL-TIME HEALTH TECHNOLOGY ASSESSMENT

All three pilot projects can been seen as 'real-time' health technology assessment projects, integrating biomedical and healthcare research with social science and policy research from the outset, comprising investigations into research program mapping, communication and technology assessment. This integration informs and supports biomedical and healthcare research with explicit mechanisms to embed social values in innovations and to allow the ethical and legal framework to evolve side-by-side with the scientific, technological and medical progress.

ADDENDUM: COURSE AND OUTCOME OF THREE KBF PILOT MULTI-STAKEHOLDER DIALOGUES

PROJECT 1
RESEARCH PRIORITIES IN TUBEROUS SCLEROSIS COMPLEX (TSC)

HOW DID WE REACH A RESEARCH AGENDA?

INVOLVING THE RIGHT PEOPLE AND EXPLORING THE FIELD

14 JUNE 2016
Kick-off meeting with 5 TSC doctors and 1 patient organisation

7 SEPTEMBER 2016
Forming the Management Committee

GATHERING THE RIGHT RESEARCH QUESTIONS

PATIENTS AND FAMILIES PROCESS

22 MARCH 2017
Focus group session in Antwerp with 8 participants

MARCH-MAY 2017
13 individual interviews

62 research questions from patients and families

PROFESSIONAL EXPERTS PROCESS

DECEMBER 2016 – MARCH 2017
17 interviews with doctors, care providers, researchers and the industry

AUGUST-SEPTEMBER 2017
Delphi I: deepening and widening of research questions with 25 national and international professional experts

49 research questions from professional experts

16 COMMON RESEARCH QUESTIONS

INTERIM PRIORITISATION OF QUESTIONS

PATIENTS AND FAMILIES PROCESS

2 JUNE 2017
EU Conference with 6 European TSC patient organisations

16 priority research questions from patients and families

PROFESSIONAL EXPERTS PROCESS

SEPTEMBER - OCTOBER 2017
Delphi II: 25 professional experts vote on disease area, age groups and ranking of research questions

16 priority research questions from professional experts

SEEKING CONSENSUS AND PRIORITISATION

18 NOVEMBER 2017
Consensus conference: with 10 patients or family members and 11 professional experts

16 research questions from patients / families

16 research questions from professional experts

TOP 15 RESEARCH QUESTIONS

REPORTING AND DISSEMINATION

REPORTING AND PUBLICATION
3 pilot projects and methodology for priority setting

ADVOCACY

SUPPORT FOR RESEARCH

FOCUS AND SCOPE: RESEARCH IN TUBEROUS SCLEROSIS COMPLEX (TSC)

Tuberous sclerosis complex (TSC) is an incurable genetic condition that affects approximately 2 million people worldwide. Patient's lives are impacted on the one hand by the threat of tumour growth in brain, kidneys and lungs, and on the other hand by the daily burden of refractory epilepsy, disfiguring skin lesions or TSC-associated neuropsychiatric disorders (TAND). The quality of life, burden of illness and socio-economic impact of TSC are poorly researched. Symptoms are highly variable between patients, and the onset and evolution of symptoms change with age, further complicating clinical management.

Despite major breakthroughs in TSC research over the past decades, treatment options remain inadequate and largely confined to targeted treatments with mTOR-inhibitors (which have important side-effects and are not universally accessible) or surgery for epilepsy, brain- or kidney lesions in selected cases (targeting only part of the disorder). Biomarkers for prediction of disease burden, timing, or choice of treatment are lacking.
But also the support for families is in many cases suboptimal, both at the clinical and the non-clinical level.

STEERING COMMITTEE

Anna Jansen, pediatric neurologist,
UZ Brussel, Vrije Universiteit Brussel
Eva Schoeters, be-TSC
Annemie T'Seyen, King Baudouin Foundation
Bénédicte Gombault, King Baudouin Foundation
Peter Raeymaekers, LyRaGen – project management
Alain Wouters, Whole Systems – project management

SPECIFICITIES ON THE DIALOGUE FORMAT

Preparatory phase:

Mapping of the existing knowledge and research by drafting a status quaestionis paper.

Patients and relatives – consultation phase

Because of the rarity of TSC and the relative short existence of the Belgian TSC patient organisation (be-TSC), only a limited number of Belgian patients and relatives were known at the time of the beginning of the project. Therefore, it was decided to gather researchable questions during the consultation phase by means of a focus group and supplementary individual interviews with patients, parents of patients and spouses.

Patient and relatives – interim prioritization

Instead of organising a poll for interim prioritizing the gathered researchable questions in the 'patient track', a workshop was organised with representatives from 6 European TSC patient organisations. This group redefined and validated the questions, followed by an interim prioritization exercise partially based on mutual discourse aiming towards consensus and partly by individual voting.

Expert track – consultation phase in 2 stages

Because of the diversity in symptomatology in TSC, 17 Belgian and international clinical experts and researchers from various backgrounds were interviewed on knowledge gaps and their own research interests in TSC. The gathered researchable questions were presented by e-mail to a panel of 25 TSC experts for validation, deepening and broadening. Members of the steering committee processed the comments and regrouped the questions.

Expert track – interim prioritization

The resulting researchable questions were prioritized by e-mail voting by an international group of 25 experts.

Consensus and prioritization

A consensus conference was held with representatives from both the patient and the expert groups to exchange questions, to seek consensus and, finally, to define the top 15 priorities in TSC research.

OUTCOME

- Top 15 research priorities in TSC with the most pressing priority research to prevent, minimize, treat and manage the different TSC Associated Neuropsychiatric Disorders (TAND) in patients.
- A comprehensive research agenda in TSC with 60 unique researchable questions in 8 different areas: health services; natural history and phenotypic heterogeneity; family support; treatment and disease management; oriented basic and preclinical research; progeny and genetic testing; collaboration, synergy and capacity building; and TSC in society.
- 10 urgent needs that can be met immediately without the need for prior research.

RESEARCH PROGRAMMING AND IMPLEMENTATION

In 2018, KBF launched a call for research projects focussing on TSC Associated Neuropsychiatric Disorders (TAND) with the aim to better understand the processes (causes and mechanisms) underpinning the neuropsychiatric disorders associated with TSC and/or to translate and implement fundamental discoveries into better prevention, diagnosis, treatment or quality of care/life for patients with TSC and their relatives.

PROJECT 2
RESEARCH PRIORITIES AROUND RETURNING TO WORK AFTER LONG-TERM WORK DISABILITY

HOW DID WE REACH A RESEARCH AGENDA?

INVOLVING THE RIGHT PEOPLE AND EXPLORING THE FIELD

Consultation KBF and RIZIV/INAMI

↓

PUTTING THE RIGHT FOCUS ON THE PROJECT

STEP 1 – QUESTIONING STAKEHOLDERS

8 focus group sessions
- Personnel managers
- People with current or previous work disability
- Doctors & support providers for psychological disorders
- Doctors & support providers for musculoskeletal disorders
- General practitioners

Additional individual questions addressed to individual specialists in psychological disorders and general practitioners

TOTAL: 75 participants

4 focus group sessions with the steering committee of the Centre of Expertise
- Researchers
- RIZIV/INAMI experts
- Employers
- Employees
- Mutual health insurers

TOTAL: 40 participants

→ Identification of 322 obstacles and 155 good practices ←

↓

44 PRIORITY RESEARCH QUESTIONS

↓

HARVEST THE RIGHT TOPICS FOR RESEARCH QUESTIONS

STEP 2 – INTERNAL PROCESSING

Listing of identified:
- Obstacles
- Good practices

→ **Conversion of priorities into research questions**

→ **Selection of questions** according to the responsibility of the Centre of Expertise

→ **19 RESEARCH QUESTIONS**

↓

SEEKING CONSENSUS AND PRIORITISATION

STEP 3 – MULTISTAKEHOLDER WORKSHOP

First priority-setting process in 3 mixed groups

→ **Second priority-setting process in 3 mixed groups**

→ **Final individual voting on the top 10 for each group**

→ **10 PRIORITY RESEARCH QUESTIONS**

↓

REPORTING AND DISSEMINATION

REPORTING AND PUBLICATION
3 pilot projects and methodology for priority-setting

HELPING TO DETERMINE THE RESEARCH AGENDA OF THE CENTRE OF EXPERTISE

RIZIV/INAMI COMMUNICATION
on 23rd May 2018

FOCUS AND SCOPE: WORK DISABILITY

As in most industrialised countries, Belgium is facing an increasing number of sick, incapacitated citizens. More insight into the causes and evolution of disability is necessary in order to develop strategies that provide appropriate support for disabled workers, help to prevent disability for work, and promote return to the labour market of incapacitated people. The Centre of Expertise on Work Disability of the Belgian National Institute for Health and Disability Insurance (RIZIV/INAMI) studies the causes of work disability, the trends and relations with other areas of social security, etc. With the help of KBF, The Centre of Expertise wanted to identify research priorities in this field taking into account the views from stakeholders.

STEERING COMMITTEE

Saskia Decuman, head of the Centre of Expertise
on Work Disability at RIZIV/INAMI
Bénédicte Gombault, King Baudouin Foundation
Yves Dario, King Baudouin Foundation
Stefan Gijssels, Seboio – project management

SPECIFICITIES ON THE DIALOGUE FORMAT

Separate stakeholder consultations

From the start, the concept was designed to be very wide-ranging and to ensure that the perspectives and points of difficulty faced by all the stakeholders were included. On the other hand, the proposed research topics had to fall within the policy competences of the Belgian Federal Minister of Health.

Focus groups or individual interviews were organized with 1) patients and people with previous work disability; 2) psychiatrists and those supporting people with psychological disorders; 3) rheumatologists and specialists in musculoskeletal disorders; 4) personnel managers and human resources specialists; 5) general practitioners; 6) representatives of organizations representing employers, employees, self-employed people, and insurers; 7) researchers; 8) RIZIV/INAMI experts and doctors.

Internal processing

Members of the steering committee translated the results of the separate stakeholder tracks into research questions and carried out a filtering process deleting topics on which research had already been carried out and which do not come within the remit of the RIZIV/INAMI.

Consensus and prioritization

Two representatives from each of the stakeholder groups were invited for a multi-stakeholder meeting, together with four representatives from each of the patient groups. At the end of the day they collectively arrived at the research priorities.

OUTCOME

The question of returning to work after a long period of work disability is seen as a complex one by most of the stakeholders. There is a need for more knowledge and information, there is a need for more consultation between all those involved, more attention needs to be paid to the driving forces for all those involved, and also to the emotional component among employees. These topics were translated in a consensual list of 10 top priorities. Above all, the stakeholders want research into pragmatic solutions that have proved to be successful.

RESEARCH PROGRAMMING AND IMPLEMENTATION

The research institute on work disability of the RIZIV/INAMI is using the results of the multi-stakeholder dialogue directly as input for developing its new research and study program for the next year(s) and for allocating appropriate research budgets to this program. The proposal has first been approved by the minister and in a second phase has to be approved by the insurance committee of the RIZIV/INAMI, which comprises all the stakeholders who have also participated to the dialogue.

PROJECT 3
RESEARCH PRIORITIES IN NON-ALCOHOLIC STEATOHEPATITIS (NASH) TO WHICH BIOBANKS CAN CONTRIBUTE

HOW DID WE REACH A RESEARCH AGENDA?

INVOLVING THE RIGHT PEOPLE AND EXPLORING THE FIELD

23 MARCH 2017 Exploratory workshop

↓

PUTTING THE RIGHT FOCUS ON THE PROJECT

30 JUNE 2017
Focus and scope meeting

Liver disease x biobank → Criteria to determine a focus (determined by citizens, patients, hepatologists and biobank managers) → **NASH** x biobank

↓

HARVEST THE RIGHT TOPICS FOR RESEARCH QUESTIONS

FOCUS GROUP BIOBANK MANAGERS (15)
4 OCTOBER 2017

FOCUS GROUP CITIZENS AND PATIENTS (14)
14 NOVEMBER 2017

FOCUS GROUP INDUSTRY (6 pharma & biotech representatives)
17 NOVEMBER 2017

SURVEY CLINICIANS
14 NOVEMBER 2017
Mailing list BASL and Belgian Week of the Liver with 21 respondents

90 NASH RESEARCH QUESTIONS

Can the research question be formulated again to avoid overlap?

Has the research question already been (partly) solved?

Can the research question be solved by research?

23 FILTERED NASH RESEARCH QUESTIONS

↓

SEEKING CONSENSUS AND PRIORITISATION

12 JANUARY 2018
Steering committee selects from the 23 NASH questions the questions with a possible contribution of biobanks

→

2 FEBRUARY 2018
Consensus meeting with all the involved stakeholders

→

25 MAY 2018
Feedback from ethics experts

↓

REPORTING AND DISSEMINATION

REPORTING AND PUBLICATION
3 pilot projects and methodology for priority-setting

FOCUS AND SCOPE: NASH & BIOBANKS

The original focus and scope of the project was to prioritize research questions in liver diseases to which biobanks can contribute. The term biobank refers to a structured collection of human biological specimens (such as tissue, bold, urine, …) and associated data (including demography, history of illness, treatment and clinical outcomes, lifestyle, health parameters…) stored for the purposes of present and future research. Liver diseases encompass infectious, malignant and chronic disease processes arising from a wide range of aetiologies, including viral hepatitis, alcohol and non-alcohol fatty liver disease. Cirrhosis and primary liver cancer represent the end-stage of most liver pathologies.

During the process, the focus and scope of the project was redirected to research priorities in non-alcoholic liver disease, also called non-alcoholic steatohepatitis (NASH), and how biobanks can contribute in answering these questions.
A second objective was to contribute to the development of a long term dialogue by identifying future challenges on biobanks, taking into account the perspective of various stakeholders, with the aim to create a dynamic and a platform for future reflexions.

STEERING COMMITTEE

Sofie Bekaert, Bimetra and Biobank, UZ Gent
Peter Starkel, hepatologist UCL Saint-Luc
Hans Van Vlierberghe, hepatologist UZ Gent
Annelies Debucquoy, BBMRI and KU Leuven
Laurent Dollé, ULB and BWB
Bénédicte Gombault, King Baudouin Foundation
Annemie T'Seyen, King Baudouin Foundation
Peter Raeymaekers, LyRaGen – project management
Alain Wouters, Whole Systems – project management

SPECIFICITIES ON THE DIALOGUE FORMAT

Focus and scope workshop

During a multi-stakeholder workshop, a number of criteria were brought forward for setting the focus and scope of the project. When applying these criteria to all liver diseases, non-alcoholic fatty liver disease (NASH) was selected to best meet the criteria (focus) since it is an upcoming liver disorder, creating an increasing burden in terms of human suffering and societal impact, for which research needs to be prioritized and for which the contribution of biobanks can play a decisive role. Within NASH, an evolving liver syndrome starting with a fatty liver and gradually moving towards liver cirrhosis and/or liver malignancy (if not stopped), all questions regarding risks factors, epidemiology, disease progression, physiopathology (also at cellular and molecular level), diagnosis, prognosis, therapy, patient support … were considered within the scope of this project. Also how premedical states like overweight, insulin resistance, high blood pressure, dyslipidemia and a sedentary lifestyle links to the formation and evolution of NASH.

Separate stakeholder tracks

Focus groups were organized with biobank managers (15 participants) and representatives from pharma and biotech (6 participants). A full day bilingual workshop with patients and citizens was also organized (14 participants). Liver specialists and researchers were surveyed with a questionnaire with open questions (21 respondents).

Internal processing

Members of the steering committee translated the results of the separate stakeholder tracks into researchable questions and carried out a filtering process, deleting topics which were already answered by previous research.

Consensus and prioritization – 2 phases

In a first phase, the complete steering committee prioritized the researchable NASH questions based on the possible contribution of biobanks. A number of questions were no longer maintained for further discussion because biobanks cannot contribute to their solution. These questions are therefore reported separately.

In a second phase, the remaining researchable questions were prioritized according to societal prominence during a multi-stakeholder consensus meeting, including citizens and patients together with hepatologists, researchers and biobank managers.

OUTCOME

During the consensus conference, 14 researchable NASH questions were retained to which biobanks can contribute. For a first group of 3 imminent researchable questions, biobanks can have an immediate and high impact. A second group of 3 highly ranked NASH-questions cannot be solved without the input from biobanks, but they need to evolve in the direction of population based biobanks (instead of hospital based) with a long term follow up of the sample donators.
Furthermore, 28 biobank challenges were retained.

RESEARCH PROGRAMMING AND IMPLEMENTATION

In a first phase, the results of the project were presented in the presence of several people who had participated in one or more phases of the project, to a number of ethicists, lawyers and philosophers who are familiar with the world of biobanks. Rather than emerging into a research programming and implementation phase, this project aims to be the start of a continued dialogue between the various stakeholder groups in order to promote and advocate the use of biobanks as a precious common good in order to advance biomedical research for the benefit of citizens, patients and society.

REFERENCES

1 **Manafò E, Petermann L, Vandall-Walker V, Mason-Lai P**. *Patient and public engagement in priority setting: A systematic rapid review of the literature.* PLoS One. 2018 Mar 2;13(3):e0193579. doi: 10.1371/journal.pone.0193579.

2 **Raeymaekers P**, **Crowe S**, **Cowan K**, **Broerse J**, **Hertz-Pannier L**. *Mind the Gap! Multistakeholder dialogue for priority setting in health research.* April 2016. https://www.kbs-frb.be/en/Activities/Publications/2016/20160426PP

3 RIZIV/INAMI is the Belgian National Institute for Health Research and Disability Insurance.

4 **Crowe S**, **Giles C**. *Making patient relevant clinical research a reality*. BMJ. 2016 Dec 23;355:i6627. doi: 10.1136/bmj.i6627.

5 **Domecq JP**, **Prutsky G**, **Elraiyah T**, **Wang Z**, **Nabhan M**, **Shippee N**, **Brito JP**, **Boehmer K**, **Hasan R**, **Firwana B**, **Erwin P**, **Eton D**, **Sloan J**, **Montori V**, **Asi N**, **Dabrh AM**, **Murad MH**. *Patient engagement in research: a systematic review.* BMC Health Serv Res. 2014 Feb 26;14:89. doi: 10.1186/1472-6963-14-89.

6 *The James Lind Alliance.* Guidebook, version 7, March 2018. http://www.jla.nihr.ac.uk/jla-guidebook/downloads/Print-JLA-guidebook-version-7-March-2018.pdf

7 **Abma TA**, **Pittens CA**, **Visse M**, **Elberse JE**, **Broerse JE**. *Patient involvement in research programming and implementation: A responsive evaluation of the Dialogue Model for research agenda setting.* Health Expect. 2015 Dec;18(6):2449-64. doi: 10.1111/hex.12213.

8 **Viergever RF**, **Olifson S**, **Ghaffar A**, **Terry RF**. *A checklist for health research priority setting: nine common themes of good practice.* Health Res Policy Syst. 2010 Dec 15;8:36. doi: 10.1186/1478-4505-8-36.

9 Participants were informed upfront that only aspects that fell within the competence of the Belgian federal Minister of Public Health would be retained in this project.

10 **Slocum N**, **Steyaert S**, **Berloznik R**, **Beyne C**, **Rauws G**. *Participatory Toolkit, a practitioner's manual, 2003.* Delphi, pp. 75-86.

11 **Arnold RD** and **Wade JP. A** *Definition of Systems Thinking: A Systems Approach.* Procedia Computer Science, 44 (2015) 669-678. doi: 10.1016/j.procs.2015.03.050

CURIOUS TO LEARN MORE ABOUT PRIORITY SETTING AND THE THREE PILOT PROJECTS? HAVE ALSO A LOOK AT OUR OTHER PUBLICATIONS

Multi-stakeholder dialogue for priority setting in health research (2016)
Working together to set research priorities around returning to work after a long-term work incapacity (2018)
Working together to set research priorities for Tuberous Sclerosis Complex (2018)
Working together to set research priorities for NASH with an optimal contribution of biobanks (2018)

MIND THE GAP!

MULTI-STAKEHOLDER DIALOGUE FOR PRIORITY SETTING IN HEALTH RESEARCH. SHARING EXPERIENCES FROM 3 PILOT PROJECTS.

A publication of the King Baudouin Foundation
rue Brederodestraat 21
B-1000 Brussels

Author **Peter Raeymaekers** LyRaGen

Coordination King Baudouin Foundation
Gerrit Rauws Director
Yves Dario Senior project coordinator
Bénédicte Gombault Senior project coordinator
Annemie T'Seyen Senior project coordinator
Laurine Vanackere Project & knowledge manager

Graphic design **Signelazer**

With the support of the (Belgian) National Lottery

Legal deposit **D/2893/2018/34**
Order number **3608**
January 2019

King Baudouin
Foundation
Working together for a better society


mind
the
gap!