**Future of evidence ecosystem series: 3. From an evidence synthesis ecosystem to an evidence ecosystem**

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**Abstract (196 words/200)**

The “one-off” approach of systematic reviews is no longer sustainable; we need to move toward producing “living” evidence syntheses (i.e., comprehensive, based on rigorous methods, and up-to-date). This implies rethinking the evidence synthesis ecosystem, its infrastructure and management. The three distinct production systems — primary research, evidence synthesis and guidelines development — should work together to allow for continuous refreshing of synthesized evidence and guidelines. A new evidence ecosystem, not just focusing on synthesis, should allow for bridging the gaps between evidence synthesis communities, primary researchers, guidelines developers, health technology assessment agencies, and health policy authorities. This network of evidence synthesis stakeholders should select relevant clinical questions considered a priority topic. For each question, a multi-disciplinary community including researchers, health professionals, guidelines developers, policymakers, patients and methodologists needs to be established and commit to performing the initial evidence synthesis and keeping it up to date. Encouraging communities to work together continuously with bidirectional interactions requires greater incentives, rewards and the involvement of healthcare policy authorities to optimize resources. A better evidence ecosystem with collaborations and interactions between each partner of the network of evidence synthesis stakeholders should permit living evidence syntheses to justify their status in evidence-informed decision-making.

**Keywords:** systematic review, evidence synthesis ecosystem, evidence ecosystem, living evidence, primary research

**What is new?**

- Reinforcing the link between trialists and systematic reviewers is a major objective to implement a virtuous circle of continuous improvement in the quality of evidence, in primary research and therefore in future evidence synthesis.
- Our expectations regarding the synthesis of evidence need to be rethought by considering a synthesis as a product in a process of continuous extension and improvement rather than a finished product valid at a single time.
- Implementing living network meta-analyses and living clinical practice guidelines will help in outlining what is not known, allow for assessing the trustworthiness of the evidence and help the research community streamline future clinical trials and focus on areas of deficient evidence.

## INTRODUCTION

An accurate, concise, up-to-date and unbiased synthesis of available evidence is arguably one of the most valuable contributions a research community can offer patients, healthcare providers, guideline developers, funders, health policy-makers or health systems managers and other decision-makers [1]. Changes in healthcare research, advancements in technology and the development of new methods are converging in new ways to produce higher-quality evidence synthesis (i.e., based on more rigorous methods and a timely, comprehensive search) for better healthcare decision-making. However, these developments imply rethinking the evidence synthesis ecosystem, its infrastructure and management and to move toward an evidence ecosystem.

For clinical research, we can no longer afford the "one-off" approach of systematic reviews relying on repeated construction and deconstruction of ephemeral review teams in a "staccato" fashion [2]. A system based on multiple initiatives arising from uncoordinated groups of researchers working to answer narrow questions focusing on only some of the various treatments of interest at one point in time is questionable. Such a state is frequently inefficient, wastes time and resources and leads to a fragmented global picture of evidence (Future of evidence ecosystem series: 1. Introduction — Evidence synthesis ecosystem needs dramatic change; this issue). We need to move toward producing "living" evidence syntheses — comprehensive, based on rigorous methods, up-to-date evidence syntheses, and updated as new research becomes available [3]. Better coordination is needed to identify enduring questions and allocate them globally. For each topic, a large, multi-disciplinary research community is needed to undertake the effort and commit to maintaining an up-to-date synthesis over time.

Crucially, there is also a need to bridge the gap between the evidence synthesis community and trialists who are positioned at the beginning of completed trials being

synthesized and future trials being planned and conducted. Currently, there are three distinct production systems that largely function in parallel and without any systematic integration: primary research (i.e., clinical studies and other research studies), evidence synthesis and guidelines development. However, these production systems are actually highly interdependent, but such interdependency is limited to data and not organisation. They all contribute to the overall evidence production system. To accelerate the pace of production of relevant evidence, improve the efficiency of this system and facilitate translation into practice, a global community of communities bridging cultures, countries and scientific disciplines needs to be built. This community would be a large-scale, global, learning health system that can continuously and routinely improve itself.

## 1. RETHINKING EVIDENCE SYNTHESIS

### 1.1 Encouraging communities to work together and co-create to allow for continuous refreshing of synthesized evidence

High-quality evidence synthesis is a public good [1] that needs to be permanently refreshed to be up-to-date and useful. Such an updating process, which is increasingly becoming cumbersome and complex, requires the involvement of many researchers. Greater incentives and rewards are needed to promote the enormous effort required to produce a high-quality systematic review and for updating over time. Furthermore, these communities would be engaged in a process of co-creation in which input from consumers but also other decision makers will play a central role from beginning to end.

### 1.2 Rethinking the link between primary research and future evidence synthesis

The link between primary evidence and evidence synthesis could be viewed differently. To adequately plan their trials, trialists should be aware that results of only a very few trials

definitively change practice. Findings from most trials help build evidence by being integrated in a systematic review. For example, estimates from systematic reviews are used to inform sample size calculation; knowledge gained in previous trials such as recruitment, retention, and outcome measurement is used to help plan and conduct new trials efficiently. Furthermore, results of initial trials published in high-impact journals are frequently contradicted or the benefits are less strong that initially suggested [4]. Trialists must anticipate that the results of their trials will be integrated later in a systematic review and meta-analysis. Therefore, in addition to ensuring that their study sample size can adequately adress the question being posed, they should also compute the trial sample size to be able to potentially change meta-analysis results and record all important outcomes even if they are belived to be not informative at the trial level (e.g., safety) [5,6]. Furthermore, creation of standards for reporting data could allow to bypass the data extraction process and include the data straight from primary producers to synthesize.

### 1.3 Optimizing the trade-off between speed and thoroughness

Evidence synthesis is an evolving field of research. Over time, the complexity and rigor of methods used in reviews have increased considerably. The mechanisms established for producing high-quality up-to-date systematic reviews are resource-intensive, and timely generation of the reviews is challenging. Dealing with multiple sources of data (Future of evidence ecosystem series: 2. Current opportunities and need for better tools and methods; this issue) further compounds the work of systematic reviewers. The delay from the decision to perform a review to its completion is increasing. However, all stakeholders (clinicians, researchers, policymakers) are making daily decisions and need syntheses of evidence that could inform these decisions. The increased complexity of the methods and quality checks delay the release of reviews and must be balanced against the benefits provided by these methods.

A good-enough version (of evidence synthesis) available before making a decision is much more valuable than a perfect version that arrives a day too late [1]. In contrast, an evidence synthesis of poor quality and insufficiently rigorous is useless or even harmful. We need to rethink our expectations regarding the synthesis of evidence by considering a synthesis as a product in a process of continuous extension and improvement (allowing us to have the best possible synthesis at all times) rather than a finished product valid at a single time. The extent of thoroughness required to address a given question may vary from one topic to another and the "one size fits all" approach is not the best option.

### 1.4 Tailoring the end-products of evidence synthesis to stakeholder needs

The end users of evidence syntheses are multiple and have different needs that must be taken into account when designing and developing the products derived from evidence syntheses. These products could have varying format and sizes, different focus of content, and different language complexity and could be translated into different languages. Beyond the full review that must be as detailed as possible for researchers, different versions of the synthesis report could be prepared for the public, physicians, policymakers and others [7]. As an example, rapid reviews (i.e. a type of knowledge synthesis for which the steps of the systematic review are streamlined or accelerated to produce evidence in a shortened timeframe) have been proposed as an approach to provide actionable evidence in a timely manner for policymakers[7]. The co-creation process would help in producing such tailored outputs.

### 1.5 Recognizing the importance of research on evidence synthesis

A culture shift in the community (research funders, research institutions, journalists etc.) is needed to recognize that evidence synthesis is intellectually challenging and must be considered a respected activity that needs to be funded and rewarded like any research activity [1]. Indeed as an example, the NLM classifies systematic reviews and research articles

differently. Furthermore, systematic reviews are rarely highlighted by journalists despite the higher level of evidence. The recognition is currently geographically inconsistent [4]. Furthermore, research on evidence synthesis methods must be recognized as an important field of research considering the permanent need to develop and validate innovative and complex methods to respond to the emergence of new data sources and data types as well as the evolution of needs and expectations of end users.

## 2 DEVELOPING A HARMONIZED INTERNATIONAL WORK PLAN

Moving toward the new evidence synthesis ecosystem and encouraging communities to work together continuously will require greater incentives and rewards for all stakeholders. To achieve this goal, mechanisms of funding, the research evaluation framework and the dissemination practices of evidence syntheses need to be better aligned.

### 2.1 Selecting priority topics and distributing workload globally

The huge amount of work requires a distribution of the workload at the international level. Multiple teams all over the world are dedicating time and resources to produce evidence syntheses, which are overlapping and redundant. We need to collectively rethink the needs of evidence community and create a marketplace for evidence synthesis in which all stakeholders will find the evidence they need on a specific topic. The evidence synthesis ecosystem must be organized at a global level with a geographically widespread reach rather than geographically localized distribution of work.

Because all topics of interest cannot be covered, priorities should be defined. The criteria for defining these priorities could be related to the burden of disease and topics for which the pace of evidence change is the fastest. For each relevant clinical question considered a priority topic by the network of evidence synthesis stakeholders, one living

evidence synthesis community needs to be set up to perform the initial evidence synthesis and keep it up to date.

Furthermore, at one point, the research question may not be relevant anymore, and consequently the living systematic review should be stopped. In other situations, the living systematic review could become an open-ended activity. Hence, communities must have a process to determine when the living systematic review should be closed.

### 2.2 Setting up living evidence synthesis communities

Groups of researchers, health professionals, guidelines developers, policymakers, patients or their representatives and methodologists interested in a particular theme could take the lead for a given topic. These living groups will commit to ensuring the long-lived rather than ephemeral maintenance of the evidence synthesis on this topic, thereby creating a unique marketplace for this topic in which all stakeholders will find the current best evidence. The community could encourage deep engagement (and in particular that of end-users) to exchange perspectives and understand priorities and help create a positive climate of collaboration. This community will be in charge of performing the initial evidence synthesis for the question of interest and keeping the synthesis up-to-date over time. This initial evidence synthesis should be a Network Meta-Analysis (NMA), namely a technique for comparing three or more interventions simultaneously in a single analysis by combining both direct and indirect evidence across a network of studies. A different approach from a one-off publication in a prestigious journal is needed for publishing such reviews, such as an online community with alerts for practice-changing updates.

To ensure both the diversity of viewpoints and the dissemination of results, involving people from different countries, specialties and cultures is especially important. The living evidence synthesis community would consist of different open embedded groups, in which contributors

can move in and out but share common research principles, scientific goals and methodological approaches. The different groups can have different backgrounds and skills (e.g., anyone interested in the disease, including patients or their representatives, clinicians, trialists, methodological experts) and so will have different specific tasks in the evidence synthesis process [8]. These communities will share the same values, methods and principles (e.g., for conflicts of interests) but would be allowed to adapt their methods and objectives to their topic of interest and to the needs of stakeholders in their specific area. Particular attention and specific safeguards should be in place to avoid the undue influence of lobby bodies such as the pharmaceutical industry. The role of each community member and their conflict of interest should be completely transparent. As an example, the need for using observational data in evidence synthesis may be different in domains for which few randomized controlled trials exist (e.g., surgery) as compared with domains for which multiple randomized controlled trials are available. Furthermore, the benefits of incorporating real-world data must be systematically considered. We have already described an example of such a community in paper 2 (section 2.2. Living network meta-analyses, and Figure 1).

Some initiatives such as the SPOR Evidence Alliance, a Canada-wide alliance of researchers, research trainees, patients, healthcare providers, policy makers and organizations who use research to inform decisions, would help to build capacity for such communities. The SPOR Capacity Development Framework offer multidisciplinary mentorship opportunities in knowledge synthesis and knowledge translation and has the goal to build a culture of interdisciplinary collaboration [9].

### 2.3 Reinventing a new reward system for living evidence synthesis

Evidence syntheses must be quickly discarded once outdated [1]. An open-access repository in which all living evidence syntheses produced collectively can be saved, shared, updated over time and retrieved by each stakeholder seems the best option for wide dissemination and

ensuring timely updates. The aggregated data extracted could also be shared to allow for data verification or re-analysis by the research community. However, the current reward system, mainly based on publication in peer-reviewed journals, is challenged because no publications per se are needed in this new system. The currently prevailing reward system could be a major barrier particularly for young contributors. Requesting digital object identifiers for the analysis results and data could be a solution [10]. We could also consider that a publication in peer-reviewed journals is necessary when evidence on benefits/harms changes, or we could propose to regularly publish a document of the state-of-the-art of available evidence for the clinical question of interest.

The usual peer-review process will also be challenged by such an approach because it would considerably delay access to information, which will not be acceptable. Alternative forms of publication (e.g., preprint publication) or peer-review (e.g., post-publication peer-review) need to be considered to allow rapid access to the information.

A collaborative reflection exercise is needed to refine the current reward system and properly reward researchers commensurate with their contribution over time.

### 2.4 Future role of organizations such as Cochrane

International organizations are the best placed to govern, organize and implement such a fundamental change to the system. The main features expected for these organizations are credibility, broad international presence, independence from the main lobby bodies, and interest in evidence building. Such organizations will have to the identify enduring questions and their allocation globally.

Cochrane has the historical legitimacy, a network of trained members and volunteer contributors, and the organizational capacity. Cochrane has demonstrated its capacity to scale evidence synthesis in health and to involve a large number of volunteers, train its volunteers, and develop and make use of the same methods by all, to ensure that the level of quality is

consistent despite the diversity of topics and contributors. Cochrane could have a potential future role in prioritization, setting up teams, hosting evidence syntheses, methodological developments, and advocacy. However, Cochrane would have to go far beyond its comfort zone (i.e., evidence synthesis) to take the lead in this area (primary evidence and evidence synthesis). In the same spirit, the Joanna Briggs Collaboration, involving 70 Collaborating Entities across 34 countries, contribute to improve in the quality of healthcare globally through the delivery of high quality programs of evidence synthesis for end users, including transfer and implementation [11].

Such organizations could act as important facilitators and essential partners with any new or existing or network of organizations (e.g., The International Network of Agencies for Health Technology Assessment) wishing to take the lead.

### 2.5 Optimizing resources by involving agencies for health technology assessment

Many actors involved in evidence synthesis (researchers, Cochrane members, Health Technology Agency staff, guideline developers) perform systematic reviews and meta-analyses in an uncoordinated manner, frequently without knowing that another team in the world is doing the same work. These syntheses are often redundant, and even if their objectives and methods may be slightly different, their overall aims and processes are very similar. Independent duplication of efforts to solve questions may be useful. However, replication/duplication is much more likely to be useful if it is an informed and reasoned choice. Coordinating these efforts would help avoid duplicate or overlapping systematic reviews. It would also help to dedicate more resources for research that at least part of the scientific community considered collegially as useful and important, thereby allowing for

faster and more efficient reviews. Furthermore, involving both systematic reviewers and the potential targeted audience throughout the process of evidence synthesis in designing the question, governing the process and interpreting the findings should help improving the relevance of reviews for decision-makers. Funding sustainable infrastructures in charge of such ecosystems rather funding short projects might also ensure that it is not a one-shot initiative.

## 3 MOVING FROM AN EVIDENCE SYNTHESIS ECOSYSTEM TO AN EVIDENCE ECOSYSTEM

Evidence synthesis requires brokerage at the interface of public life and academia. Improving collaboration will bring academics, policymakers, practitioners, funders and publishers closer to a world in which decision-making can be built on solid ground [1]. Currently, primary research, evidence synthesis and guidelines development and adoption of evidence into clinical practice are largely siloed. However, they are interdependent, and any improvement in one component of the system will benefit the whole system. A natural objective would be to bring the different communities together for their mutual benefit. As an example, we could assume that collecting data on the transparency of trials during a systematic review and disclosing these data will eventually improve the transparency of primary research and therefore the quality of subsequent systematic reviews. In the same way, developing living meta-analyses will help accelerate the production of up-to-date guidelines. The living evidence synthesis communities would be extended to living evidence communities involved in evidence synthesis and also in primary evidence generation and evidence translation to guidelines. This development would be conceived in the context of the broader system with bidirectional interactions with stakeholders.

### 3.1 Creating feedback loops between living evidence synthesis and primary research communities

Reinforcing the link between trialists and systematic reviewers is a major objective to implement a virtuous circle of continuous improvement in the quality of evidence, improvement in primary research and therefore improvement in the quality of future evidence synthesis. Moreover, highlighting the unsolved clinical questions gives pointers to scientists, policymakers and funders on potential lines of enquiry to fill knowledge gaps [12].

- **Living monitoring of methodological quality of trials**

Asking systematic reviewers to collect a limited number of additional data when they are performing their review should be doable. The incremental cost of collecting additional data at this stage represents a limited and manageable effort with significant potential long-term benefits.

Some of the data necessary for monitoring the methodological quality of trials are already extracted for most reviews (e.g., items to assess the Cochrane Risk of Bias tool [RoB]). For example, systematic reviewers could check whether a Core Outcome Set is proposed for the disease and recorded in the trial report or could identify major methodological issues.

Providing access to this information will help trialists improve the planning of their future trial by avoiding reproducing some methodological errors or forgetting essential outcomes and therefore decrease the waste in future research. In fact, we are convinced that no trialist would be satisfied with planning a trial that will later be considered at high risk of bias or that could not be included in evidence synthesis because outcomes were not recorded and that they would modify their design if they were aware of it before the trial began.

- **Living monitoring of transparent reporting of trials**

In the same way, we could perform a living monitoring of the transparent and complete reporting of trials by assessing the quality of reporting for the most important items. We could perform a permanent audit of the rate of publications and posting of trials, their compliance with the 2007 US Food and Drug Administration Amendments Act (FDAAA) that requires sponsors of trials in the United States to post results on ClinicalTrials.gov and the European Union requirement to post results on the European Clinical Trials Database (EudraCT).

Furthermore, we could use the RoB assessment as a marker of the completeness of reporting. Indeed, with the new version of the RoB tool (RoB 2.0), all signaling questions rated by systematic reviewers as "No information" are considered poorly reported. The evaluation of the completeness of reporting and the extraction of results as soon as a trial is published could be performed systematically. An immediate contact with investigators could clarify the reporting. Investigators contacted immediately after the trial is published would probably be more likely to clarify the information as opposed to several years after the end of the trial when a systematic review is performed. Finally, it would be useful to ask the investigators of each trial if they would give access to the protocol of their trial or if they would agree to share their data and under which conditions.

- **Living reporting system of the quality, transparency and accessibility of data**

All these data would then be used for a living disclosure of the quality and transparency of reporting. The mapping and disclosure by medical specialties, journals, funders or universities of research transparency would likely have a positive effect on various stakeholders and would help raise awareness about the waste related to poor reporting, thereby motivating actors to develop quality improvement programs. In the same way, a mapping of the stakeholders who make their data publicly available would be useful [13].

We can also have a more proactive and incentive approach to improve transparency by identifying on ClinicalTrials.gov and EudraCT all trials as soon as they are terminated and systematically encouraging principal investigators via automatically generated emails to post their results on registries within 1 year after the end of the trial. This approach has already demonstrated its impact in a randomized trial [14]. We could also encourage investigators to give access to their protocols, publish their results and archive their data and direct them to practical repository solutions to share their data if needed.

- **Living mapping of research**

Having a global view of the research already carried out or in progress (and its state of advancement) is crucial for researchers who will plan a research project, funders who will decide whether or not to fund new research and institutional review boards who will assess its ethical nature. Accessing this information is not straightforward because the data needed to perform this mapping are scattered, and creating a global observatory for health research and development has been advocated [15]. Living mapping of evidence for one specific topic of interest can be built to represent both current (all existing trials) and also ongoing evidence (all ongoing trials). This mapping would improve the coordination of clinical research by helping trialists plan their future trial and choose the most relevant comparator and inclusion/exclusion criteria as well as guide the allocation of public resources by funders. Funders might also think more imaginatively by funding research ecosystems around a prioritized topic rather than separate evidence syntheses and primary research. Such a research "programme" is likely to require more funds than the small amounts available for answering specific isolated questions, and many funders' budgets will simply not cover all conditions in this way. Nevertheless, such a joined-up system of funded evidence syntheses, platform trials [16] that can quickly add a new drug, or a comparison identified in an NMA, and a living guidelines group and clinical research community could be a very powerful and

efficient way for conducting research rather than the piecemeal and "stop/start" culture than currently prevails.

- **Living individual participant data network meta-analysis**

For some specific and well-chosen questions (i.e., when the additional work is justified by its benefit to the end user), the ultimate goal would be to access individual participant data (IPD) rather than aggregated data and to perform living individual participant data NMA. IPD data are considered the gold standard for evaluating the intervention effects in pairwise meta-analysis and NMA because they allow for properly evaluating assumptions and handling the potential for bias from several sources; furthermore, they would allow for assessing the effect of interventions in subgroups of patients. This goal, which seemed completely unrealistic and unattainable only a few years ago, now seems more likely to be achievable, even within a few years. The lack of data sharing is recognized as a waste in research and is becoming increasingly politically inappropriate. Several organizations, funders and pharmaceutical companies have been brought together in an effort to support large-scale data sharing, and this is expected to boost the availability of IPD data in the wider research community.

### 3.2 Bridging the gaps between evidence synthesis communities, clinical practice guidelines developers, agencies for health technology assessment, health policy authorities and primary researchers

A new evidence ecosystem should allow for bridging the gap between not only systematic reviewers and trialists but also with developers of clinical practice guidelines.

Living NMA provides a network of current evidence for the clinical question of interest representing all treatments assessed and trials performed in this setting**.** It offers constant access to updated global evidence synthesis and may help improve real-time knowledge transfer from systematic reviews and meta-analyses to clinical practice guidelines.

This living NMA repository would be the marketplace for evidence synthesis, whereby groups of guideline developers will find the best evidence and access to the data that were extracted. They could re-use these data, reanalyse all or some of these data, add other data and thus produce locally relevant and applicable guidelines. For example, they could decide to consider only data of trials performed in relevant settings according to their geographic area. The ultimate goal will be to reach the step of implementing "living clinical practice guidelines" [17–19].

Currently, only a small number of clinical guidelines are based on a high certainty of evidence [20–24] as mentioned in paper 2. Therefore, we need to bridge the gaps between guidelines developers and primary researchers. Implementing living NMA and living clinical practice guidelines will help in outlining what is not known, will allow for assessing the trustworthiness of the evidence underlying each recommendation and will therefore help the research community streamline future clinical trials and focus on areas of deficient evidence to expand the evidence base from which clinical practice guidelines are derived.

### 3.3 Create links between living evidence synthesis communities and decision-makers

The creation of a partnership with decision-makers, such as guidelines developers, regulators and governments, will help support, promote and sustain the paradigmatic and cultural shift to living evidence synthesis for each priority topic selected [25]. All stakeholders, including decision-makers, should be involved throughout the whole process.

### 3.4 Moving toward a global learning health system

From a broader perspective, we need to set up a global learning health system with positive feedback loops in real time to improve the global system of evidence production. For each topic or question of interest, a community can be constituted and a learning system developed. All these systems contribute to the overall learning system. Cochrane seems naturally in an

excellent position to coordinate this learning system. However, some activities of such living evidence communities would require Cochrane to step far outside its current scope, agree to extend its field of action and accept a fundamental change in its activity and organization. This move would imply profound questioning and changes to remain innovative, competitive and attractive in an expanding marketplace of evidence.

Figure 1 summarizes the idea of a continuous improvement of clinical research and Box 1 the different steps to facilitate the implementation of this new evidence ecosystem.

## CONCLUSION

Despite the multiple challenges, the network of evidence stakeholders must bring their longer-horizon efforts in line with the pragmatic questions of importance to patients, physicians and decision-makers. This new approach may offer an innovative solution to the current problems with and the imperative need to provide up-to-date evidence synthesis of all available treatments for a specific clinical question.

Reinventing the global system of producing evidence needs to overcome the scientific, technical and logistical challenges and the constraints of the current scientific system.

A better evidence ecosystem will require collaborations and interactions between each partner of the network of evidence synthesis stakeholders. Links between the living evidence synthesis community and agencies for health technology assessment, health policy authorities, primary researchers and clinical practice guidelines developers with facilitation by the Cochrane collaboration should allow for living evidence syntheses according to the high standards needed to justify their status in evidence-informed decision-making.

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**Figure 1: Developing a culture of continuous improvement of clinical research for a specific disease**

**Box 1. Different steps to facilitate the implementation of this new evidence ecosystem**

**To create a living community dedicated to one condition**

- The community shall gather clinicians, systematic reviewers, patients, trialists, methodologists, statisticians and guidelines experts willing to join their efforts to improve the production of evidence in a specific field
- The community should define specific safeguards to avoid the undue influence of lobbies such as pharmaceutical industry. The role of each community member and their conflict of interest should completely transparent.
- The community should agree on
    - The research questions to be explored in priority
    - The sources of data to be used
    - The types of data (randomized trials, observational data, individual-patient data) to consider
- The community should distribute the work to diverse teams disseminated worldwide
- The community should agree on a new reward system to properly reward researchers commensurate with their contribution over time

**To set-up a living mapping of research (ongoing and completed research) and a living network meta-analysis** of all available treatments, continuously updated for a specific condition or therapeutic indication to

- Perform the initial evidence synthesis (initial network meta-analysis)
- Organize updates at a pace adapted to their topic and the speed of knowledge production
- Organize the knowledge transfer toward the various stakeholders
    - To tailor the end-products to stakeholders needs and develop a different version for each stakeholder. For example, the end product for trialist could be tools to help guide the sample size calculation, chose the outcomes measurements, chose the comparator, set up eligibility criteria, chose centers etc.
    - To provide access to the most updated results and to the data immediately on an open platform
    - To publish results when relevant

**To organize the living monitoring and feedback to all stakeholders (funders, trialists, journal editors, institutions etc.) of trials quality and transparency**

- The living monitoring of trials conducting quality will consist of assessing and reporting whether
    - Outcomes used are consistent and in line with the core outcomes set
    - The trials identified are at high risk of bias according to the risk of bias tool, why and how methodological errors identified could be avoided.
    - Patients are involved in the study design
- The living monitoring of trials transparency and completeness of reporting will consist of assessing and reporting whether
    - Trials protocols are available
    - Trials data are archived and where
    - Trials results are available (e.g., posted or published)
    - Trials are completely reported
    - Individual-patient data are accessible and under what conditions
- The feedback could consist of
    - A living disclosure of trials quality and transparency
    - A tailored feedback to specific stakeholders (funders, institutions, journal editors)
    - Reminders for posting trial results on registries
    - Tailored guidance for data reporting and data sharing

**To organize the process for the development of living guidelines**

- Giving access to the data that were extracted to guidelines developers who could re-use these data, reanalyse all or some of these data, add other data and thus produce locally relevant and applicable guidelines.