

# **Evaluation of NIHR investment in Cochrane infrastructure and systematic reviews**

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**10 February 2017**

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## LIST OF ABBREVIATIONS

|          |   |
|----------|---|
| ACP      | American College of Physicians  |
| AEs      | adverse events  |
| AHTA     | Adelaide Health Technology Assessment                                 |
| AHP      | Allied health professional  |
| AHRQ     | Agency for Healthcare Quality and Research                            |
| ARI      | Acute Respiratory Infections CRG                                      |
| AVALIA-T | Galician Agency for Health Technology Assessment                      |
| BACP     | British Association for Counselling & Psychotherapy                   |
| BMJT     | Bone, Joint and Muscle Trauma CRG                                     |
| BSC      | best supportive care  |
| CADTH    | Canadian Agency for Drugs and Technologies in Health                  |
| CDSR     | Cochrane Database of Systematic Reviews                               |
| CENTRAL  | Cochrane Central Register of Controlled Trials                        |
| CEU      | Cochrane Editorial Unit   |
| CI       | confidence interval   |
| CIHR     | Canadian Institutes of Health Research                                |
| CMD      | Common Mental Disorders CRG   |
| CMO      | Chief Medical Officer   |
| CR       | complete response   |
| CRD      | Centre for Reviews and Dissemination                                  |
| CRG      | Cochrane Review Group   |
| CRSU     | Complex Review Support Unit   |
| CQPT     | (NICE) Cochrane Quality and Productivity Topic                        |
| DAR      | Diagnostics Assessment Report   |
| DARE     | Database of Abstracts of Reviews of Effects                           |
| DALY     | Disability-Adjusted Life Year   |
| DIMDI    | Deutsches Institut für Medizinische Dokumentation und Information     |
| DMO      | Diabetic macular oedema   |
| DoH      | Department of Health  |
| EAG      | External Assessment Group   |
| EBHC     | Evidence-based healthcare   |
| EBM      | Evidence-based medicine   |
| EHCBS    | Effective Health Care Bulletin  |
| EME      | Efficacy and Mechanism Evaluation                                     |
| EPOC     | Effective Practice and Organisation of Care CRG                       |
| EPPI     | Evidence for Policy and Practice Information and Co-ordinating Centre |
| ERG      | Evidence Review Group   |
| ESRC     | Economic and Social Research Council                                  |
| FN       | false negative  |

|         |  |
|---------|--|
| FP      | false positive   |
| GIN     | Guidelines International Network                                   |
| GP      | General Practitioner   |
| GRADE   | Grading of Recommendations Assessment, Development & Evaluation    |
| HDA     | Health Development Agency  |
| HEE     | Health Education England   |
| HEI     | Health Education Institute   |
| HEOR    | health economics and outcomes research                             |
| HRA     | Health Research Authority  |
| HRQoL   | health-related quality of life                                     |
| HRs     | hazard ratios  |
| hrs     | hours  |
| HSDR    | Health Service and Delivery Research                               |
| HSR     | Health Services Research   |
| HST     | Highly Specialised Technology                                      |
| HTA     | Health Technology Assessment                                       |
| HTAi    | Health Technology Assessment international                         |
| ICER    | incremental cost-effectiveness ratio                               |
| ICS     | (Cochrane) Impact Case Study                                       |
| INAHTA  | International Network of Agencies for Health Technology Assessment |
| INESSS  | Institut national d'excellence en santé et en services sociaux     |
| JBC     | Joanna Briggs Collaboration  |
| JBI     | Joanna Briggs Institute  |
| JRF     | Joseph Rowntree's Foundation                                       |
| KSR Ltd | Kleijnen Systematic Reviews Ltd                                    |
| MECIR   | Methodological Expectations of Cochrane Intervention Reviews       |
| MRC     | Medical Research Council   |
| MRS     | Methods for Research Synthesis                                     |
| MTA     | Multiple Technology Appraisal                                      |
| N/A     | not applicable   |
| NCC     | National Co-ordinating Centre                                      |
| NDC     | NIHR Dissemination Centre  |
| NHS     | UK National Health Service   |
| NHS EED | National Health Service Economic Evaluation Database               |
| NHS III | NHS Institute for Innovation and Improvement                       |
| NICE    | National Institute for Health and Care Excellence (UK)             |
| NIHR    | National Institute for Health Research                             |
| N/R     | not reported   |
| NRT     | nicotine replacement therapy                                       |
| ORR     | overall response rate  |

|          |  |
|----------|--|
| OS       | overall survival   |
| PaPAS    | Pain, Palliative and Supportive Care CRG                 |
| PCB      | Pregnancy and Childbirth CRG                             |
| PHR      | Public Health Research Programme                         |
| PROSPERO | International Prospective Register of Systematic Reviews |
| PRP      | Policy Research Programme                                |
| QALY     | quality-adjusted life year                               |
| QoL      | quality of life  |
| QQR      | Quinquennial Review                                      |
| QUADAS   | Quality Assessment of Diagnostic Accuracy Studies        |
| QS       | (NICE) Quality Standards                                 |
| RCT      | randomised controlled trial                              |
| RD       | risk difference  |
| REF      | Research Excellence Framework                            |
| RevMan   | Review Manager software                                  |
| RoB      | Risk of Bias   |
| ROBIS    | Risk of Bias in Systematic Reviews tool                  |
| RR       | relative risk  |
| SCIE     | Social Care Institute for Excellence                     |
| SD       | standard deviation                                       |
| SDO      | Service Delivery and Organisation                        |
| SIGN     | Scottish Intercollegiate Guidelines Network              |
| SoF      | Summary of Findings                                      |
| SRPAG    | (NIHR) Systematic Reviews Programme Advisory Group       |
| STA      | Single Technology Assessment                             |
| TAG      | Technology Assessment Group                              |
| TAR      | Technology Assessment Review                             |
| TN       | true negative  |
| TP       | true positive  |
| TSC      | Trial Search Co-ordinator                                |
| UK       | United Kingdom   |
| UKCC     | UK Cochrane Centre                                       |
| USA      | United States of America                                 |
| VFM      | Value for Money  |
| VOIM     | Value of implementation                                  |
| VSLY     | Value of a statistical life year                         |
| WHO      | World Health Organisation                                |

## EXECUTIVE SUMMARY

The Chief Medical Officer (CMO) for the Department of Health requested an evaluation of the NIHR investment in Cochrane infrastructure and systematic reviews (SRs). The committee were tasked with examining NIHR investment in Cochrane in meeting the key clinical and policy questions in the NHS, taking into account the wide variety of global review producers and commissioners. The objectives of this evaluation were as follows:

1. To review how the performance of systematic reviews could be improved.
2. To review the broader landscape of systematic reviews and consider the role of Cochrane, and the NIHR investment, compared to other global providers of reviews; in particular in meeting the key clinical and policy issues facing the NHS.
3. To review the performance of the NIHR funded Cochrane Review Groups (CRGs) and Cochrane UK:
  - a. quantity and quality of outputs.
  - b. impact in influencing NHS practice/policy and (in so far as is possible) NHS culture
4. To consider current and planned developments in Cochrane, and how and if, NIHR might wish to continue to influence these, to ensure better value for the NHS.
5. To consider the content and implementation of the Cochrane strategic plan in ensuring better value for the NHS.
6. To advise on whether the current NIHR investment in Cochrane is well spent or should be allocated in other ways or to other areas.

This report considers these objectives in six chapters. This review had to be proportionate in resources, and therefore drew largely on readily available sources of evidence, including reports, interviews and the Committee's own expert knowledge of the field. This information was supplemented as considered necessary by the Committee, and a series of interviews with stakeholders was conducted. A researcher collated data following directions of the lead and the Committee. The Committee met regularly to discuss findings, data, interpretation and recommendations; and participated in recommendation formulation. The Committee responded to the objectives above in the following sections:

### 1. [The global landscape of systematic reviews](#)

Cochrane has had an enormous impact on SRs production since it was established, accounting for 6,906 reviews in issue 5/2016 of the Cochrane Library. The NIHR and its predecessors have provided funding to Cochrane since 1992 and the NIHR has committed £16 million funding for 21 CRGs over the current five year contract period (2015-2020), representing a total of 40% of CRGs worldwide (21/52). Cochrane has made a significant contribution to other processes, including methods developments, and, indirectly, guideline production. Cochrane has been central to the development of the science of research synthesis, and Cochrane

participants have contributed to helping develop the unified transparent GRADE approach to guideline development.

Recognition of the value of systematic reviews at a governmental level has resulted in much wider infrastructure investment across a range of SR producers in the UK. These are often focused around specific policy questions, eclipsing the total number of SRs produced by Cochrane. Technology Assessment Review (TAR) teams produce reviews for NICE around specific questions and NIHR has committed £38.5 million over five years from April 2016 to TAR teams. Worldwide, systematic reviews are now mainstream for academic medical research, and around 11,000 SRs are produced every year worldwide.

Cochrane's continued contribution to the development of methods is important, but the product of the systematic review is less unique, given the many other SR providers. Cochrane reviews are unique in terms of a commitment in principle to keeping them up-to-date, but this has proven difficult to implement fully.

Without a doubt, Cochrane is a reliable first port of call with a strong history, reputation and brand and is relatively inexpensive. However, there are many other SR producers in the UK, making up a large SR playing field. In order to maintain and strengthen its place, the Committee recommends that Cochrane should more clearly identify its niche and redefine where it fits in this changing environment.

## 2. The performance of NIHR funded Cochrane Review Groups (CRGs)

The Committee appraised the performance of CRGs in relation to the following:

- SR production
- Quality (whether outputs were reliable, rigorous, readable and relevant to the NHS)
- CRG managerial efficiency

It was clear that there was considerable variation between reviews in terms of quality and between CRGs in terms of performance and coverage. Whilst there have been attempts to address these critical concerns through the efforts of the CRGs and the Cochrane Editorial Unit, the committee considered that this variation had not been addressed well to date.

Quality is a critical point, which requires openness and transparency. Whilst quality of the 7,000 Cochrane reviews is good relative to non-Cochrane reviews, not all of Cochrane reviews are good quality. One independent analysis showed that 88% of Cochrane reviews are rated to have a low risk of bias, compared to only 12% of non-Cochrane SRs, which is something Cochrane can be very proud of. However, specific groups of non-Cochrane reviews such as those for NICE and other HTA agencies are also likely to be rated at low risk of bias. Nevertheless, internal screening within the Central Editorial Unit of Cochrane has shown that 5% of NIHR-funded SRs signed off by the CRG Co-ordinating Editor still required major amendments before they met methodological expectations.<sup>4</sup>

Timeliness of review production remains a concern for the Committee. For reviews to address questions relevant to NHS decision-makers, they need to be completed for policy windows. Unfortunately delays in review production impairs an organisation's ability to ensure policy windows are met. This also linked to problems concerning relevance of reviews and coverage of topics and assuring timely updating of high priority topics. Timeliness of reviews is essential to achieve impact, and requires CRGs to prioritise review production and updating carefully.

Timely updating of reviews represents a significant challenge. During the 2014 assessment process, 1,250 reviews were assessed as requiring an update, which were either in-progress or awaiting sufficient resources to complete them. Coverage is impaired by reviews missing in important topic areas, and also because a number of important reviews are out of date.

Level of interest in NIHR-funded CRG work is high; nine of the top 10 most accessed Cochrane reviews of 2014 were produced by NIHR-funded CRGs. This number of accesses refers to downloads of PDFs or HTML files from the Cochrane Library. An analysis of the impact of Cochrane SRs on policy examined the number of NIHR-funded CRG reviews cited in NICE and SIGN Guidelines published between 2013 and February 2016. This showed 415 Cochrane reviews from 19 of the 21 UK-based NIHR-funded Cochrane Review Groups were cited in 103 guidelines (74 NICE; 29 SIGN).<sup>5</sup> Whilst this shows guideline producers identify and cite Cochrane SRs, this does not directly demonstrate influence or impact on behalf of Cochrane.

An enduring criticism of policy-makers and funders is that some CRGs consistently exclude other sources of effectiveness data when randomised controlled trials are absent; and that Cochrane do not carry out reviews in areas that are also important for policy development. Cochrane needs to more widely address the scope of evidence being used if it intends to be seen as the 'home of evidence'; encouraging more focus on sources of data other than RCTs, including observational studies, indirect comparisons, economics, and adverse effects evidence. Of concern are empty reviews if they have overly restrictive inclusion criteria concerning the types of studies, such as only RCTs, in situations where other types of studies addressing the question exist.

A study conducted in 2010 found that nearly 9% of all reviews published in CDSR had no included studies meeting the inclusion criteria.<sup>6</sup> The study found that NIHR-funded CRGs produced 52% of all reviews on CDSR (2,249/4,320, based on data from Yaffe<sup>6</sup>) however these CRGs also contributed nearly 66% of all empty reviews (248/376, based on data from Yaffe<sup>6</sup>).

The Committee identified mixed author experiences with CRGs. There were many expressions of positive experiences, there are also tensions between authors and CRGs. Some feedback about CRGs remains critical, especially where prospective reviewers are dismissed because of CRG workload and where long delays occur in dealing with protocols and draft reviews; this means that NIHR investment is put at risk where reviews cannot get through the editorial pipeline in reasonable time. The committee recommends that data about transit times from workflow should be included in NIHR monitoring requirements, and some benchmarks for turnaround established so performance can be measured against this.

Surveys of quality against Cochrane standards (MECIR), readability studies and the number of reviews that are signed off by editorial groups but then are pulled from publication by the Central Editorial Unit are not disclosed internally or publically. The Committee recommends public disclosure of CRG performance. A number of low quality Cochrane SRs exist and can be identified from existing and future MECIR and readability studies.

These data provided invaluable insight into the CRGs who perform well consistently producing high quality reviews, and distribution of these indicators will help groups take remedial action, provide the CEU with an opportunity for dialogue, and NIHR to adjust funding in relation to performance.

### 3. Cochrane's impact on key clinical and policy issues in the NHS

To date, Cochrane has had an impact on people, methods, policy, research, and health outcome. Cochrane is seen as a trusted source by healthcare professionals, clinicians, guideline developers, information producers and infomediaries.<sup>2, 7, 8</sup> Cochrane evidence is also valued by health commissioners, policy developers, NHS managers and the public, however they find it more challenging to use in a practical sense. Consequently, they value it less than could be the case, leaving room for additional improvement.<sup>2</sup>

For many, but not all, NHS institutions, Cochrane is a primary source of evidence; such apparent impact needs to be assessed in a meaningful way, and Cochrane should be more proactive in its planning or anticipation of impact.

Impact will only happen if CRGs prioritise. Existing processes in Cochrane are helpful, but the Committee feels these could be more successful if there is a more explicit, transparent and centralised strategy that establishes what the Priority List is for and how the NHS needs can be incorporated into CRG priority review decisions. Prioritisation needs to continue to build on examples of good practice and the organisation needs to challenge parts of Cochrane that are not active or transparent in prioritisation, or implementing existing priorities, especially in processes that acknowledge NHS needs. Cochrane has had, and continues to have, substantial collateral impact having influenced methodological developments. Looking forward, Cochrane needs to proactively embrace other approaches (use of best available evidence; economic data) within its full systematic reviews.

The Committee is well aware that Cochrane is a worldwide organisation and that the activities of UK based CRGs have a worldwide focus. Funding UK based CRGs gives benefits worldwide, and simultaneously the NHS benefits from Cochrane work done elsewhere in the world.

However, some of Cochrane's activity does not have an impact, often due to timing. Cochrane should be encouraged to consider upcoming guideline questions to identify review title priorities. It is essential to get an overall profile of Cochrane impact as a whole, rather than focussing on single impactful reviews. Furthermore, Cochrane has a number of resources, generated with support of NIHR funding, which are not fully accessible, such as specialised registers. The Committee recommends that Cochrane look into ways to increase sharing of resources.

More involvement of Cochrane Consumers, and other stakeholders in the whole systematic review process, but specifically question formulation, scoping, outcomes, and dissemination products (beyond the Plain Language Summary) may improve the relevance and uptake of reviews. Increasing uptake may improve impact of reviews. Questions remain whether CRGs are proactive enough to sustain these impacts, and whether reported impacts are due to serendipity, or due to planning. There are many resources and examples of public involvement in research that Cochrane could build on in this regard.

Cochrane UK (formerly the UK Cochrane Centre) has played a crucial role in training and accomplishing culture change to using evidence in decision making in the NHS. Cochrane UK should continue with further training of NHS staff, and should engage with both NHS prioritisation initiatives and CRGs in order to play a major facilitating role to match Cochrane review production to topics relevant to the NHS, making sure these reviews are prepared in a timely manner and are being kept up-to-date.

#### 4. The economic impact of systematic reviews

The economic impact of SRs was considered in four case studies. The case studies were highly selective, and selective information was used for each case study. The case studies showed that for Cochrane to represent value for money it would need to recommend only a small number cost-effective interventions a year. However, the Committee considered that justifying all Cochrane activities and reviews as worthwhile on the back of a small number that have impact is a weak rationale. It would be useful to see more routine Cochrane work that uses economic evaluation to determine whether reviews can lead to savings in the NHS. Cost savings are not the only possible outcome, methods may show effective treatments which cost the NHS money. It also should be borne in mind that reviews exist that evaluate standard practice, which could result in savings to the NHS. On average, Cochrane reviews come out with relatively low unit costs, but these estimates need to take relevance and quality in to account, and the time of health or academic staff carrying out the review.

#### 5. Current and planned developments in Cochrane and stakeholders' views

The Committee asked NIHR to commission some stakeholder interviews (34) to assess the views and experiences of Cochrane review users and producers based in the UK and the NHS.<sup>2</sup> The results are summarised later in Chapter 5. The themes, in most cases, added weight to evidence in this review and the findings of Cochrane and Wiley commissioned stakeholder exercises<sup>7, 8</sup> (which were worldwide, with less UK and NHS focus). The overlaps in findings between the three exercises are summarised below\*;

**Cochrane brand;** trusted source of evidence with independence and addressing conflicts of interest.

**Quality of Cochrane reviews;** review users strongly value the rigour, transparency and clarity of Cochrane reviews, but there was less consensus (across all stakeholder exercises) about

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\* Unless stated these refer to all three of the included exercises.<sup>2, 7, 8</sup>

value of access to the underlying source data and widening source data (health economics and real world data from different healthcare settings).

**Cochrane relevance;** many find Cochrane reviews relevant, although it can be frustrating when there is no conclusion, or reviews are 'empty'. For some groups in the UK (commissioners, policy makers and consumer/patient organisations) they find reviews less relevant. Two reports conclude that a range of stakeholder representations in review processes and production would potentially help address relevance issues.

**Priority setting;** two of the exercises highlighted the need for a more systematic use of priority setting and stakeholder representations (i.e. health professionals, consumers, patients and the public, funders, policy makers and guideline developers) utilising existing and current health priorities, objective data on burden of disease and healthcare, and identified gaps in published evidence.

**Dissemination of Cochrane reviews and products;** Cochrane could offer more products or services that would promote review uptake among different groups, customised according to target group e.g. commercial media channels, partnerships with medical journals, briefing papers for policy makers, professional and community networks, high profile bloggers. Comments were also made on presenting reviews with narrative synthesis, clinical summaries, graphical content, contextual information, and emphasis on the interpretation of the evidence (including metrics used by practitioners). An ongoing challenge is for Cochrane to be able to respond to the changing needs of the review user community.

Cochrane's Strategy to 2020 should determine and highlight Cochrane's niche and unique selling points, and provide clear direction to realise these. Cochrane should work on developing expertise and processes to get better and quicker at producing reviews. Cochrane should revisit some of its goals as there seem to be many different objectives in many areas. The Committee feels that an explicit focus is needed on relevance to patient care, as a primary goal. The Committee recommends that Cochrane keeps full SRs as its primary product and makes sure that activities to develop new products do not have a negative impact on timely, relevant full systematic reviews. This is echoed in stakeholder feedback; a new output is not required, just the existing product delivered quicker and with high relevance.

Centralisation versus decentralisation (roles of the Central Editorial Unit and the CRGs) is a core consideration for Cochrane's future and should be transparently and swiftly discussed. Clarifying areas in CRGs for consistency and areas for flexibility is critical to Cochrane's roles and functionality moving forward.

The nature of funding dictates where responsibilities lie and funding sources should be openly considered when thinking about future direction of travel, capacity and accountability. Key considerations should focus on measures of impact; emphasising the need for groups to plan and think more strategically moving forward in order to maximise their impact on the NHS.

## Conclusions

- Many recommendations in this report may be in line with, or in progress with, the Cochrane strategy to 2020, however the Committee feels that progress needs to speed up, be more definite and more transparent and linked to a clear vision of Cochrane's place in the world of systematic review production.
- The Committee recommends to continue funding Cochrane. However, this funding should be linked to key performance indicators to ensure optimal value for money. These should focus on measures of impact; emphasising the need for groups to plan and think more strategically moving forward in order to maximise impact in the NHS.
- Impact should be assessed in terms of impact on policies, practice change, culture change, and methodology change. For realising such impact, improving communication with the public, health professionals and policy makers will be key for Cochrane UK, individual review groups, and Cochrane worldwide.
- If warranted, variation of funding be it either increased or decreased should be swiftly implementable. If Cochrane improves on addressing NHS priorities an increase of funding makes sense.
- A revised structure of CRGs could impact dramatically on efficiencies, outputs and future funding models, and should be explored, and pursued more proactively by Cochrane. For example fewer, larger groups could overhaul efficiencies.
- In the Committee's opinion, the past has shown good value. With critical changes in quality, prioritisation and changing structure, the organisation could maintain its important role. Therefore, key performance indicators should be crucial in securing funding.

## Recommendations and considerations for NIHR Cochrane funding

### Recommendations to Cochrane

Cochrane should more clearly identify its niche and redefine where it fits in the changing environment of SRs. The Committee recommends that Cochrane keeps full SRs as its primary product and makes sure that activities to develop new products do not have a negative impact on timely, relevant full systematic reviews. Continue focus on maintaining and improving quality in the domains:

- Relevant: relevance to the NHS (use best available evidence, try to avoid empty reviews)
- Reliable: includes the review conclusions reflecting the findings
- Rigorous: low risk of bias
- Readable: clearly written for identified audiences

Cochrane should improve transparency around assessments of quality and CRGs' performance; continue funding/supporting well performing CRGs, stop funding/supporting to poorly performing CRGs, consider reorganisation of NIHR-funded CRGs (see options below).

Address priority setting for new reviews and updating existing reviews:

- Consider a more explicit, transparent and centralised prioritisation strategy, while maintaining wide coverage in line with NHS and global priorities
- Establish how the NHS' needs can be incorporated into CRG priority setting
- Cochrane UK should help to improve the performance of CRGs in meeting the evidence needs of core UK relationships

Address timeliness of reviews and updates:

- Reviews should be as much as possible ready and up-to-date at the point in time of decision-making and policy windows
- Implement changes aimed at faster editorial turnaround times

### Recommendations to NIHR

#### *Evaluation of performance*

NIHR funding to CRGs should be based on each group's performance in relation to quality (relevant, reliable, rigorous and readable), priority setting, relationship to the NHS, and timeliness.

NIHR should work with Cochrane UK and the Editor in Chief's Office and CRGs in implementing the strategic plan,<sup>9</sup> in relation to improving CRG performance. Evaluation of performance by NIHR funded Cochrane entities has in the past focussed too much on quantity of outputs such as numbers of reviews and updates. A shift is needed towards more focus on impact for the NHS. Concrete options may include:

- Use measures of quality (relevant, reliable, rigorous and readable)
- Use measures of timeliness, including faster editorial turnaround time at every step of the editorial processes
- Use measures that demonstrate activities to improve NHS relevant priority setting
- Put more emphasis on metrics that capture NHS impact via all the supporting agencies and organisations

#### *Possible future funding arrangements*

The Committee suggests a number of options for future funding arrangements:

- Increase incentive awards, these have been shown to have considerable impact on timeliness. Consider linking the awards to NICE and other existing NHS priorities; Cochrane UK (see below) should play a role in this process.
- Have fewer but larger groups, while maintaining wide coverage in line with NHS and global priorities. This will yield economies of scale and increase consistency.
- Stop funding underperforming groups, only fund well performing groups.
- Let groups compete for funding and award funding proportionally to NHS relevance and timeliness. Cochrane UK could play a major role in this allocation process.

#### *Future role of Cochrane UK*

Cochrane UK (Cochrane Centre in Oxford) should play a more central role in developing the strategy, implementation and monitoring, to improve CRG performance, as specified above.

In addition, Cochrane UK has a major role in assuring prioritisation and timeliness to meet the needs of the NHS. This can be done by being an intermediary between for example NICE, medical charities, the NHS and Cochrane Groups. Formal liaisons with NICE and relevant NHS bodies should be set up. Feedback mechanisms to Cochrane Groups should be put into place.

## INTRODUCTION

Systematic reviews (SRs) are the cornerstone of all new medical research and health policy ensuring that the best available evidence is used to inform decisions in health and care services. Since 1992, the National Institute for Health Research (NIHR, formerly NHS Research and Development) has funded Cochrane UK's systematic reviews infrastructure and supported systematic reviews across a number of programmes. NIHR currently spends approximately £6m a year supporting Cochrane UK and 21 UK Cochrane Review Groups (CRGs) out of 52 worldwide.

Given the changes in healthcare and needs of the UK National Health Service (NHS) and policy makers, the Chief Medical Officer (CMO) for the Department of Health, has requested an evaluation of the NIHR investment in Cochrane infrastructure and systematic reviews. An independent committee has been formed to lead the evaluation, which includes Professor Jos Kleijnen (Chair), Professor Paul Garner, Dr Phil Alderson, Ms Sally Crowe, Dr Jane Aubin, and Professor John Cairns.

The evaluation will consider the health and economic impact of Cochrane reviews from 2005-2014 by assessing the quantity, quality and impact of reviews on policy, practice and research, their relevance to the NHS, and the wider benefits which contribute to the return on the NIHR investment.

### Objectives

1. To review how the performance of systematic reviews could be improved.
2. To review the broader landscape of systematic reviews and consider the role of Cochrane, and the NIHR investment, compared to other global providers of reviews; in particular in meeting the key clinical and policy issues facing the NHS.
3. To review the performance of the NIHR funded CRGs and Cochrane UK:
  - a. quantity and quality of outputs.
  - b. impact in influencing NHS practice/policy and (in so far as is possible) NHS culture.
4. To consider current and planned developments in Cochrane, and how and if, NIHR might wish to continue to influence these, to ensure better value for the NHS.
5. To consider the content and implementation of the Cochrane strategic plan in ensuring better value for the NHS.
6. To advise on whether the current NIHR investment in Cochrane is well spent or should be allocated in other ways or to other areas.

### Better reviews: relevant, timely and high quality

In 2013 at the Cochrane UK and Ireland 21<sup>st</sup> Anniversary Symposium, the CMO Dame Sally Davies reflected on whether Cochrane has successfully met the challenges identified by Archie Cochrane in 1979. She set out her perspective of the challenges faced by Cochrane in the future, and gave advice on how Cochrane could adapt to meet these demands in a

changing environment.<sup>10</sup> She made the point that Cochrane reviews in the UK represented very good value, at an estimated cost of approximately £15,000 of infrastructure funding for every new or updated systematic review.

The recognition of the role of volunteers and contribution from other funders was key in attaining such value for money. There was considerable variation in outputs and activity between the different NIHR-funded CRGs, with the numbers of new systematic reviews produced by UK CRGs ranging from 1 to 30 in 2011. The CMO emphasised the challenges ahead for Cochrane, as well as the need for better reviews that are relevant, timely and of high methodological quality.

Table 1: Key challenges facing Cochrane

***Patient involvement***

The NHS Constitution gives patients the right to join in and participate with all aspects of the research cycle from question formulation and importance to dissemination and implementation. Self-management of long term conditions and prevention of lifestyle-related ill-health highlight the importance of patient involvement. The Collaboration must ensure that there is effective public and patient involvement to identify the patient-relevant questions for Cochrane reviews and patient important outcomes. In the UK there is an established network and infrastructure of public involvement in research and in the NHS, with a co-ordinating centre based in the University of Southampton, Wessex Institute. Medical research charities also advocate for patient needs and increasingly involve patients in their research strategy development and commissioning. Increased collaboration with INVOLVE, the public involvement processes and networks in the NIHR, and the Association of Medical Research Charities are an important way for Cochrane to meet this challenge. Project ACTIVE by gathering examples of good practice within Cochrane but needs also to embrace what is happening outside Cochrane and where there can be enhanced collaboration. The UK remained the global leader of international Cochrane activity and NIHR was the leading funder. Attempts have been made by the CMO to encourage other countries to increase their funding to help the Collaboration go forward. The Collaboration must ensure that the questions addressed by reviews are not only interesting to researchers, but also questions that matter to the public, patients, and the frontline practitioners delivering health care.

***Collaboration with NICE***

Systematic reviews are essential building blocks for guidelines and guidance.<sup>10</sup> Seventy-three percent of NICE guidelines published from 2008 to 2013 referenced Cochrane reviews (range: 1 to 46 Cochrane reviews). A review of nicotine replacement therapy (NRT)<sup>11</sup> produced by the Cochrane Tobacco Addiction Group demonstrated considerable impact in the field of public health. The NRT review<sup>11</sup> was cited in NICE Guidance on brief interventions and referral for smoking cessation,<sup>12</sup> as well as being cited by the WHO as high quality evidence of effectiveness. As a consequence of the review,<sup>11</sup> NRT was added to the WHO List of Essential Medicines.<sup>13</sup>

### ***Prioritise to topics of greatest importance***

Cochrane faces challenges as the UK population is enlarging and ageing, and there is a demanding financial situation. Combined, these factors place significant pressure on the NHS, placing greater importance on prevention, including screening and vaccination. Lifestyle-related ill-health and self-management must also be addressed. Higher-value health care is required, and potentially austerity will drive real innovation. The role of NIHR as a key Cochrane funder means that the focus should be on the public and NHS. This focus may be valid worldwide, however efforts should be prioritised into areas of the greatest importance for health and healthcare. Utilising existing priority sets that have this focus such as the James Lind Alliance are a good start but review groups may and need to undertake their own dialogue and process for establishing priorities, and there is no current agreed gold standard for ways to go about this. The Cochrane Prioritization Methods Group has relevant resources to assist review groups, but a better shared understanding of what the central Cochrane Priorities List is for, and about, would enable this objective to be realised more fully.<sup>14</sup>

### ***Keep more reviews up-to-date***

Cochrane used to be the only player in the systematic review market, but now there are others such as the World Health Organisation (WHO), the Agency for Healthcare Research and Quality (AHRQ) and the American College of Physicians (ACP), who produce either standalone systematic reviews or reviews underpinning guidance. Cochrane's unique selling points are ongoing updates of reviews, completeness for certain topics, and its thread into the health service. Often real practitioners are undertaking reviews. NICE have started to carry out their own reviews, when an available and up-to-date Cochrane systematic review is not available. In 2012, the Collaboration investigated some of the issues around updating Cochrane reviews.<sup>15</sup> Only 36% of systematic reviews in the Cochrane Database of Systematic Reviews (CDSR) were deemed to be up-to-date. Within the Collaboration, there is a view that reviews that are only of historical interest should be labelled as such. Priority should be given to the more important reviews, some of which will need updating more than every two years. Should a significant trial come out, there may be a need to update a review very quickly to ensure responsiveness and appropriate prioritisation.<sup>15</sup>

### ***Prepare reviews more rapidly***

The same Cochrane editorial<sup>15</sup> gave the median production time as 23 months from protocol registration to publication. For some priority topics, two years might seem an unreasonably long time to wait for an answer to a question. When reviews are commissioned using programme grants and undertaken by professional reviewers, timely returns are expected and required.

### ***Use best available evidence, beyond RCTs***

In some circumstances, the best evidence available to answer a question may not come from an RCT. The Cochrane Non-Randomised Studies (NRS) for Interventions Methods

Group's role is to advise the Cochrane Steering Group to set a policy/formulate guidance about the inclusion of non-randomised studies (NRS) of the effectiveness of health care interventions in Cochrane Reviews.<sup>16</sup>

Source: CMO (2013)<sup>10</sup>

These points will be returned to in Chapter 6. The Committee will address the key issues facing Cochrane in the future, and propose strategic options for the consideration of commissioners, funders and Cochrane itself.

### Methods and sources to inform the evaluation process

This review had to be proportionate in resources, and therefore drew largely on readily available sources of evidence, supplemented as considered necessary by the Committee. The time period covered by this report is 2005-2014, and data were considered for inclusion up to Spring 2016. The Committee acknowledges that some of these data will soon be or already are out of date. These sources included:

- Factual output figures from the last NIHR quinquennial review (QQR) of Cochrane funding and more recent annual reports.
- Relevant recent publications, e.g.: “The impact of Cochrane Reviews: a mixed-methods evaluation of outputs from Cochrane Review Groups”<sup>3</sup> and “The Cochrane Collaboration: an institutional analysis.”<sup>17</sup>
- Bibliographic information
- Stakeholder interviews and two other stakeholder reports commissioned by Cochrane and Wiley
- Impact statements identified from NIHR funded CRGs including details of relevance for and impact on national UK guidelines from NICE, SIGN etc.
- Economic impact of selected reviews
- A survey of NHS patients and practitioners about the relevance to the NHS of NIHR funded CRG outputs
- Quality of Cochrane reviews: assessments of the quality of Cochrane reviews with the ROBIS checklist<sup>18</sup> against Cochrane’s MECIR checklist.<sup>19</sup>
- Document review: using Cochrane policy documents, assessing progress towards these policies, and relevance to the NHS.

## CHAPTER 1 – SYSTEMATIC REVIEWS IN HEALTH: THE GLOBAL LANDSCAPE

### Overview

*As a first step in evaluating Cochrane's contribution and value to UK and international SR production, this chapter will describe the various organisations, funding streams, commissioners and programmes engaged in the ever-changing SR environment. Points covered in this chapter will include:*

- *The dramatic increases in SR production over the last two decades*
- *Cochrane as one of many in the UK and internationally preparing SRs*
- *UK's contribution to the Cochrane landscape*
- *UK funding in other SRs programmes*

Systematic reviews (SRs) aim to identify, evaluate and analyse the best available evidence in a transparent, methodical and reproducible way, and play a vital role in informing decision making.

Since the first use of the phrase "systematic review" (PubMed<sup>20</sup>), international publication rates of SRs have increased exponentially in recent years, from 232 in 1990 up to 11,314 in 2015 (PubMed estimate based on adapted Bastian<sup>21</sup> approach).

Figure 1: Estimated publication rate of systematic reviews from 1990-2014 [data collected 24.3.15]

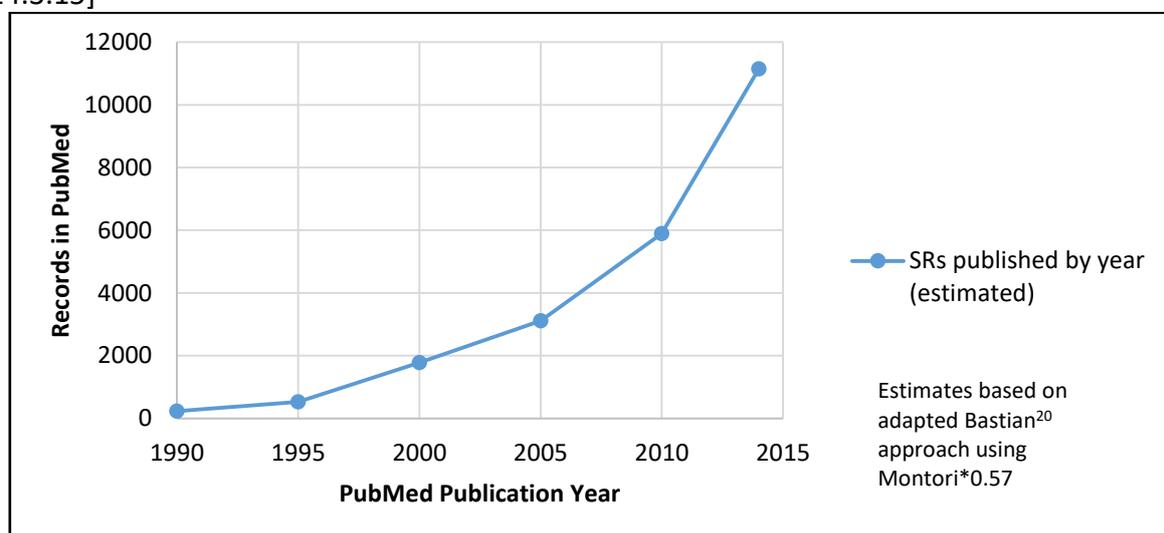
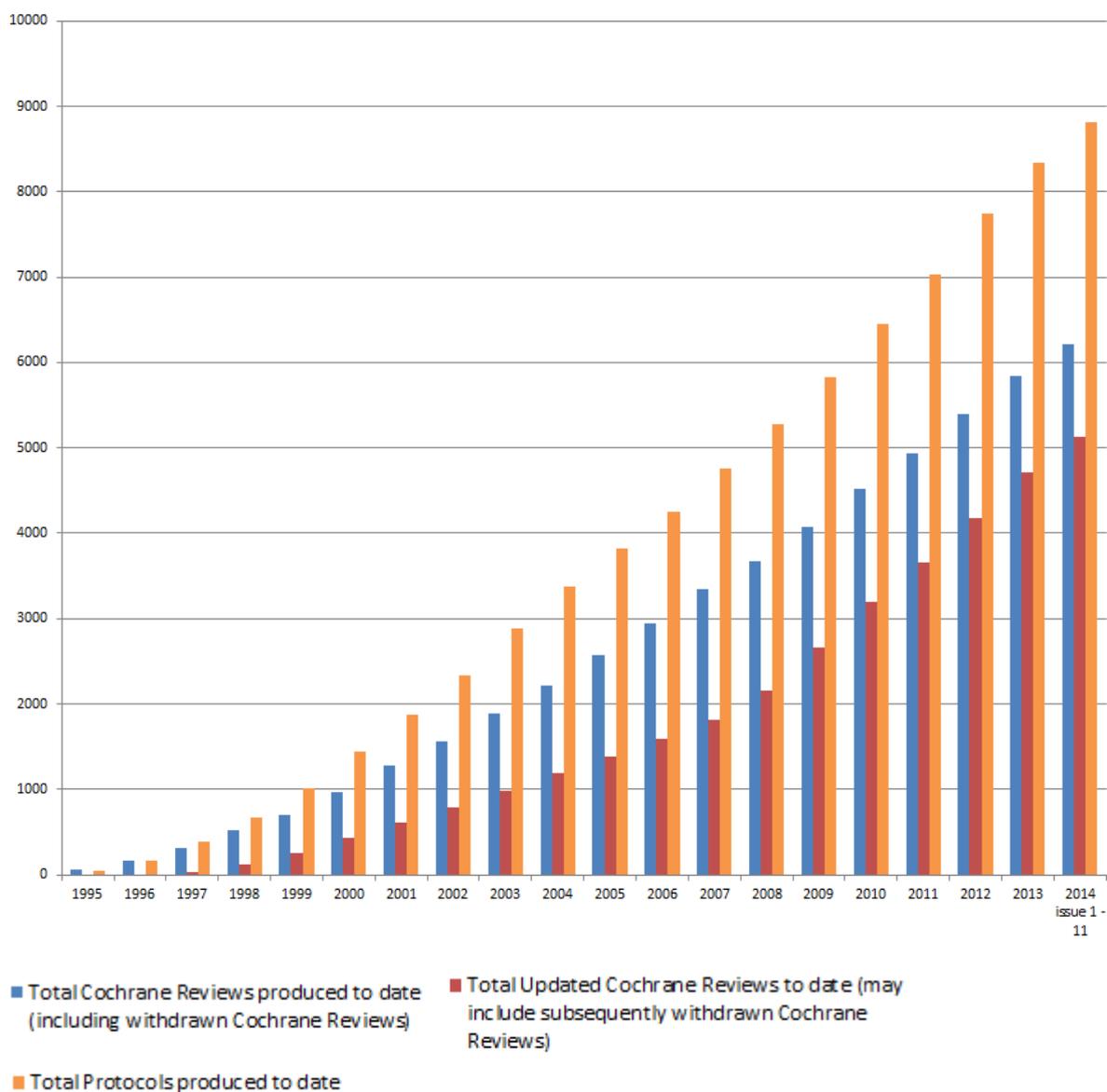


Figure 2 presents the cumulative prevalence of Cochrane reviews and protocols (excluding withdrawn publications) and illustrates a similarly marked increase in the number of reviews produced and updated by Cochrane reviewers.

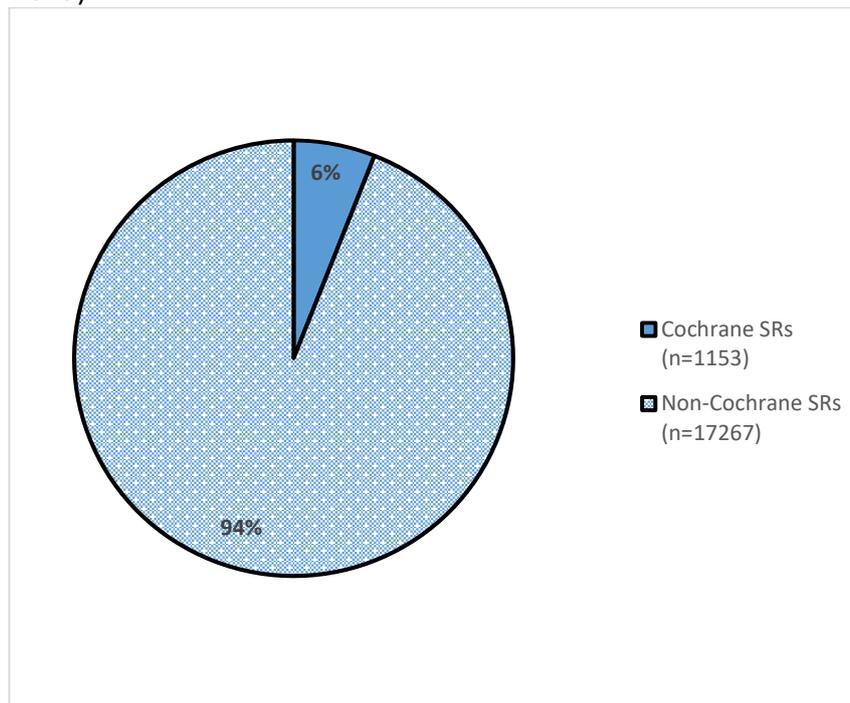
Figure 2: Cochrane Database of Systematic Reviews: total Cochrane Reviews and Protocols\*



Source: Cochrane (2014)<sup>22</sup> \*Cochrane Reviews can be withdrawn from the active database when they become out of date or are replaced by new Cochrane Reviews in a similar subject area.

Further analysis conducted for this report (see Appendix 3: KSR Evidence database bibliometric analysis), identified 18,420 potential SRs.<sup>23</sup> For all SRs retrieved with a publication year of 2010-2015 (n=18,420), 6% (n=1,153) were published in the Cochrane Database of Systematic Reviews,<sup>24</sup> and 94% (n=17,267) were published in a different format, such as journal article, thesis or report.

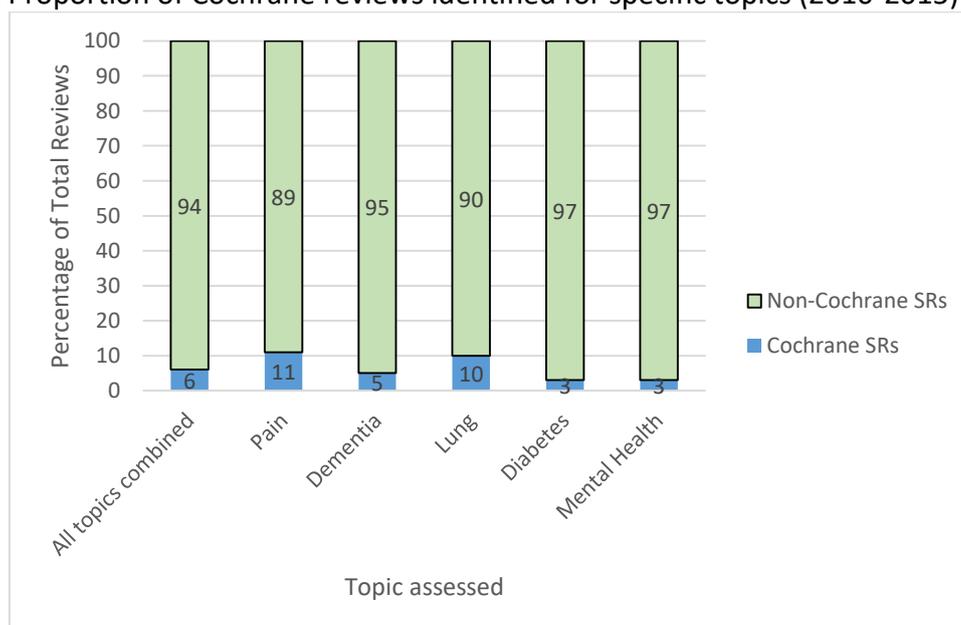
Figure 3: Percentage of all SRs retrieved produced by Cochrane and other producers (total = 18,420; 2010-2015)



Source: Kleijnen Systematic Reviews Ltd (2016)<sup>23</sup>

The contribution Cochrane Review Groups (CRGs) made to publications of SRs varied across topics. Bibliographic analysis of publication distribution across a sample of five separate topics, showed that Cochrane reviews made up between 3-11% of published reviews.

Figure 4: Proportion of Cochrane reviews identified for specific topics (2010-2015)



Source: Source: Kleijnen Systematic Reviews Ltd (2016)<sup>23</sup>

The topics of mental health and diabetes both contributed a yield of 3% Cochrane reviews (257/7,411, and 72/286 respectively). The lung disease and pain fields had the highest percentage of Cochrane reviews at 10% and 11% respectively (403/4,176, and 373/3,463). These data illustrate Cochrane's comparative role in the production and publication of SRs in the global marketplace, and indicate how competitive review production is becoming.<sup>25</sup>

This report will focus on reviews on health and health-related topics, however systematic reviewing is increasingly being adopted outside of health in education, social care, agriculture and other areas of policy-making.<sup>26-30</sup> Within the UK, and progressively on an international basis, guidelines are increasingly becoming 'evidence-based' and many guidelines and guidance publications are underpinned with systematic reviews.<sup>31</sup> Therefore a great deal of SR production and activity is involved in guidelines production and this will also be included in this chapter.

Increasingly public and patient perspectives and information needs have become important factors to be considered when commissioning and undertaking reviews. User and patient experiences can be invaluable sources from review inception to uptake and dissemination. Ensuring appropriate topics are prioritised for review, and that the research questions address interventions and outcomes that are relevant to patients, their carers, and consumers in general, depend on consultation with and involvement of users and patients.<sup>32</sup> In addition to consideration of patient experiences and insights, users and patients can be encouraged to become involved as participants in the production of reviews, for example providing input to ensure the message of reviews are clearly accessible and easy-to-read by a wide audience.<sup>33, 34</sup>

Cochrane has a rich history of involving patients and the public (consumers) in their review processes and this is something to celebrate; however practice across Cochrane varies and, with some notable exceptions, it has not kept pace with the world of Patient and Public Involvement in clinical research outside Cochrane. In addition the current cohort of UK based Cochrane Consumers are unlikely to sufficiently represent NHS users and their priorities.

With some exceptions consumer contributions are largely made by commenting on abstracts and Plain Language Summaries.<sup>35</sup> However the recent Consumer Structure and Function review,<sup>7</sup> and stakeholder consultations has underlined the need to expand this contribution to span the systematic review process, and Strategy 2020<sup>9</sup> supports this ambition. Project Active which started just at the inception of this review seeks to collect and share examples of good practice in consumer involvement in Cochrane and it remains to be seen how much of this ambition will be translated into more widespread activities and impact on reviews.

#### [Organisations funding or preparing systematic reviews in the UK](#)

SR funding streams in the UK are complex, with multiple programmes funding different providers to produce SRs, health technology assessments, technology appraisals and guidelines. Table 2 below provides an overview of the key funders, SR producers, outputs and the relationships between them. Where available, an indication of funding allocations is

given. A more detailed description of the main funders, SR producers and their related outputs is presented in Appendix 1. Further ways of accessing existing systematic reviews are presented in Appendix 2.

Table 2: Summary of organisations funding or preparing systematic reviews in the UK

|      | Programme                    | Remit   | Approximate Annual Budget (£) |
|------|------------------------------|---|-------------------------------|
| NIHR | SR Programme                 | Budget to support the updating of existing SRs, and the production of new SRs. Funding is allocated through several work streams (listed below).  | £13.6m                        |
|      | Cochrane Review Groups (CRG) | Conduct of SRs and provision of editorial support and peer review.  | £3.2m                         |
|      | Cochrane UK                  | Does not undertake SRs, but supports CRGS and other to do so.   | £0.8m                         |
|      | Cochrane Project funding     |   |                               |
|      | Cochrane Programme Grants    | Provision of high-quality new and updated SRs of direct benefit to users of NHS in England. Each grant is spread over 3 years (up to £140,000 max p.a.)<br>Approximately 10 grants are awarded each year. | £1.4m                         |
|      | Cochrane Engagement Awards   | To strengthen engagement between Cochrane SR producers and SR users within the NHS.   | £0.8m                         |
|      | Cochrane Incentive Awards    | Facilitation and acceleration of SRs that are already planned or underway.  | £5,000 per award              |
|      | Complex Review Support Unit  | Provision of specialist expert advice to those producing methodologically complex SRs.  | £0.4m                         |
|      | TARs                         | Conduct of SRs, reviews of economic evaluations and cost-effectiveness models to inform DARs and MTAs. Conduct of STAs and HSTs to inform decision-making.  | £8m                           |
|      | HTA                          | Funds independent research for the NHS about clinical effectiveness, cost effectiveness and impact of healthcare interventions. Primary studies and SRs.  | £74m                          |
|      | HSDR                         | Production of rigorous, relevant evidence to improve accessibility, quality and organisation of health services, and to   | £18.5m                        |

|                          | Programme                 | Remit   | Approximate Annual Budget (£) |
|--------------------------|---------------------------|---|-------------------------------|
|                          |                           | support decisions by managers and clinical leaders. Projects may include SRs.   |                               |
|                          | PHR                       | Funds research to generate evidence to inform delivery of non-NHS interventions to improve public health and to reduce health inequalities. Projects may include SRs.           | £9.9m                         |
| NICE                     | Clinical Guidelines       | Support provided by the National Co-ordinating Centres (NCCs); work involves SR of evidence.  | N/A                           |
|                          | Social Care Guidelines    | Support provided by the National Co-ordinating Centres (NCCs); work involves SR of evidence.  | N/A                           |
|                          | Public health             | Work involves SR of evidence.   | N/A                           |
| DH                       | Policy Research Programme | Commissions timely, cutting edge research focussing on the current needs of policy makers and ministers. Both primary research and SRs are produced.                            | N/A                           |
| Academic Groups          |                           | Conduct of SRs and methodological work. Financial support from a range of funding sources.  | N/A                           |
| Charities                |                           | Conduct or commissioning of SRs, to utilise primary research and produce SRs to reinforce a relevant and reliable message.  | N/A                           |
| Commercial Agencies      |                           | Conduct of SRs, meta-analyses, network meta-analyses and health economics outcomes research. Outputs might be unpublished, published, or used to compile regulatory submissions | N/A                           |
| Healthcare professionals |                           | As part of continuing professional development (CPD) activities.  | N/A                           |

N/A = information not available.

### Organisations funding or preparing systematic reviews globally

A range of organisations are involved in systematic reviews globally, some important players are mentioned below. Cochrane has existing partnerships with most of these groups. These are described in Appendix 1.

Table 3: Summary of organisations funding or preparing systematic reviews globally

| Programme                       |   | Remit  |
|---------------------------------|---|--|
| Cochrane worldwide              |   | Conduct of SRs and provision of editorial support and peer review. Varied sources of funding from multiple funders.  |
| Joanna Briggs Institute         |   | Conduct of SRs and provision of support to others undertaking SRs. Provision of methodological expertise and develops new methods.   |
| International HTA organisations | INAHTA                                  | Collaborative network of international HTA agencies; encourages information sharing about HTA methods and encourages co-operation between agencies.  |
|                                 | HTAi                                    | Professional society representing anyone involved in HTA and SR production and use. Forum for collaboration and sharing of expertise.  |
|                                 | Regional and national HTA organisations | Other collaborative networks on a regional or national basis.  |
| Guideline organisations         | GIN                                     | Collaborative association of organisations and individuals involved in the development and implementation of evidence-based guidelines and health care information. Does not conduct SRs, but encourages information sharing and methodological development. |
| Governmental                    |   | Conduct or commissioning of research to inform decisions and policy-making in education, health, infrastructure social care, and humanitarian aid. Projects may include SRs.   |
| Commercial agencies             |   | Conduct of SRs, meta-analyses, network meta-analyses and health economics outcomes research. Outputs might be unpublished, published, or used to compile regulatory submissions  |
| Academic Groups                 |   | Conduct of SRs and methodological work. Financial support from a range of funding sources.   |
| Charities                       |   | Conduct or commissioning of SRs, to utilise primary research and produce SRs to reinforce a relevant and reliable message.   |
| Healthcare professionals        |   | As part of CPD activities.   |

## Cochrane Review Groups

SRs conducted by Cochrane are undertaken by 52\* Cochrane Reviews Groups (CRGs)<sup>36</sup> worldwide, of which 21 currently receive infrastructure costs funded by the NIHR,<sup>37-39</sup> and 24 have an editorial base in the UK.<sup>40</sup>

### Funding

NIHR have committed £16 million funding for CRGs over the five year contract period (2015-2020).

Table 4: NIHR-funded Cochrane Review Groups

| Cochrane Review Group                                 | Web address   |
|---|---|
| 1. Airways  | <a href="http://airways.cochrane.org/">http://airways.cochrane.org/</a>             |
| 2. Bone, Joint and Muscle Trauma                      | <a href="http://bjmt.cochrane.org/">http://bjmt.cochrane.org/</a>                   |
| 3. Cystic Fibrosis and Genetic Diseases               | <a href="http://cfgd.cochrane.org/">http://cfgd.cochrane.org/</a>                   |
| 4. Dementia and Cognitive Improvement                 | <a href="http://dementia.cochrane.org/">http://dementia.cochrane.org/</a>           |
| 5. Common Mental Disorders                            | <a href="http://cmd.cochrane.org/">http://cmd.cochrane.org/</a>                     |
| 6. Ear, Nose and Throat Disorders                     | <a href="http://ent.cochrane.org/">http://ent.cochrane.org/</a>                     |
| 7. Epilepsy   | <a href="http://epilepsy.cochrane.org/">http://epilepsy.cochrane.org/</a>           |
| 8. Effective Practice and Organisation of Care (EPOC) | <a href="http://epoc.cochrane.org/">http://epoc.cochrane.org/</a>                   |
| 9. Eyes and Vision                                    | <a href="http://eyes.cochrane.org/">http://eyes.cochrane.org/</a>                   |
| 10. Gynaecological Cancer                             | <a href="http://gnoc.cochrane.org/">http://gnoc.cochrane.org/</a>                   |
| 11. Heart   | <a href="http://heart.cochrane.org/">http://heart.cochrane.org/</a>                 |
| 12. Incontinence                                      | <a href="http://incontinence.cochrane.org/">http://incontinence.cochrane.org/</a>   |
| 13. Injuries  | <a href="http://injuries.cochrane.org/">http://injuries.cochrane.org/</a>           |
| 14. Neuromuscular Disease                             | <a href="http://neuromuscular.cochrane.org/">http://neuromuscular.cochrane.org/</a> |
| 15. Oral Health                                       | <a href="http://ohg.cochrane.org/about-us">http://ohg.cochrane.org/about-us</a>     |
| 16. Pain, Palliative and Supportive Care              | <a href="http://papas.cochrane.org/">http://papas.cochrane.org/</a>                 |
| 17. Pregnancy and Childbirth                          | <a href="http://pregnancy.cochrane.org/">http://pregnancy.cochrane.org/</a>         |
| 18. Schizophrenia                                     | <a href="http://schizophrenia.cochrane.org/">http://schizophrenia.cochrane.org/</a> |
| 19. Skin  | <a href="http://skin.cochrane.org/">http://skin.cochrane.org/</a>                   |
| 20. Tobacco Addiction                                 | <a href="http://tobacco.cochrane.org/">http://tobacco.cochrane.org/</a>             |
| 21. Wounds  | <a href="http://wounds.cochrane.org/">http://wounds.cochrane.org/</a>               |

Source: NIHR Evaluation Trials and Studies (2015)<sup>40</sup>

A further four CRGs, based in the UK, are funded by commissioners other than NIHR:

- Infectious Diseases
- Methodology
- Vascular
- Stroke

There is also field-based activity that is not funded through NIHR.

\* During 2015 the Cochrane Infectious Diseases Group took over the editorial base of the HIV/Aids Group. Sources that pre-date this change referred to 53 CRGs, and sources consulted after 2015 referred to 52 CRGs.

### *Global landscape of systematic review production: Main points*

- *Cochrane has had an enormous impact on SR production over time*
- *NIHR investment has made this possible for Cochrane*
- *Cochrane contributors have made an important contribution to methodology and other processes, advocating change and improving guideline production*
- *There are many other SR producers in the UK, making up a large systematic review playing field*
- *On average the cost of Cochrane reviews to NIHR is low (around £15,000) compared to TARs (£175,000) but this does not take into account quality or relevance of the review product*
- *Cochrane is a reliable first port of call with a strong history, reputation and brand.*

## CHAPTER 2 - PERFORMANCE OF NIHR FUNDED CRGS AND COCHRANE UK

### Overview

*To assess and appraise the performance of NIHR-funded CRGs and Cochrane UK, this chapter will explore the outputs and activities of the CRGs, issues surrounding quality assurance and timeliness, and propose options for defining and measuring quality in the future. Points covered in this chapter include:*

- *Activity and outputs from NIHR-funded groups and Cochrane UK.*
- *Variability between CRGs and how this is being addressed within Cochrane*
- *Challenges in terms of timely delivery of SRs*
- *Assessment of performance and quality; measurement of appropriate and transparent key outcome metrics*

### Outputs

#### Publication of reviews by NIHR-funded Cochrane Review Groups

Analysis of output by NIHR-funded CRGs cannot solely be judged on number of reviews and protocols, as the size of topics and scope of work varies between CRGs. The number of 'empty' reviews, those with no included studies, must be considered; alongside broad reviews that 'lump' together multiple interventions on a topic, and more specific reviews that 'split' down into much narrower questions. Consequently, output of CRGs can be assessed using measures of clinical relevance and general workload. Much of the information presented below has been drawn from comprehensive analysis undertaken by the Cochrane Editorial Unit to inform the QQR of UK CRGs undertaken by NIHR in 2013.<sup>41</sup>

The table below presents the number of active reviews (reviews that have not been withdrawn) registered by each of the NIHR-funded CRGs in Issue 1/12 of the CDSR (January 2016).

Table 5: Number of active reviews and protocols by NIHR-funded CRG (up to 26.1.16)

| Cochrane Review Group                              | Active Reviews | Active Protocols |
|--|----------------|------------------|
| Airways  | 302            | 52               |
| Bone, Joint and Muscle Trauma                      | 118            | 30               |
| Cystic Fibrosis and Genetic Diseases               | 149            | 29               |
| Dementia and Cognitive Improvement                 | 125            | 55               |
| Common Mental Disorders                            | 154            | 60               |
| Ear, Nose and Throat Disorders                     | 101            | 47               |
| Epilepsy   | 83             | 26               |
| Effective Practice and Organisation of Care (EPOC) | 106            | 63               |
| Eyes and Vision                                    | 150            | 56               |

| <b>Cochrane Review Group</b>         | <b>Active Reviews</b> | <b>Active Protocols</b> |
|--------------------------------------|-----------------------|-------------------------|
| Gynaecological Cancer                | 162                   | 41                      |
| Heart                                | 152                   | 49                      |
| Incontinence                         | 79                    | 16                      |
| Injuries                             | 138                   | 38                      |
| Neuromuscular Disease                | 121                   | 34                      |
| Oral Health                          | 149                   | 47                      |
| Pain, Palliative and Supportive Care | 203                   | 51                      |
| Pregnancy and Childbirth             | 533                   | 84                      |
| Schizophrenia                        | 198                   | 86                      |
| Skin                                 | 77                    | 45                      |
| Tobacco Addiction                    | 73                    | 12                      |
| Wounds                               | 122                   | 54                      |
| <b>Total</b>                         | <b>3,295</b>          | <b>973</b>              |

Source: Cochrane Database of Systematic Reviews: Issue 1 of 12, January 2016, (searched 26.1.16)<sup>42</sup>

The QQR<sup>41</sup> presented another workload indicator: the number of included studies per review. The table below shows that new reviews produced by the top five ranked NIHR-funded CRGs included between 12.3-21 studies.

Table 6: Number of included studies per new review for NIHR Funded CRGs. From April 2008 - March 2013: top 5 CRGs

| <b>Rank</b> | <b>NIHR Funded CRG</b>  | <b>Studies/new review</b> |
|-------------|---|---------------------------|
| 1           | Heart   | 21.0                      |
| 2           | Skin  | 20.0                      |
| 3           | Depression, Anxiety and Neurosis (now called Common Mental Disorders) | 18.8                      |
| 4           | Tobacco Addiction   | 18.6                      |
| 5           | Schizophrenia   | 12.3                      |

Source: Quinquennial review (July 2013)<sup>41</sup>

#### [Maintenance and updating workload](#)

In addition to overall output and included studies, current workload can be analysed according to the number of active reviews and active protocols maintained by each CRG (reviews and protocols that have not been withdrawn). Table 5 presents the maintenance and updating burden by NIHR-funded CRGs, represented as the number of active protocols. Withdrawn reviews and protocols were omitted from the analysis.

#### [Most accessed Cochrane reviews](#)

Nine of the top 10 most accessed Cochrane reviews of 2014 were produced by NIHR-funded CRGs. A number of these are substantially out of date.

Table 7: Top 10 most accessed Cochrane reviews of 2014

| Cochrane Review  | NIHR-funded CRG                                 | Number of accesses* |
|--|---|---------------------|
| 1. Gillespie LD, et al. <b>Interventions for preventing falls in older people living in the community</b> (2012) CD007146. <sup>43</sup>   | Yes, BJMT                                       | 15,121              |
| 2. Cooney GM, et al. <b>Exercise for depression</b> (2013) CD004366. <sup>44</sup>   | Yes, CMD  | 13,867              |
| 3. Moore ER, et al. <b>Early skin-to-skin contact for mothers and their healthy newborn infants</b> (2012) CD003519. <sup>45</sup>   | Yes, PCB  | 13,610              |
| 4. Jefferson T, et al. <b>Neuraminidase inhibitors for preventing and treating influenza in adults and children.</b> (2014) CD008965. <sup>46</sup>                                      | No, ARI (however the review was funded by NIHR) | N/A                 |
| 5. Waters E, et al. <b>Interventions for preventing obesity in children</b> (2011) CD001871. <sup>47</sup>   | Yes, Heart                                      | 9,414               |
| 6. Reeves S, et al. <b>Interprofessional education: effects on professional practice and healthcare outcomes (update)</b> (2013) CD002213. <sup>48</sup>                                 | Yes, EPOC                                       | 12,461              |
| 7. Zwarenstein M, et al. <b>Interprofessional collaboration: effects of practice-based interventions on professional practice and healthcare outcomes</b> (2009) CD000072. <sup>49</sup> | Yes, EPOC                                       | 10,275              |
| 8. Moore ZEH, et al. <b>Risk assessment tools for the prevention of pressure ulcers</b> (2014) CD006471. <sup>50</sup>   | Yes, Wounds                                     | 10,011              |
| 9. Sandall J, et al. <b>Midwife-led continuity models versus other models of care for childbearing women</b> (2015) CD004667. <sup>51</sup>  | Yes, PCB  | 9,898               |
| 10. Shepperd S, et al. <b>Discharge planning from hospital to home</b> (2013) CD000313. <sup>52</sup>  | Yes, EPOC                                       | 9,828               |

Source: Cochrane Collaboration (2015)<sup>1, 53</sup>

\*"The term 'accesses' in the table refers to full text downloads of the PDF and html versions of a Cochrane review via Wiley Online Library."<sup>1</sup>

### 'Empty' reviews

'Empty' reviews refer to SRs that found no studies suitable for inclusion. These reviews represent considerable workload in undertaking the review process up to the point of study inclusion. Whilst useful in identifying gaps in the research evidence, and need for further research, empty reviews may present no conclusions, or conclusions based on excluded studies that were not quality assessed. Therefore these reviews may be of limited use to clinicians and decision-makers.<sup>6, 54, 55</sup>

The number of 'empty' reviews conducted by each CRG varies. In 2013, the Cochrane Editorial Unit presented the number of 'empty' new or updated reviews produced by the top five UK-based\* CRGs.<sup>41</sup>

Of concern are empty reviews with overly restrictive inclusion criteria concerning the types of studies, such as only randomised controlled trials, in situations where other types of studies addressing the question exist. Empty reviews, in policy terms, are uninformative. While it was not possible to fully investigate this issue in the timeframe allowed, examples of an empty review produced by an NIHR-funded CRG were identified. A review of vision-screening<sup>56</sup> found no RCTs therefore concluded that there was no evidence available. As a consequence, a European organisation<sup>57</sup> had to commission a new independent review to include evidence from observational studies to provide evidence to inform their decision-making.<sup>58, 59</sup> To date, this Cochrane review still contains no data and has not been updated since 2009.

Table 8: Proportion (and total number) of new or updated reviews that are 'empty' (have no included studies)

| Rank | CRG  | Empty reviews |        |
|------|--|---------------|--------|
|      |  | % Total       | Number |
| 1    | Cystic Fibrosis and Genetic Diseases                                 | 34.1%         | 73     |
| 2    | Eyes and Vision  | 23.0%         | 26     |
| 3    | Neuromuscular Disease  | 21.6%         | 29     |
| 4    | Developmental, Psychosocial and Learning Problems (not NIHR-funded)* | 21.3%         | 16     |
| 5    | Oral Health  | 19.1%         | 17     |

Source: Hilton (2013)<sup>41</sup> \*Please note this table included one non-NIHR funded CRG.

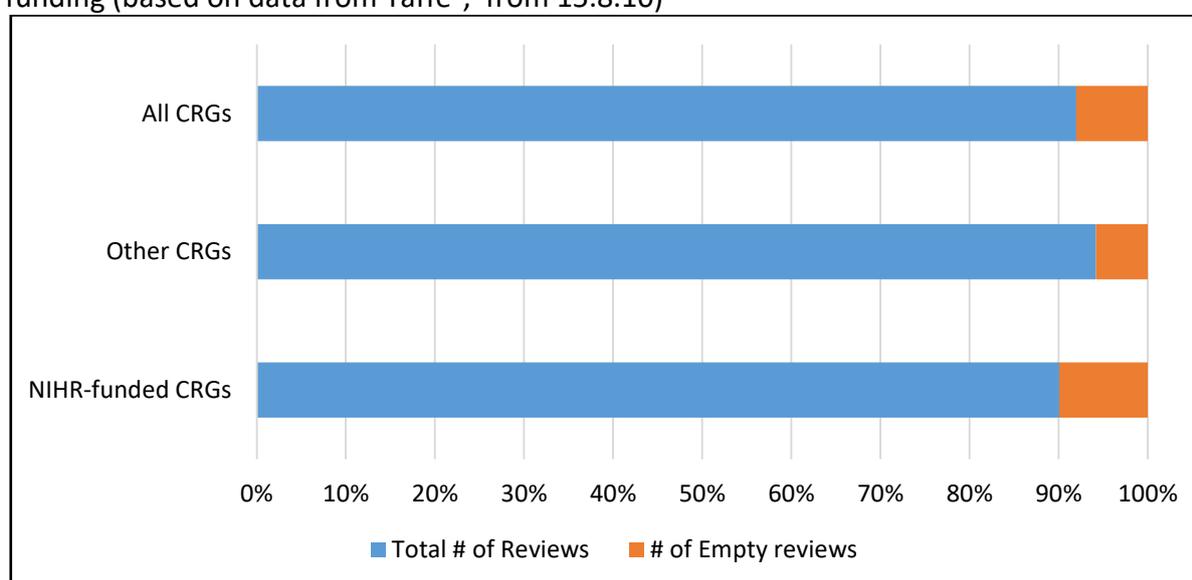
A study conducted in 2010 found that nearly 9% of all reviews published in CDSR had no included studies meeting the inclusion criteria.<sup>6</sup> The study found that NIHR-funded CRGs produced 52% of all reviews on CDSR (2,249/4,320, based on data from Yaffe<sup>6</sup>) however these CRGs also contributed nearly 66% of all empty reviews (248/376, based on data from Yaffe<sup>6</sup>).

Table 9: Reviews and Empty Reviews by NIHR-funded CRG (based on data from Yaffe<sup>6</sup>, from 15.8.10)

| Cochrane Review Group   | Total # of Reviews | # of Empty reviews | % of Empty reviews |
|---|--------------------|--------------------|--------------------|
| Airways   | 223                | 26                 | 12                 |
| Bone, Joint and Muscle Trauma                                       | 92                 | 3                  | 3                  |
| Cystic Fibrosis and Genetic Diseases                                | 93                 | 25                 | 27                 |
| Dementia and Cognitive Improvement                                  | 88                 | 12                 | 14                 |
| Common Mental Disorders (formerly Depression, Anxiety and Neurosis) | 111                | 6                  | 5                  |
| Ear, Nose and Throat Disorders                                      | 65                 | 7                  | 11                 |
| Epilepsy  | 54                 | 6                  | 11                 |
| EPOC  | 68                 | 5                  | 7                  |
| Eyes and Vision   | 80                 | 19                 | 22                 |
| Gynaecological Cancer   | 85                 | 7                  | 8                  |
| Heart   | 87                 | 4                  | 5                  |
| Incontinence  | 66                 | 2                  | 3                  |
| Injuries  | 103                | 14                 | 14                 |

| Cochrane Review Group                | Total # of Reviews | # of Empty reviews | % of Empty reviews |
|--------------------------------------|--------------------|--------------------|--------------------|
| Neuromuscular Disease                | 83                 | 14                 | 17                 |
| Oral Health                          | 108                | 18                 | 17                 |
| Pain, Palliative and Supportive Care | 134                | 16                 | 12                 |
| Pregnancy and Childbirth             | 394                | 35                 | 9                  |
| Schizophrenia                        | 148                | 18                 | 12                 |
| Skin                                 | 48                 | 3                  | 6                  |
| Tobacco Addiction                    | 53                 | 3                  | 6                  |
| Wounds                               | 66                 | 5                  | 8                  |
| <b>Total for NIHR-funded CRGs</b>    | <b>2,249</b>       | <b>248</b>         | <b>11</b>          |
| <b>Total on CDSR for all CRGs</b>    | <b>4,320</b>       | <b>376</b>         | <b>9</b>           |

Figure 5: Reviews and empty reviews for NIHR-funded CRGs and CRGs with other sources of funding (based on data from Yaffe<sup>6</sup>, from 15.8.10)



These data highlight the underlying issue concerning empty reviews: NIHR-funded CRGs undertake a greater percentage of empty reviews than non-NIHR funded CRGs, and each empty review represents considerable work up to the point of study exclusion.

#### Number of guidelines based on SRs

Usage and citation of Cochrane reviews in clinical guidelines and guidance acts as an important measure of impact. On an ongoing basis, Cochrane UK assess the extent to which clinical guidelines by key guidelines developers, are informed by Cochrane SRs. An assessment of this impact measure looked at guidelines by NICE, SIGN and WHO.<sup>41</sup>

Table 10: Cochrane reviews from UK CRGs that inform NICE guidelines, August 2013: top five CRGs

| Rank | CRG                                | Number of reviews informing NICE guidelines |
|------|------------------------------------|---|
| 1    | Pregnancy and Childbirth           | 158   |
| 2    | Schizophrenia                      | 31  |
| 3    | Incontinence                       | 28  |
| 4    | PaPAS                              | 27  |
| 5    | Dementia and Cognitive Improvement | 26  |

Source: Hilton (2013)<sup>41</sup>

Table 11: Number of Cochrane reviews informing NICE, SIGN or WHO guidelines, August 2013: top five CRGs

| Rank | CRG                              | Number of reviews informing NICE, SIGN or WHO guidelines |
|------|----------------------------------|--|
| 1    | Pregnancy and Childbirth         | 202  |
| 2    | Schizophrenia                    | 68   |
| 3    | Airways                          | 66   |
| 4    | Depression, Anxiety and Neurosis | 51   |
| 5    | Stroke                           | 49   |

Source: Hilton (2013)<sup>41</sup>

Table 12: Number of NICE, SIGN, or WHO guidelines informed by UK CRG reviews: top five CRGs

| Rank | CRG                              | Number of guidelines informed by reviews |
|------|----------------------------------|--|
| 1    | Pregnancy and Childbirth         | 42                                       |
| 2    | Depression, Anxiety and Neurosis | 35                                       |
| 3    | Schizophrenia                    | 20                                       |
| 4    | EPOC                             | 16                                       |
| 5    | Wounds                           | 15                                       |

Source: Hilton (2013)<sup>41</sup>

An analysis was carried out to identify the number of NIHR-funded CRG reviews cited in NICE and SIGN Guidelines published between 2013 and February 2016. This showed 415 Cochrane reviews from 19 of the 21 UK-based NIHR-funded Cochrane Review Groups were cited in 103 guidelines (74 NICE; 29 SIGN).<sup>5</sup> See Table 1 in Appendix 4 for more detailed information. Whilst this shows guideline producers identify and cite Cochrane SRs, this does not directly demonstrate influence or impact on behalf of Cochrane.

## Quality of reviews produced by NIHR-funded Cochrane Review Groups

Cochrane has undertaken the following projects to assess variation in quality of review output and benchmark methods and processes:

- Methodological Expectations of Cochrane Intervention Reviews (MECIR) audit<sup>4</sup>
- Readability study<sup>60</sup>

Working on the assumption that the higher quality a review is the greater impact and usage it will have, the Cochrane Editorial Unit commenced routine quality screening for all new Cochrane reviews of interventions. Currently diagnostic reviews are excluded from this programme. New SRs are screened against a subset of MECIR standards.<sup>4</sup>

Although this exercise has provided invaluable insight into the CRGs who perform well consistently producing high quality reviews,<sup>1</sup> the Committee notes a lack of transparency in disseminating the findings of these exercises. It remains unclear what remedial action was put in place to support those CRGs performing less favourably.

### Readability study

The Cochrane Editorial Unit (CEU) has invested significant time in assessing 'readability' of Cochrane review abstracts against a number of key indicators.<sup>60</sup> Abstracts of new SRs published in October 2011 and 2012 were compared, and for the most part fewer of the more recent abstracts failed to meet the basic indicators required, such as reporting the search sources and dates, describing the number of included studies and setting out the review objectives as a PICO question. Areas of weakness identified in more of the 2012 reviews included failing to report risk of bias, failing to describe harms and not giving absolute data by comparison group. As a consequence of this readability audit, the CEU made the statement, "Transparency is the best arbiter of quality". The CEU further recommended that based on the findings of the Risk of Bias (RoB) audit, integration of the Methodological Expectations of Cochrane Intervention Reviews (MECIR) standards should be supported with training materials and greater prominence of MECIR and Cochrane Handbook advice in RevMan.<sup>60</sup> The Methodological Expectations of Cochrane Intervention Reviews (MECIR) are methodological standards developed by Cochrane, to which all Cochrane Protocols, SRs, and SR updates are required to meet. The MECIR standards cover both the conduct and reporting of Cochrane SRs. As well as clearly setting out the best practice methods expected to be followed within Cochrane, MECIR also offers external readers a transparent guide to the requirements for Cochrane reviews.<sup>61</sup>

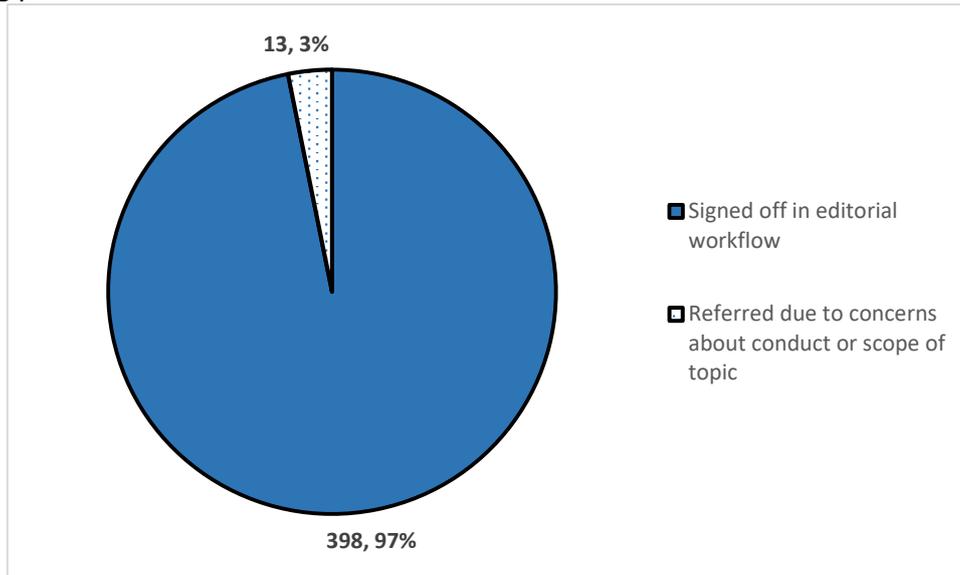
### MECIR evaluation

The following year after making those recommendations, the Cochrane Editorial Unit undertook a pre-publication quality assessment and assurance project, to appraise reviews by NIHR-funded CRGs prior to publication in CDSR. The CEU's team of editors screened 411 SRs between September 2013 and September 2015 to see how well the reviews conformed the standards required, the Methodological Expectations of Cochrane Intervention Reviews (MECIR).<sup>19</sup> Reviews were classified into three groups:

- Triaged: no or very minor amendments required
- Minor amendments
- Major amendments

Where amendments were required, further action involved referral to an editor from the CEU quality team, and additional work was required to ensure SRs were revised to a sufficient standard.

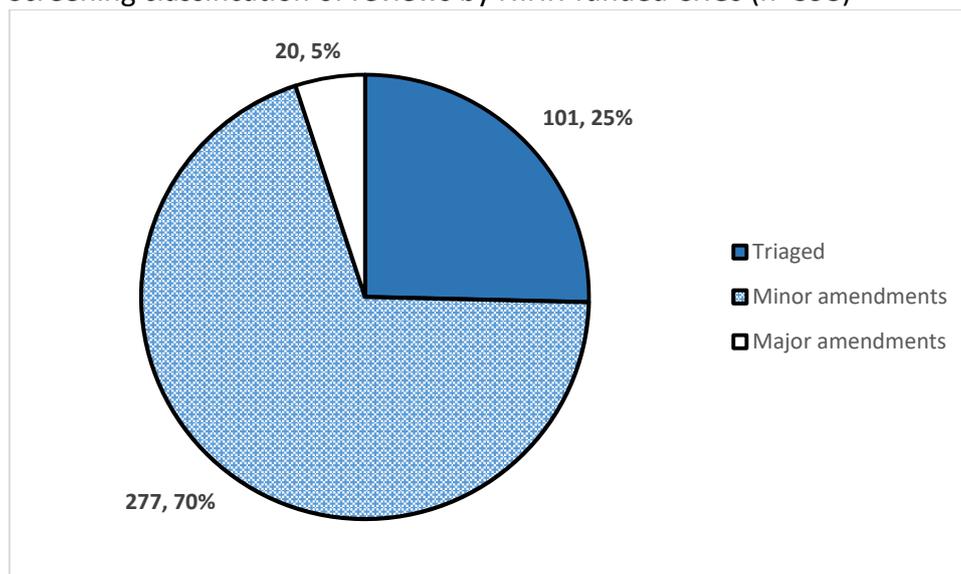
Figure 6: Stage of pre-publication process for NIHR-funded reviews submitted to the MECIR screening process



Source: Cochrane Collaboration (2015)<sup>4</sup>

The majority of reviews (97%, n=398) submitted for MECIR screening had been signed off in the editorial workflow, prior to copy-editing. These reviews were considered the best indicator of average quality prior to publication. Thirteen SRs (3%) were referred for screening because the CRGs had issues with the way the reviews were being conducted, or because there were particular concerns about how the review might be judged if it addressed a particular controversial review question.

Figure 7: Screening classification of reviews by NIHR-funded CRGs (n=398)



Source: Cochrane Collaboration (2015)<sup>4</sup>

According to the Cochrane Editorial Unit Quality report (2015): "*Minor amendments were defined as: where reviews have been assigned to an editor from the quality team in the CEU. Typically, these reports include more detailed comments on the abstract, PLS, Summary of Findings tables, and main conclusions. All the items picked up here are easily fixed, but the reports can vary in length from 3 pages to 6 or 7 in extreme cases. The vast majority of the issues identified relate to inconsistencies of interpretation or clarification of how methods were implemented. These reports point to issues that are fixable with edits to the text or revisions to the GRADE assessments*".<sup>4</sup>

The Committee wondered to what extent 3-7 pages can still be considered "minor" but as a whole, the overall results of the screening project were positive. Ninety-five percent of all assessed NIHR-funded SRs required no or minor amendments. Halfway through the MECIR screening project, the CEU quality team excluded reviews from the following CRGs from pre-publication screening, having decided their SRs were consistently high quality:

- Airways
- Bone, Joint & Muscle Trauma
- Developmental, Psychosocial & Learning Disorders (not in receipt of NIHR-funding)
- ENT
- EPOC
- Eyes & Vision
- Infectious Diseases (not in receipt of NIHR-funding)
- Oral Health
- Pregnancy & Childbirth
- Wounds

During 2015, two further CRGs were exempted from screening, as their reviews were considered to have consistently reached a sufficient standard:

- Common Mental Disorders
- Peripheral Vascular Disorders (now Vascular, not in receipt of NIHR-funding)

The number of SRs screened for each NIHR-funded CRG varied considerably (3-40 SRs). The results of the MECIR screening project showed variability between NIHR-funded CRGs. Classification of reviews requiring major amendments (0-3 SRs), minor amendments (2-28 SRs) and triaged (0-14 SRs) varied between the assessed CRGs. The results presented in the CEU MECIR report<sup>4</sup> showed that for all but one NIHR-funded CRG, the proportion of assessed reviews requiring revision (whether minor or major amendments) was greater than those requiring no change (triaged). Considering the majority of assessed reviews (97%) had already progressed through the editorial workflow process, this raises concerns about how thorough the editorial checks and processes are to ensure SRs are robust and error-free.

Figure 8: Classification of pre-publication screening reports by NIHR-funded CRGs<sup>4</sup>

CONFIDENTIAL CONTENT FROM COCHRANE – MADE AVAILABLE TO NIHR

Source: Cochrane Collaboration (2015)<sup>4</sup>

The MECIR screening project appraised a subset of SRs against specific MECIR requirements, and categorised the proportion of reviews fulfilling these criteria (Y), partially fulfilling criteria (P), failing to fulfil criteria (N), or presenting insufficient information to allow formulation of a clear judgement (U). These assessments were presented for two time periods (August 2013 and August 2014). Of 56 SRs included in the original audit, 28 were published by 15 NIHR-funded CRGs over the two assessment months.

Areas of concern existed in key items relating to planned protocol methods, which included search methods, subgroup analyses, inclusion criteria and deviations from the protocols. The proportion of reviews assessed as being fully or partially compliant with all the audit items was higher in 2014 than in 2013. The latter cohort of reviews showed improvements in the implementation of GRADE, including summary of findings (SoF) tables. These reviews were also assessed as being more internally consistent (MECIR standards for conduct).<sup>19</sup> However, there was a lack of transparency in the reporting of the MECIR subset assessment, and only limited data were presented on the findings for a few select domains. The Committee noticed the lack of openness in reporting how well each NIHR-funded CRG performed on all the MECIR measures.

The MECIR project highlighted issues of variability in the way that reviews were conducted by NIHR-funded CRGs and supported Yaffe's observations about empty reviews with no included studies.<sup>6</sup> The number of included studies in reviews assessed between 2013-2014 ranged between 0-181 studies.<sup>4</sup> Variation also existed in the way reviews were reported; summary of findings (SoF) tables were included in 53% of SRs in 2013, increasing to 64% in 2014 (mean: 57%).

In addition to producing an internal report on the timeliness and quality of assessed reviews by NIHR-funded CRGs,<sup>4</sup> the CEU has also produced a table of common errors and good practice that is publicly available.<sup>62</sup>

#### Concordance between Cochrane and non-Cochrane meta-analyses

To assess the concordance between Cochrane versus non-Cochrane reviews Useem and colleagues<sup>63</sup> conducted a matched pair analysis, comparing pairs of meta-analyses in cardiovascular disease that had examined the same set of interventions and outcomes. Their objectives included to contrast the two literatures in terms of sample size, numbers of included subjects, date of publication, and the degree to which the studies included in each member of the pair overlapped. Furthermore, they compared the magnitude of effect sizes and shifts in the confidence intervals that would lead to differences in a reader's interpretation of the results; and differences in terms of summary effect size and statistical precision. Finally, they assessed how frequently meta-analyses were cited as a function of whether and how the results between each matched pair differed.

Forty matched pairs of reviews were analysed. The two sets were similar in terms of which was first to publication, how many studies were included, and average sample sizes. The paired reviews included a total of 344 individual clinical trials: 111 (32.3%) studies were included only in a Cochrane review, 104 (30.2%) only in a non-Cochrane review, and 129 (37.5%) in both. Overall, 37.5% of pairs had discrepant results. Non-Cochrane reviews reported significantly higher effect sizes and lower precision than their matched Cochrane reviews. Reviews reporting an effect size at least two-fold greater than their matched pair were cited more frequently.<sup>63</sup>

#### Comparative Risk of Bias (RoB) analysis of Cochrane and non-Cochrane reviews

An analysis of RoB in Cochrane and non-Cochrane reviews was undertaken to assess the methodological quality using a dataset compiled at Kleijnen Systematic Reviews Ltd. Risk of bias was assessed using the ROBIS tool.<sup>18</sup> This tool consists of four domains:

1. Study eligibility criteria
2. Identification and selection of studies
3. Data collection and study appraisal
4. Synthesis and findings.

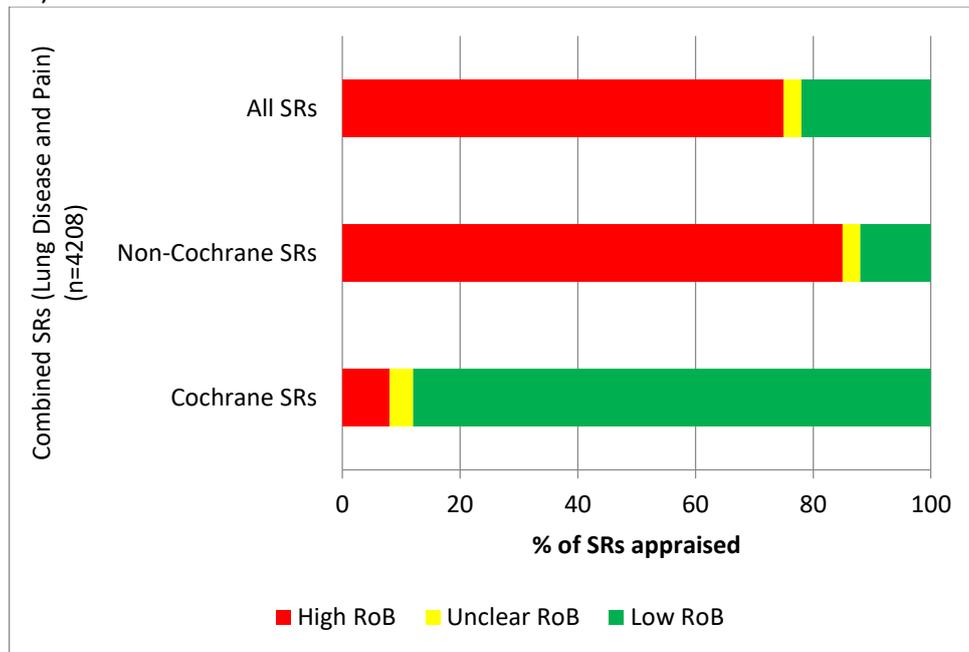
A bibliometric analysis was undertaken and is reported in Appendix 3. The internal version of KSR Evidence,<sup>23</sup> containing in-process and completed assessments, was analysed to look at comparative publication rates of reviews published by Cochrane and those conducted by all other review producers (non-Cochrane reviews) on the topics of pain and lung disease. Reviews classified as "non-Cochrane SRs" are a large group made up of work undertaken by all other SR producers; these may include specific organisational subsets, for example those in the NIHR TAR programme.

Further analysis of the three levels of RoB summary was also conducted for completed appraisals only. It is important to note that assessment of RoB relates to assessment of

methodological quality of each review based on reported methods. The summaries of overall RoB were graded as:

- Low risk of bias
- High risk of bias
- Unclear risk of bias

Figure 9: Risk of Bias (RoB) appraisals for SRs on the combined topics of pain and lung disease (2010-2015)



Data were not available to conduct a RoB assessment by NIHR-funded CRGs, however it was possible to look at overall RoB assessment for Cochrane and non-Cochrane SRs published on the topic of pain, which may be representative of the work of the NIHR-funded CRG, PaPAS. Figure 10 presents these data, and shows that Cochrane SRs have a much lower percentage of SRs rated as high RoB (10%), when compared to non-Cochrane reviews (80%). For SRs on the topic of lung disease, the rate of Cochrane reviews rated at high RoB was even lower (7%), compared to non-Cochrane SRs (89%).

When both topics are considered together (Figure 9), it is reassuring to note that 88% of Cochrane reviews are rated to have a low RoB, compared to only 12% of non-Cochrane SRs. The finding that 8% of Cochrane reviews (both topics combined) were assessed at high risk of bias was in line with the findings of the CEU's MECIR Screening Project, which found 5% of NIHR-funded SRs assessed required major amendments.<sup>4</sup>

Figure 10: Risk of Bias (RoB) appraisals for SRs on the topic of pain (2010-2015)

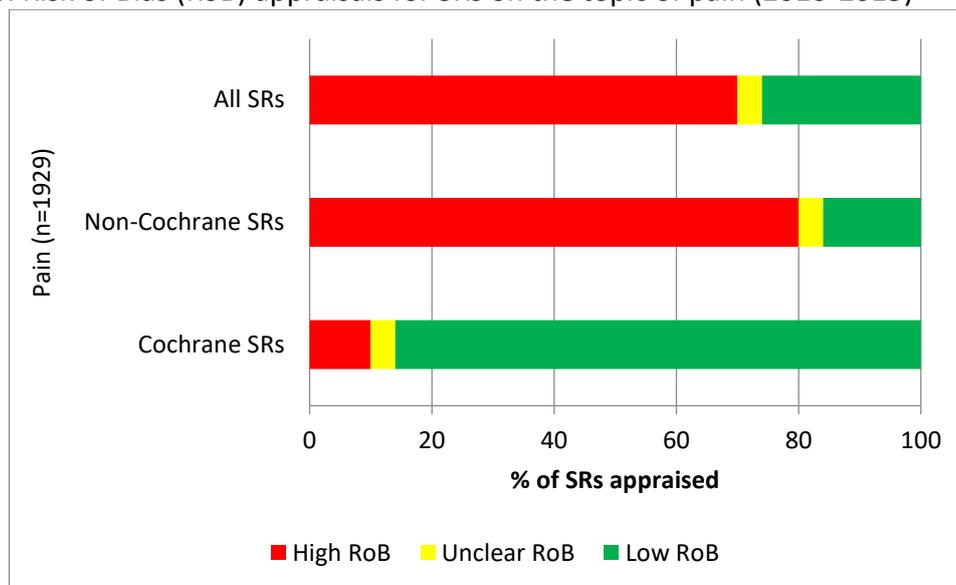
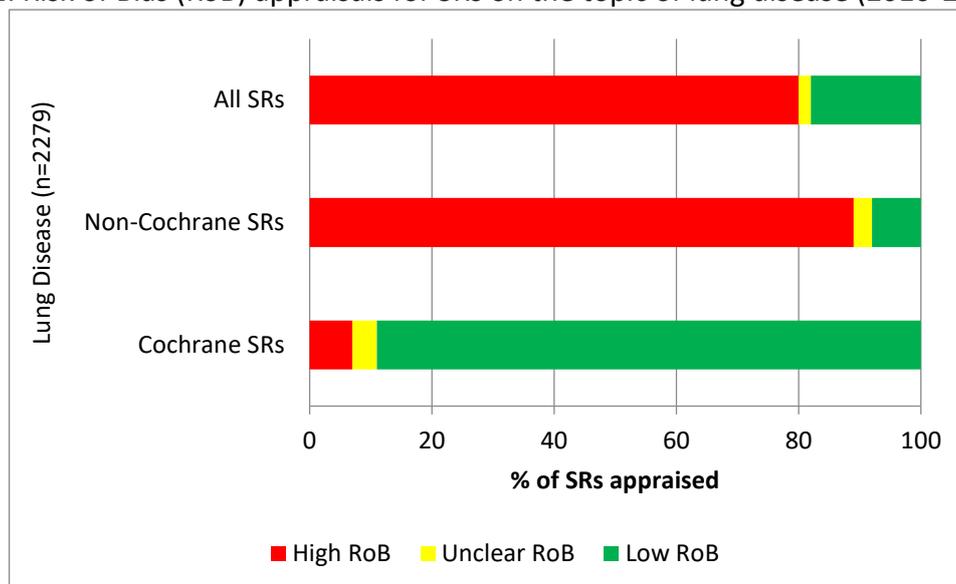


Figure 11: Risk of Bias (RoB) appraisals for SRs on the topic of lung disease (2010-2015)



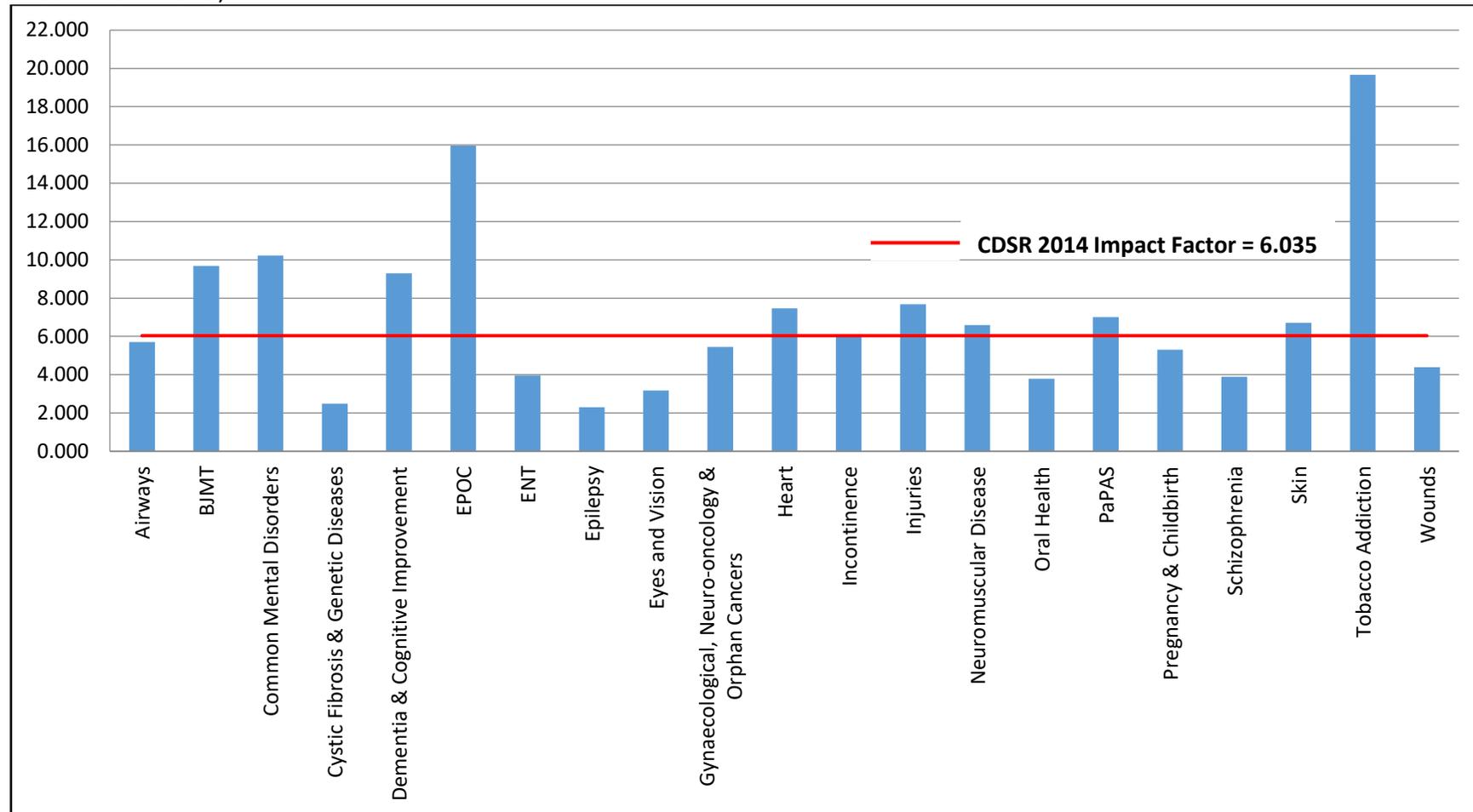
### Impact factors

Another measurable comparative metric of impact relates to citation usage of publications. The most commonly used journal-level citation impact measure is Impact Factor (IF),<sup>64</sup> however there are other impact measures, such as H-index (at author-level) and Altmetrics (based on article-level usage and social media activity).

The CDSR IF for 2014 was calculated as 6.035<sup>65</sup> with the five year IF impact factor of 6.539.<sup>66</sup> The CDSR IF of 6.035<sup>65</sup> can be interpreted as a review published in the CDSR in 2012 or 2013 being cited, on average, 6.035 times during 2014. CDSR was ranked 13<sup>th</sup> out of 153 journals in the "Medicine, General and Internal" category, identified by Thomson Reuters.<sup>67</sup> This placed CDSR in the top 5% of all titles listed in the Journal Citation Report.<sup>67</sup> The IF of CDSR between 2007-2014 is presented in Figure 1 of Appendix 5.

The latest 2014 data are presented in the figure below, and show that Wiley "IF" ranging from 2.308 to 19.667 for NIHR-funded CRGs; with an average Wiley "IF" of 6.99.<sup>68</sup> During 2014 all NIHR-funded groups achieved an impact factor that exceeded their five year average score.<sup>1</sup> It is possible that a CRG's IF may be driven by a single highly-cited review. More information on the Wiley calculated "Impact Factor" is presented in Appendix 5.

Figure 12: Wiley "Impact Factor" for each UK CRG (i.e. number of cites to reviews published in 2012-2013, divided by the number of reviews published in 2012-2013)



Source: Stewart (2016)<sup>68</sup>

UK-based CRGs in receipt of NIHR funding are well-represented in the top 10 most cited SRs of 2014, making up 70% of CRGs.<sup>67</sup> The most cited SR<sup>43</sup> was produced by the Bone, Joint and Muscle Trauma CRG, funded by the NIHR. The SR was also included in the value of investment analysis included in Chapter 4 of this report.

## Activities

### Activity of NIHR-funded CRGs<sup>1</sup>

On an annual basis, an analysis of annual reports produced by all NIHR-funded CRGs is conducted and presented to the NIHR Systematic Reviews Programme Advisory Group (SRPAG).<sup>1</sup> The analysis highlighted several key achievements and activities for 2014.<sup>1</sup>

### Infrastructure grants

Infrastructure grants contribute to costs of the editorial bases of all 21 CRGs discussed in this report (funding in place from 1 April 2015).<sup>1</sup> During 2014, 65% of the 20 CRGs receiving NIHR infrastructure funding were within £5,000 of their budgets. Of these, five groups spent 100% of their budget, 12 CRGs reported an overspend (ranging from £99 to £29,000) and eight CRGs reported an underspend (ranging from £430 to £33,000).<sup>1</sup>

### Updating

As part of the infrastructure review process, information was collated for each CRG on whether their reviews were in need of updating.

It is apparent that CRGs face challenges in review capacity to deal with such numbers of reviews assessed as in need of updating. During the 2014 assessment process, 1,250 reviews were assessed as requiring an update, which were either in-progress or awaiting sufficient resources to complete them.<sup>1</sup>

Table 13: NIHR-CRG reviews assessed as requiring updating

| NIHR-funded CRGs*                                 | Reviews assessed as not requiring an update | As % | Reviews assessed as requiring an update (either underway or awaiting available resources) | As % |
|---|---|------|---|------|
| Airways   | 49  | 73%  | 18  | 27%  |
| Bone, Joint and Muscle Trauma                     | 36  | 51%  | 35  | 49%  |
| Cystic Fibrosis and Genetic Disorders             | 16  | 36%  | 28  | 64%  |
| Dementia and Cognitive Improvement                | 35  | 55%  | 29  | 45%  |
| Common Mental Disorders                           | 45  | 49%  | 47  | 51%  |
| ENT   | 2   | 3%   | 70  | 97%  |
| Epilepsy  | 1   | 3%   | 39  | 98%  |
| Eyes and Vision                                   | 21  | 32%  | 45  | 68%  |
| Gynaecological, Neuro-oncology and Orphan Cancers | 12  | 48%  | 13  | 52%  |

| <b>NIHR-funded CRGs*</b> | <b>Reviews assessed as not requiring an update</b> | <b>As %</b> | <b>Reviews assessed as requiring an update (either underway or awaiting available resources)</b> | <b>As %</b> |
|--------------------------|--|-------------|--|-------------|
| Heart                    | 6  | 8%          | 74   | 93%         |
| Incontinence             | 2  | 7%          | 26   | 93%         |
| Injuries                 | 6  | 6%          | 91   | 94%         |
| Neuromuscular Disease    | 12   | 15%         | 70   | 85%         |
| Oral Health              | 48   | 48%         | 51   | 52%         |
| PaPAS                    | 63   | 47%         | 70   | 53%         |
| Pregnancy and Childbirth | 30   | 9%          | 312  | 91%         |
| Schizophrenia            | 19   | 13%         | 125  | 87%         |
| Skin                     | 10   | 16%         | 52   | 84%         |
| Tobacco Addiction        | 19   | 40%         | 29   | 60%         |
| Wounds                   | 4  | 13%         | 26   | 87%         |

Source: NIHR Evaluation Trials and Studies Coordinating Centre (n.d.)<sup>1</sup>\* Data from 2014 Infrastructure funding summary,<sup>1</sup> therefore EPOC Group is not included.

Further information on Cochrane's criteria for considering where an update is required can be found in section '3.4: Considerations when updating a Cochrane review' of the Cochrane handbook.<sup>69</sup>

## Editorial support and managerial processes

Each CRG has an editorial team who provide advice and support to reviewers and authors. Within a CRG, the editorial team help prospective authors to select and refine their review questions, develop and write protocols, and act in an advisory capacity throughout the review process. Many authors highly value this support and undoubtedly such support is one of the main reasons why Cochrane has built up its reputation of producing high quality reviews. The CRG editorial team is ultimately responsible for the decision to publish each protocol and review within their group's module, and therefore adopts a supervisory role to ensure the review is conducted according the Cochrane Handbook methods<sup>69</sup> and that the review meets MECIR requirements<sup>19, 70</sup> both for the conduct and reporting of the complete review. Methodological rigour is assessed through peer review, audit

and other managerial quality assurance processes. Access to statistical expertise and support from the CRG's trial search co-ordinator or information specialist should also be available.

CRGs report working towards reducing delays and time manuscripts spend in the editorial process; the Injuries CRG have made progress here in their transition towards rapid review production. On average a manuscript spends 5.7 months in their editorial process.<sup>1</sup>

The Cochrane Editorial Unit assessed the time taken by 49 CRGs from receipt of title applications, to registration of titles, publications of protocols and reviews. Only CRGs using the workflow system were included, and workflows completed by 26.12.14 were included in the analysis (1,130 reviews and 1,472 protocols). The results of the analysis showed variation between CRGs for all stages of the review production process.

The results presented below were not restricted to NIHR-funded CRGs; results were anonymised and sorted by the total of the two medians (for protocol and review development workflows). These results show that for over half the review groups, the median time for the review to be in the hands of the editorial base was more than a year, and for the majority of

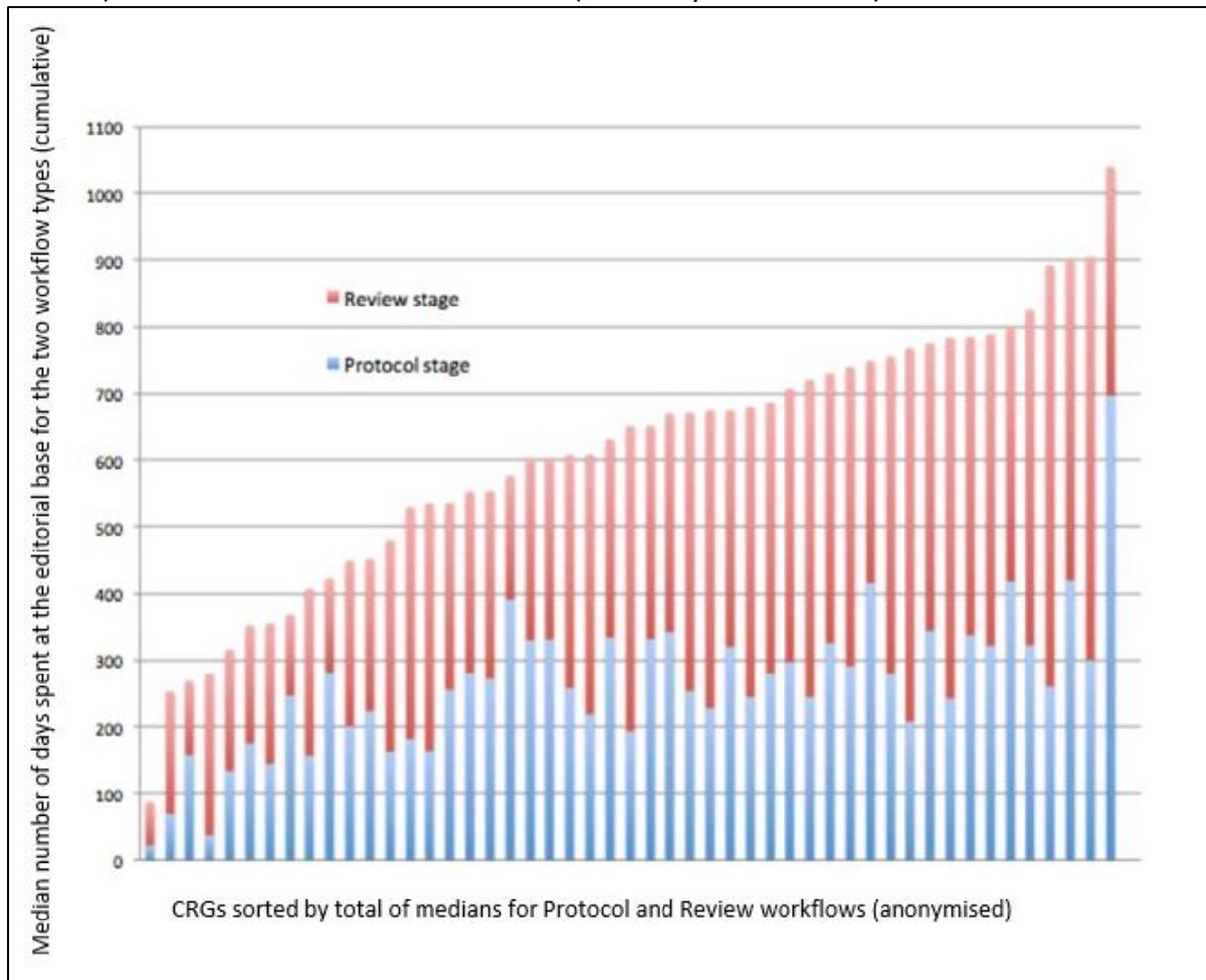
### *Experiences of authors*

Although many authors receive excellent support from the CRGs, the Committee has also received several anecdotal submissions of negative encounters review authors have experienced with poor support from CRG editorial teams. Reports received include excessive delays in receiving editorial feedback on submitted protocols; one group of authors were told to expect feedback no sooner than four months after submission. Other reports mentioned occurrences of inappropriate rigidity concerning inclusion of observational studies in circumstances where non-randomised evidence would be entirely appropriate to the review's scope. This has also been supported by evidence from stakeholder interviews.<sup>2</sup>

Where review authors voluntarily give of their time to undertake review, frequently on top of existing professional and clinical "day jobs", a more supportive and interactive model of editorial support might encourage their continued engagement with Cochrane, and future involvement in review production.

groups, the median time for protocol and review combined to be in the editorial base hands was more than 18 months.

Figure 13: Protocol and review development workflows: time spend at editorial base (days; median) for those CRGs that use workflows (sorted by time at base)



Source: Cochrane Collaboration (2015)<sup>71</sup>

Several CRGs have expanded their review capacity and reach by establishing satellite groups; seven of the UK-based CRGs have done so already.<sup>1</sup> The Common Mental Disorders CRG (previously known as the Depression, Anxiety and Neurosis CRG) reported a new Suicide and Self Harm satellite based at the College of Medicine at Swansea University (funded by NISCHR).<sup>1</sup> Three NIHR-funded CRGs have established two satellites: the Eyes and Vision CRG have a DTA-focused group in Italy and a 'mini-CRG' in the US. The Schizophrenia Group have satellites in China and India, and the Pregnancy Group has satellites in Australia and Japan.<sup>1</sup> The Skin Group have one established satellite in France and are hoping to set up another in the US in the future.<sup>1</sup> Although not classified as a satellite, the Wounds Group is supporting a group in Queensland to undertake reviews of high priority to both the UK NHS and the Australian health system.<sup>1</sup> As well as helping to build and expand review capacity, share resources and workload and raise a CRG's profile, satellites can also be instrumental in the

dissemination of SRs and outcomes. The Heart Group reported their satellite assisted in increasing the reach and impact of the CRG's research.<sup>1</sup>

### Workshops and training

Training plays an important role in developing and maintaining SR expertise and capacity building.

Cochrane UK employs a small core team who are supported by a wider network of training faculty and partner organisations.<sup>72</sup> This allows Cochrane UK to offer a flexible approach to specific learning needs, but drawing on a wider range of skills and expertise. A range of training programmes are provided to meet the learning needs of those preparing SRs, as well as support for dissemination activities.<sup>72</sup>

In addition to review author training, examples of tailored training activities aimed at health professionals, undertaken and supported by Cochrane UK include:<sup>72</sup>

- NIHR Academic Clinical Fellows (ACF);
- Workshops in partnership with the Critical Appraisal Skills Programme (CASP), in London, Oxford, Birmingham, Glasgow and Plymouth;
- Cochrane Fellowships, including the Oxford Deanery Cochrane Fellowship;
- Medical Trainees Project;
- Social media interaction via #WeCATS and Tweet Chats; and
- other forms of ad hoc training.

Training provided and received by staff at NIHR-funded CRG editorial bases is assessed on an annual basis and reported to the NIHR SRPAG.<sup>1</sup>

Training given by staff at CRG editorial bases included protocol development, meta-analysis, Cochrane and advanced methodology, RevMan, and search strategy workshops. This training was delivered in the UK and internationally. Several CRGs also offered to contribute to SR and critical training in the UK and internationally, as well as providing one-to-one author support and teaching medical students in the UK.<sup>1</sup> Training activities by CRGs are mixed. Both the Epilepsy and Neuromuscular CRGs reported that no formal training had been provided by the editorial base during 2013-2014, although new author training continued and existing authors received support whenever methodological and software changes occurred. The Gynaecological CRG conducted a health economics workshop for attendees from UK CRGs, as well as methodologists, authors and co-ordinating editors.<sup>1</sup> Most of the training is rather basic and there is increasing demand for higher level training in editing skills and higher level author skills.

### Specialised registers maintained by NIHR-funded CRGs

The editorial base of each CRG is tasked with developing and maintaining a specialised register of RCTs relevant to the group's particular topic or health problem of interest, as an essential core function.<sup>73</sup> Often a CRG's trial search co-ordinator will facilitate the search process for compiling and updating the specialised register, namely by developing and running complex

search strategies to retrieve relevant RCTs on the topics and conditions outlined in the CRG's inclusion criteria. Records are also identified from other sources, for example, hand searching of journals and conference proceedings, and checking of reference lists and other external trial registers. Typically CRG specialised registers are restricted to RCTs, however some groups are beginning to consider inclusion of other relevant study designs. The EPOC Group has made progress in this area. On a quarterly basis, data from CRG specialised registers are aggregated to form with Cochrane Central Register of Controlled Trials (CENTRAL),<sup>42</sup> available as part of the Cochrane Library.<sup>74</sup>

The number of reports held in a CRG's specialised register could be used as an indicator of workload and output, however this approach has certain limitations.<sup>41</sup> Different CRGs compile, maintain and use their specialised registers in different ways, which may impair comparability. Between CRGs there are variations in their group's scope, some may be narrow and quite specialised (e.g. Cystic Fibrosis and Genetic Diseases), whereas others may be broad encompassing a wider range of topics (e.g. Pregnancy and Childbirth). For these reasons, direct comparison of specialised register content and output may not be a true measure of CRG activity. Nevertheless, the size of a CRG's register may provide some indication of the research activity within each CRG's scope.<sup>41</sup>

Considerable NIHR-funded CRG activity goes into compilation and maintenance of specialised registers. The UK CRG's Quinquennial Review Report<sup>41</sup> rated the PaPAS CRG register as the largest in the UK, containing the most studies (45,025 studies in 2013; see Table 1, Appendix 6).<sup>41</sup> Rankings were also presented to identify the top five UK CRGs, calculated as the ratio of number of active reviews per 1,000 register records.<sup>41</sup> The Gynaecological Cancer CRG was ranked as the top NIHR-funded CRG with 30.04 reviews per 1,000 register entries (see Table 2, Appendix 6).<sup>41</sup>

For more information on the number of studies in NIHR-funded CRG specialised registers, please see Appendix 6.

### *Performance of NIHR-funded CRGS and Cochrane UK: Main points*

- *Cochrane has had a substantial output*
- *Cochrane needs to articulate and define its core business and products better; users value timely, high quality, full systematic reviews that are relevant to NHS decision making. Relevance of reviews, and coverage of topics remains an issue*
- *Nine of the top 10 most accessed Cochrane reviews of 2014 were produced by NIHR-funded CRGs.*
- *Considerable variability in procedures, customer service, and quality exists between reviews and CRGs, however this is not well addressed*
- *Editorial groups are often slow with turn arounds to authors*
- *Quality is a critical point, which requires openness and transparency.*
- *Quality of Cochrane reviews is good relative to non-Cochrane reviews, a small proportion of Cochrane reviews are not good quality*
- *The relationship between CRG performance and volume of specialised register activity remains unclear*
- *Groups are not able to maintain updating of all reviews, and some important reviews remain out of date*
- *Cochrane needs to more widely address the scope of evidence being used; encouraging more focus on sources of data other than RCTs, such as data from observational studies, indirect comparisons, economics, or adverse effects evidence.*

## CHAPTER 3 - MEETING KEY CLINICAL AND POLICY QUESTIONS IN THE NHS

### Overview

*This chapter will discuss how much impact NIHR-funded CRG reviews and Cochrane UK has had on health care and policy-making, and how well this work aligns with the aims and priorities of the NHS. Impact will be discussed in terms of:*

- *Policy and NHS Planning*
- *Methodology development and progression for systematic reviews in Cochrane (better reviews, timely etc.)*
- *Research*
- *Health outcomes*

### Current NHS plans

The purpose of Cochrane as a whole is to prepare, maintain and promote SRs to inform healthcare decisions,<sup>69</sup> and by doing so, improving people's health and wellbeing. Within the UK, NHS England set out its plan for the future of the NHS in the document the "NHS Five Year Forward View".<sup>75</sup> Developed in partnership with health and care organisations such as the Care Quality Commission, Public Health England and NHS Improvement (previously Monitor and National Trust Development Authority), the Five Year Forward View strategy proposes new models of integrated health and social care intended to close "widening gaps in the health of the population, quality of care and the funding of services."<sup>75</sup>

For Cochrane UK (i.e. the Cochrane Centre in Oxford) to meet its aim of informing healthcare decision-making, it needs to align its priorities, actions and output with those of NHS England, which are summarised and presented in Appendix 7. Cochrane UK functions as the "front door" contact for relationship building. A key area for expansion is to function as an interface between review groups and policy/decision makers. Cochrane UK should provide assistance in terms of facilitating, enabling and delivering priority reviews. Mechanisms should be put in place to deal with any delays.

Alongside the Five Year Forward View's vision<sup>75</sup> for shared care sits the NHS England Research and Development (R&D) Strategy, currently in a draft form following an extensive consultation process.<sup>76</sup> The Research and Development Strategy draws a clear process for promoting and building a culture within NHS England that values and promotes research and innovation. It notes the importance of engaging with partner organisations and building on existing relations with the NIHR, Health Education Institutes (HEIs), Public Health England, Local Authorities and other stakeholders. Many of the aims of the R&D Strategy sit within the potential strengths of Cochrane, including promoting uptake of research skills, training providers, collaboration between individuals and organisations, and engagement with patients and the public.

### Better reviews: relevant, timely and high quality

Although Cochrane reviews in the UK represented very good value, there is reliance on volunteers and support from other funders, and between-CRG variation in outputs and activity. Cochrane must address the need for better reviews that are relevant, timely and of high methodological quality, to support decision-makers, guidelines writers, patients, clinicians and managers. The specific issues Cochrane must deal with include:

- a. Patient/public involvement for review scoping and context
- b. Collaboration with NICE
- c. Prioritise to topics of greatest importance
- d. Keep more reviews up-to-date
- e. Prepare reviews more rapidly
- f. Use best available evidence, beyond RCTs

### What impact has Cochrane had in meeting clinical and policy issues in the NHS?

Impact of Cochrane SRs should not be solely measured in citations within guidelines and guidance.<sup>1</sup> For any review to be considered having impact, it should result in the following outcomes:

- a) Results in a clear research recommendation; leading to further commissioned research
- b) Results in a change in practice or behaviour; measurable impact on NHS healthcare
- c) Contributes to the research portfolio of evidence; which in turn may result in either of the above

### Policies

One method of assessing Cochrane impact on UK policy-making and practice involves quantifying the impact SRs have on NICE Quality Standards (NICE QS).<sup>41</sup> NICE defines their quality standards as:<sup>77</sup>

*"... concise sets of prioritised statements designed to drive measurable quality improvements within a particular area of health or care. They are derived from the best available evidence such as NICE guidance and other evidence sources accredited by NICE. They are developed independently by NICE, in collaboration with health and social care professionals, their partners and service users."*

It should be noted that NIHR-funded CRGs are not directly comparable due to the intrinsic differences between groups; i.e. some CRGs relate to a broad topic area, whereas other might focus on a single condition. When examining CRG impact on NICE QS, some CRGs might be restricted to one or two standards (e.g. the Cystic Fibrosis and Genetic Diseases Group), whereas others may relate to many standards (e.g. the Heart Group). Consideration of other CRGs, such as the Wounds or the EPOC Groups, required a degree of subjectivity to match the CRG to the published NICE QS.<sup>41</sup>

Within the top five ranked UK-based CRGs for this assessment, four were in receipt of NIHR-funding and one was not (based in Ireland).

Table 14: NICE quality standards and how they relate to UK CRGs, as assessed by Hilton and Tovey for their report: top 5 CRGs

| Rank | CRG   | Relevant NICE Quality Standards (QS) |
|------|---|--------------------------------------|
| 1    | Pregnancy & Childbirth  | 14                                   |
| 2    | Heart   | 12                                   |
| 3    | Depression, Anxiety and Neurosis (now called Common Mental Disorders) | 11                                   |
| 4    | Psychosocial (not NIHR-funded)*                                       | 11                                   |
| 5    | Gynaecological Cancer   | 7                                    |

Source: Quinquennial review (July 2013)<sup>41</sup> \*Please note this table included one non-NIHR funded CRG.

An important and high impact NICE guidance document, about preventing falls and assessing risk in older people, was published in 2013<sup>78</sup> The guidance was informed by an SR published by the NIHR-funded BJMT CRG, which was last updated in 2012.<sup>43</sup> Evidence surveillance undertaken within NICE has identified a minimum of 35 new trials potentially eligible for inclusion in an update of the Gillespie SR, however an update of this review is not planned to be completed until 2017. The review in question was the most cited SR on CDSR during 2014,<sup>67</sup> Given the relevance to the NHS, resource use, health impact and research funding, this SR should be prioritised for an expedited update, not least to ensure currency of NICE Guidance.

NIHR-funded CRGs who produced high impact reviews during 2013 which led to further primary research, included the Heart, Incontinence, Oral Health and Wounds groups<sup>1</sup>

Alderson and Tan examined the extent of citation of Cochrane reviews in NICE guidelines.<sup>79</sup> There were 731 citations of Cochrane reviews in the 106 guidelines, ranging from no citations to 44 citations, with a mean of 6.90 (standard deviation 9.23). Some Cochrane reviews were cited more than once in different guidelines; therefore, the figures do not represent the number of Cochrane reviews cited. Although the data show an impressive level of use of Cochrane reviews in NICE clinical guidelines, there is scope for better use of the knowledge contained in CRGs when NICE draws up the scope for guidelines, and to encourage more involvement from Cochrane review authors on NICE guideline development groups. Cochrane and NICE could do more to ensure that Cochrane reviews and guideline questions are better aligned, work harder at sharing knowledge from Cochrane reviews and guidelines in development, and try to speed up the editorial process of turning relevant Cochrane protocols into Cochrane reviews, or updates of Cochrane reviews, so that they can be considered for a clinical guideline.

#### [Reviews that change practice and change or save lives](#)

##### *Relevance to NHS*

An evaluation to rate selected reviews completed by NIHR-funded CRGs was conducted by the NIHR Evaluation Trials and Studies Co-ordinating Centre (NETSCC).<sup>80</sup> The purpose of this exercise was to determine how relevant to the NHS a sample of Cochrane reviews was judged to be by clinicians, policy-makers and members of the public. A cross-section of raters from

the NDC 'College of Raters' were asked to explore where a selection of reviews from each of the NIHR-funded CRGs were considered of relevance to the NHS. Review titles were selected from the CRG 2015 annual reports, which detailed all reviews published in 2014 against their infrastructure grant. This referred to reviews not funded via any other funding scheme or grant. The first three reviews reported from each CRG were selected for relevancy rating. No further selection criteria were followed.

Raters were asked to answer Yes, No or Unclear; and were given the following definition of relevance to follow:

***"By relevance to the NHS we mean, in your opinion, the research is likely to be of use to (all or some of) clinicians, patients, commissioners and policy makers within the NHS setting"***

Two users were approached from each of the following categories of raters within the NDC College of Raters:

- Public rater
- GP/AHP rater (GP, nurse, allied health professional, specialist practitioner)
- Commissioning rater (commissioner, allied health policy, manager)

Despite aiming to include two individuals from each of these categories, some invitations received no response. As such not all reviews received a full six relevance ratings.

Once rating was completed, each review was classified according to the following opinion-based relevancy coding, so that an overall rating could be achieved using a 'traffic light' system, presented below:

Table 15: NETSCC Relevancy coding, number and percentage reviews ranked by judgement of relevance

| Key | Relevancy code                                  | Number of assessed reviews | % of assessed reviews |
|-----|---|----------------------------|-----------------------|
|     | Relevant, no more than one No or Unclear rating | 25                         | 42                    |
|     | More than one No or Unclear rating              | 34                         | 57                    |
|     | All No or Unclear ratings                       | 1                          | 1                     |
|     | <b>Total</b>                                    | <b>60</b>                  | <b>100%</b>           |

Source: NETSCC (2016)<sup>80</sup>

Of the 60 SRs assessed, only one was rated as 'not relevant' to the NHS (all responses given as "no" or "unclear"). Forty-two percent of assessed Cochrane SRs were graded as relevant, and 57% of assessed SRs were classified as having no or unclear relevance by more than one respondent. As previously detailed the number of ratings received differs for each review assessed, which skews the overall results. The raw data is included in Appendix 8.

This was a rapid exercise conducted to inform the NIHR evaluation. As such, there are some limitations due to the rapid timeline for completion of the rating process, including arbitrary selection of systematic reviews from each CRG, which potentially may not be representative of each CRG's work programme, together with missing data from a lower than expected response rate. Despite these considerations, nearly all the assessments rated the SRs as green or yellow for relevance, and only one SR was rated as not relevant.

A benefit of an organisation driven by individual reviewers and clinicians, rather than by funding bodies, is the focus on both patient- and clinician-relevant topics. A hypothetical scenario to illustrate this might involve Cochrane volunteers undertaking a review of footcare for diabetics in the community. Topic prioritisation at a top-down commissioner-level may not identify this as a priority topic, however patients and frontline healthcare professionals would be more aware of the positive impact such a service can have on diabetes-related complications and quality of life.

Engaging health care professionals and health care organisations has additional benefits; participation of clinicians in health research has been linked to improvements in the delivery of health care and patient outcomes.<sup>81</sup> Successful engagement appears to work at two levels; firstly at an organisational level, and secondly by way of close working between researchers and clinicians.<sup>81</sup>

#### *Addressing burden of disease*

In order to assess UK CRGs whose scope matched the priority areas for clinicians, decision-makers, patients and public, the CEU undertook analysis of topics covered by UK CRGs, to see how they performed against two measures of disease burden.<sup>41</sup> The performance measures selected to assess clinical priority were:

- Years of life lost to premature mortality (YLL), and
- Years lived with disability (YLD).

A key benefit of Cochrane's collaborative model of working alongside reviewers who are also health care professionals is that the review authors based within the health care system gave in-depth and acute knowledge of their particular topic of interest that top-down researchers may not be aware of. The reviewer/clinician-level approach enables insight and innovation at this level, increasing relevance to the NHS and impact on health care.

As the analysis included all CRGs based in the UK, the remit was broader than that of this report, as CRGs based in the UK but funded by organisations other than NIHR were included, such as the Infectious Diseases and Stroke Groups.

When the top 10 causes of YLLs in the UK for 2010 were ranked against UK CRGs, four of the five UK CRGs were funded by NIHR (80%, see Table 16 below). This represented coverage of 40% of top 10 causes of YLLs.

Table 16: Top 10 causes of YLLs in the UK in 2010 and how they related to UK, and NIHR-funded, CRGs

| Mean rank | Condition/clinical priority area   | NIHR Funded CRG   |
|-----------|------------------------------------|---|
| 1.0       | Ischaemic heart disease            | Heart   |
| 2.3       | Lung cancer                        |   |
| 2.7       | Stroke                             | (Stroke: not funded by NIHR)  |
| 4.4       | COPD                               | Airways   |
| 4.6       | Lower respiratory tract infections |   |
| 6.0       | Colorectal cancer                  |   |
| 7.1       | Breast cancer                      |   |
| 9.3       | Self-harm                          | Depression, Anxiety and Neurosis (now called Common Mental Disorders) |
| 9.3       | Cirrhosis                          |   |
| 9.3       | Alzheimer's disease                | Dementia and Cognitive Improvement                                    |

Source: Hilton (2013)<sup>41</sup>

Analysis of causes of YLDs in the UK in 2010, indicated that four NIHR-funded CRGs were included in the top 10 rankings, and two of those CRGs covered two topics each. This represented 60% coverage of the top 10 causes of YLDs, as an indicator of relevance to clinical priority areas.

This analysis failed to indicate what percentage of SRs were not ranked as relevant, and this remains an area of uncertainty.

Table 17: Top 10 causes of YLDs in the UK in 2010 and how they related to UK, and NIHR-funded, CRGs

| Mean rank | Condition/clinical priority area | NIHR Funded CRG   |
|-----------|----------------------------------|---|
| 1.0       | Low back pain                    |   |
| 3.7       | Falls                            | BJMT  |
| 3.8       | Major depressive disorder        | Depression, Anxiety and Neurosis (now called Common Mental Disorders) |
| 3.9       | Neck pain                        |   |
| 4.7       | Other musculoskeletal disorders  |   |
| 6.1       | Anxiety disorders                | Depression, Anxiety and Neurosis (now called Common Mental Disorders) |
| 7.1       | COPD                             | Airways   |
| 8.5       | Drug use disorders               |   |
| 8.7       | Asthma                           | Airways   |
| 8.9       | Migraine                         | PaPAS   |

Source: Hilton (2013)<sup>41</sup>

Unfortunately information was not available presenting how many NIHR-funded did not match to related YLDs.

*Behaviour change: professional/clinical/public*

An assessment into how stakeholders value Cochrane SRs<sup>3</sup> showed that although policy-makers use the reviews to inform clinical guidance in the UK and internationally, the reviews are judged to be less helpful when they are out of date or the research question is too restrictive. Certain Cochrane reviews were found to have contributed to identification of gaps in the evidence base, and subsequently stimulating new research in the area. Bunn et al (2015)<sup>3</sup> identified several impacts and likely impacts of Cochrane reviews. Among these, the most well-defined were targeting research gaps and health-care policy. There was less evidence of a direct impact on clinical practice and the organisation and delivery of NHS services.

While reviewers and researchers should consider how they could increase the influence of their reviews, impacts such as these are difficult to measure.<sup>3</sup> The Committee feels that more work is required into suitable methods for impact analysis, and in Chapter 6, suggests the need for clearer definition and monitoring of performance and impact measurement.

The Neuromuscular, PaPAS, Injuries and Tobacco Addiction CRGs all produced high impact or breakthrough reviews which have a potential for a change in practice.<sup>1</sup> A notably influential review that impact on guidance was a review on nicotine replacement therapy (NRT).<sup>11</sup> The review, published by the NIHR-funded Tobacco Addiction CRG, was noted as being cited in the NICE Guidance on brief interventions and referral for smoking cessation.<sup>82</sup> Furthermore, the NRT SR<sup>11</sup> was also cited by WHO as high quality evidence of effectiveness, and NRT was added it to their list of essential medicine. This SR has been incorporated into international guidelines from the US and Australia, and is an excellent example of a high impact SR.<sup>10</sup>

NICE developed the Cochrane Quality and Productivity (QP) topics<sup>83</sup> to aid the NHS in identifying practices that could be stopped or reduced significantly, freeing up funding and/or resources without a negative effect on the quality of NHS care. All QP topics are available in the public domain,<sup>83</sup> and each was derived from a Cochrane SR that has concluded the evidence showed a practice to be harmful or ineffective, and that the practice should not be used, or that there was insufficient evidence to support widespread adoption of the practice. Each QP considers the cost to the NHS, a current estimate of NHS use, levels of productivity savings anticipated, any costs to implement the recommended changes, the potential impact to the NHS and the likely ease and timeframe of implementation of the recommended changes.

A sample of QPs were assessed, identifying practice changing reviews from over half of the NIHR-funded CRGs (13/21 CRGs). A selection of these QPs identified practice changing recommendations from recent SRs and are described in Appendix 9. A full list of the NICE QPs, together with an illustrative example, are presented in Appendix 10.

### *Reviews relevant to social care*

Cochrane needs to recognise the importance of social and community care in underpinning health. Some CRGs are already undertaking SRs of relevance in these areas.<sup>10</sup> One of the key challenges faced by Cochrane in the future, is the ageing population and increasing demands on health and social care.<sup>10</sup> Reassuringly, stakeholders acknowledge that engagement with Cochrane to focus on topics, such as multi-morbidity, ageing and long-term conditions, will be key in answering these "big questions" faced in the future by the NHS.<sup>2</sup>

### *Culture change: concept of scientific rigour and independence*

#### *Cochrane as a gold standard*

The perception of Cochrane as a gold standard of evidence and SR methodology is widespread, and this was endorsed by many of the stakeholder interviewees.

The Committee asked NIHR to commission some stakeholder interviews about their views of Cochrane.<sup>2</sup> Thirty-four interviews were conducted with a range of Cochrane review users and producers, many of whom have multiple roles and interests in evidence synthesis and how the products of this are used in health care in the UK. The full report is included in Appendix 11. The following quotes from the report are relevant to the perception of Cochrane as a gold standard:

- *"Cochrane was in the vanguard of suggesting that research is not just for researchers and has contributed to the wider health and research culture in this regard."*<sup>2</sup>

Although Cochrane as a whole is seen as a recognisable brand endorsing best evidence, concern exists among stakeholders that timeliness and relevance to policymaking is variable.

- *"You have pieces of very well done research that have limited use and interest to policy and practice development and/or commissioning".*<sup>2</sup>

As scope and complexity of reviews increases, stakeholders are increasingly questioning Cochrane's flexibility to deal with differing sources of evidence, including observational studies.

Cochrane UK has offered week long training programmes for Academic Clinical Fellows (ACF) and provided opportunities for local trainees to participate in a six month full-time placement as a 'Cochrane Fellow'. This training placement has been held in high regard and designated by the UK Faculty of Public Health as a "National Treasure".<sup>84</sup>

Fostering transferrable skills in the NHS is highly valued, however as noted before, negative author experiences may discourage reviewers from participating in Cochrane reviews in the future.<sup>2</sup>

### *Promote understanding of EBM and systematic reviews among end-users, in particular the public*

Cochrane UK has worked to build greater recognition of the need and use of SR evidence, and to develop Cochrane's profile as an advocate for evidence-informed healthcare.<sup>85</sup> One way to achieve this at a grass-roots level is to engage students and future clinicians. The 'Students 4

Best Evidence' (S4BE) initiative involves an international network of students with an interest in learning about evidence-informed health care, who develop their skills by reviewing online resources, and engaging in discussions and student-led tutorials.<sup>85</sup>

Cochrane UK encourages engagement with charities, professional bodies and NHS organisations. Examples of this work include a weekly list of new and updated review titles to patient and consumer charities, e.g. the National Childbirth Trust (NCT), and to membership organisations, such as the Association of Medical Research Charities (AMRC). Where possible, Cochrane UK works alongside organisations to produce evidence-informed materials and publications to support their aims.<sup>85</sup>

Cochrane UK has commissioned independent research to inform and improve communication and collaboration with NHS organisations involved in policy-making and commissioning. This research will aid further development of networks and relationships within the NHS.<sup>85</sup>

Despite these efforts, work still needs to be done to promote the value of SRs to the public and especially to policy-makers<sup>10</sup> and health commissioners, who are interested in having dialogue about how to achieve this.<sup>2</sup>

#### Communicating with relevant audiences

Many of the NIHR-funded CRGs reported that the Cochrane Consumer Network<sup>32</sup> acted as a link to establish and maintain links with consumers, although the level of consumer involvement varied greatly across groups, and was described as being dependent on how much of the CRG's overall budget had been allocated to such activity.<sup>1</sup> CRGs noted that consumers played an important role in identifying and highlighting gaps in research, and consumers were increasingly becoming involved in areas such as:<sup>1</sup>

- Input to topic prioritisation
- Impact of treatment on patients
- Membership of advisory panels
- Development of plain language summaries
- Refereeing protocols and reviews
- Outcomes development

In reality, there seems to be variable experience in implementing consumer involvement, and this should be the focus of the Consumer Network 2020 strategy.

#### Open access

Cochrane is working in partnership with Wiley, and has established a mechanism for open access. The strategic plan states all reviews and protocols will be open access by 2020.<sup>86</sup> But the actual steps to achieve this and whether the financial model will hold remains unclear. As a first step towards full open access, all new Cochrane reviews became free to access for all readers 12 months after publication, from February 2013.<sup>9</sup> On 12 April 2016 a PubMed search identified 519 records within the Cochrane Database of Systematic Reviews as available via open access.<sup>87</sup> Cochrane has informed the Committee that 2,572 reviews were available as open access, as of Q3 2016. Although this transformative initiative will enable freely available

Cochrane SRs for all globally, there are concerns regarding possible impact of loss of Cochrane Library royalties on the financial stability of Cochrane. Funders and Cochrane (and the publisher of the Cochrane Library) need to do work on how to move towards open access to increased accessibility to Cochrane Reviews. Transparency in proposed plans is encouraged.<sup>10</sup>

#### *Plain language summaries*

Plain language summaries are produced to offer a format easily accessible and understandable by patients and the public. Improvements in the format and content of lay summaries can be achieved by engaging consumers in the planning, writing and production of the summaries.<sup>10</sup>

#### *Social media*

Cochrane as a whole has adopted new technologies and social media to engage and communicate with a variety of audiences.<sup>88</sup> Twitter and blogging have proved useful media to reach Cochrane users and commissioners.

Twitter is being utilised as an easily accessible medium for frequently, daily communications aimed at clinical staff. The majority of social media activity is undertaken centrally by CEU and Cochrane UK or by CRGs, rather than at an individual review author-level, with many CRGs interacting with external review users and stakeholders via Twitter and other web-based forms of communication. This communication activity is often facilitated by Cochrane UK, who have also offered social media training to further enable successful exploitation of social media as a dissemination tool.<sup>1</sup>

Furthermore, some CRGs have also been successful in setting up and contributing on a regular basis to “Cochrane Corners” within high impact, relevant journals.<sup>1</sup>

Many NIHR-funded CRGs, including the Common Mental Disorders Group in particular, published SRs which were highly cited or received considerable media attention and social media activity.<sup>1</sup>

Cochrane UK's twitter campaign includes focussed regular communication about commonplace and frequently occurring topics, on trends such as:

- Evidence for Everyday Midwifery (#EEMidwifery)
- Evidence for Everyday Nursing (#EENursing)

In addition to designated threads, Cochrane UK have hosted tweetchats, such as @WeNurses<sup>89</sup> tweetchat about re-siting cannulae.

Cochrane as a whole has developed a relationship with Wikipedia, aimed at closer engagement between Cochrane and the Wikimed community. Wikipedia represents a well-known and well-used internet resource, and the partnership allows Cochrane to raise its profile, ensure articles are accurate, up-to-date and informed by review evidence. Cochrane UK continue to support the Wikipedia project by giving details of new and updated reviews on a Wikipedia task list, and support to Wikipedia editors is provided by Cochrane's Wikipedian-in-Residence (WiR).<sup>85</sup>

The Evidently Cochrane initiative<sup>90</sup> features weekly blogs aimed at patients, carers, the general public, clinicians, researchers, decision- and policy-makers. Blogs cover findings of specific reviews in an accessible news-style format, as well as explaining the reasoning behind undertaking reviews to answer uncertainties in health and health care. Evidently Cochrane UK has been using a successful format for communication, winning a UK Health Blog Award in 2015.

Two high-impact blogs highlighted important engagement between Cochrane and patients, carers and the public. The first resulted from a collaboration between Cochrane UK and a carer of a person with Motor Neurone Disease (MND), and was published during MND Awareness Month. The blog investigated evidence from Cochrane reviews of MND treatment and disease management, within the context of the patient's experiences.<sup>85</sup> The second impactful blog, written by a young person with cystic fibrosis (CF) linked the work of the NIHR-funded Cystic Fibrosis and Genetic Diseases CRG, with the real-life experiences of a child living with CF.<sup>85</sup>

The next step would be more consistent social media 'conversations' about aspects and impact of SRs with Cochrane learning from end users what their interests and experiences are with using evidence generally and Cochrane evidence in particular.

### Methodology

Although NIHR does not fund methods groups, Cochrane as an organisation has acted as a key driver of research synthesis methods development and actively promoted adoption of many aspects of systematic review methodology. Innovations developed within Cochrane have been adopted by reviewers on a global scale.

Table 18: Methodologies developed within Cochrane and/or facilitated by Cochrane (for example, meetings at Cochrane Colloquia)

- Cochrane tool for assessing risk of bias in randomised trials<sup>91</sup>
- Cochrane risk of bias assessment tool: for non-randomised studies of interventions (ACROBAT-NRSI)<sup>92</sup>
- Cochrane Highly Sensitive Search Strategy (HSSS) for identifying randomised controlled trials in Medline<sup>93</sup>
- Prediction study Risk Of Bias ASsessment Tool (PROBAST)<sup>94</sup>
- Risk of bias in systematic reviews tool (ROBIS)<sup>18</sup>
- Indirect and mixed treatment comparisons<sup>95 96</sup>
- Network meta-analysis<sup>97, 98 96</sup>
- QUADAS-2<sup>99</sup>
- Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD)<sup>100, 101</sup>
- Quality in Prognostic Studies (QUIPS)<sup>102</sup>
- Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS)<sup>103</sup>

- Screening Embase for RCTS using Crowdsourcing<sup>104</sup>
- Methods to identify reports of adverse effects (AE)<sup>105-109</sup>

There are areas where reviews are being undertaken by other producers where Cochrane has yet to carry out many SRs. These areas include aetiology, diagnostics and prognostics. However, Cochrane has helped develop methodologies for conducting diagnostic<sup>110</sup> and prognostic reviews.<sup>111</sup> Cochrane has also carried out considerable work in developing methods to systematically investigate adverse events (AE).<sup>112</sup>

Personal communication from Stefan Lange at the Institute for Quality and Efficiency in Health Care (IQWiG) in Germany indicated that IQWiG highly values Cochrane for their methodological contribution and that senior methodological staff from IQWiG specifically attend the Cochrane Colloquium for this purpose.<sup>113</sup>

#### *Cochrane Methodology Group*

The Cochrane Methodology Group aims to "summarise the empirical basis for decisions about methods for systematic reviews and evaluations of healthcare, including preventive, diagnostic, therapeutic, rehabilitative and educational interventions".<sup>114</sup> The main focus is to examine methodological studies that make use of empirical data derived from SRs. The Cochrane Methodology Group compiles the Cochrane Methodology Register (CMR) which is available as part of the Cochrane Library.<sup>42</sup> The Group provide structured abstracts of methodological studies and reviews in the annual 'Cochrane Methods' publication,<sup>115</sup> which acts as a supplement to the CDSR.<sup>24</sup>

#### *Cochrane as a benchmark*

##### *For conduct and reporting of SRs*

Many SRs refer to following the principles laid out in both the Cochrane Handbook<sup>69</sup> and the Centre for Reviews and Dissemination's guidance for undertaking SRs in health care.<sup>116</sup> The Cochrane Handbook is viewed as the dominant source for SR methods guidance. A pragmatic citation search undertaken using Google Scholar<sup>117</sup> suggests in excess of 20,000 documents cite the Cochrane Handbook.<sup>117</sup>

International guidance produced by the US Agency for Healthcare Research and Quality (AHRQ),<sup>118</sup> the Institute of Medicine for the National Academies of Sciences (IoM)<sup>119</sup> and the Institute for Quality and Efficiency in Health Care (IQWiG)<sup>120</sup> each refer to the Cochrane Handbook as the gold standard source.

Similarly the Cochrane tool for assessment of risk of bias in randomised studies<sup>91</sup> has been adopted by thousands of review producers.

#### *Seen as trustworthy*

Cochrane is seen as a trusted source by healthcare professionals, clinicians, guideline developers, information producers and infomediaries.<sup>2</sup> Cochrane evidence is also valued by health commissioners, policy developers, NHS managers and the public, however they find it

more challenging to use in a practical sense. Consequently, they value it less than could be the case, leaving room for additional improvement.<sup>2</sup>

### *Meeting key clinical and policy issues in the NHS: Main points*

- *Impact needs to be assessed in a meaningful way, and Cochrane should be more proactive in its planning or anticipation of impact*
- *Impact will only happen if prioritisation is done better. Existing processes are helpful but the Committee feels these could be more successful if there is a more centralised strategy to bring structures together.*
- *Cochrane has had substantial collateral impact having influenced methodological developments. Looking forward, Cochrane needs to proactively embrace other approaches such as incorporating cost-effectiveness information and using the best available evidence, which includes observational studies where RCTs are missing.*
- *Uncertainties exist surrounding the proportion of NHS vs academic reviewers. The opportunity costs of utilising NHS clinicians should be balanced against the benefits of embedding research into practice. A research-active clinician is a better clinician for improved patient outcomes.*
- *A large volume of Cochrane activity does not have an impact, often due to timing. Cochrane should be encouraged to consider upcoming guideline questions to identify review title priorities. It is essential to get an overall profile of Cochrane impact as a whole, rather than focussing on single impactful reviews.*
- *For many NHS institutions Cochrane is the first port of call; an important impact message*
- *To date Cochrane has had an impact on people, methods, policy, research, and health outcome. Are CRGs proactive enough to sustain these impacts? Were reviews impactful due to serendipity, or due to planning?*

## CHAPTER 4 – CASE STUDIES OF THE ECONOMIC IMPACT OF SELECTED SYSTEMATIC REVIEWS

### *Overview*

*The chapter describes four case studies to evaluate the economic value of Cochrane reviews to the UK and the value of increased/faster adoption of healthcare interventions in the NHS resulting from the publication of Cochrane reviews, key points include:*

- *The value of implementing four healthcare interventions recommended in four exemplar Cochrane reviews is estimated by applying the value of implementation Value of Investment Model (VOIM) framework described in Fenwick et al.<sup>121</sup>*
- *This framework operates by seeking to assess the value per patient of implementing a healthcare intervention. These benefits are scaled up to the population level by considering the size of current and future population eligible to receive the intervention.*
- *Value for money of Cochrane reviews*
- *Considerations for Cochrane to incorporate economic evaluations*
- *Possible outcomes of implementing Cochrane reviews*

For this chapter, NIHR commissioned work from the University of York, Centre for Reviews and Dissemination (CRD) and the Centre for Health Economics (CHE), which aimed to evaluate the value of Cochrane reviews to the UK and specifically to evaluate the value of increased/faster adoption of healthcare interventions in the NHS resulting from the publication of Cochrane reviews.

### *York CRD/CHE study*

This study<sup>122</sup> has estimated the value of implementing four healthcare interventions recommended in four exemplar Cochrane reviews by applying the value of implementation Value of Investment Model (VOIM) framework described in Fenwick et al.<sup>121</sup> This framework operates by seeking to assess the value per patient of implementing a healthcare intervention. These benefits are scaled up to the population level by considering the size of current and future population eligible to receive the intervention. The full report is in Appendix 12.

Four Cochrane reviews were selected for the analysis. The selection of the four reviews was carried out by the committee from a short list of 16 reviews; eight of which were put forward by the committee, and eight of which were put forward by the York team. The reviews selected were chosen as exemplars because they are considered to have had a major impact in either in shaping NICE guidelines or have significant implications in terms of improvements in health. However it was difficult to find acceptable examples of impactful Cochrane reviews that could be matched to corresponding economic models.

The questions to be addressed were as follows:

1. What is the value, in terms of both health and monetary value, of implementing the health care intervention identified as effective in the four Cochrane reviews?
2. Given plausible values for the degree to which a Cochrane review may influence practice what is the value of each of these Cochrane reviews both in terms of improved health and economic value?
3. What factors are likely to influence the value of implementing the health care intervention identified as effective?

In order to meaningfully apply the VOIM framework the selected reviews also were required to meet the following three criteria:

- The Cochrane review draws unequivocal conclusions regards the clinical benefits of one or more healthcare interventions;
- An existing UK based assessment of cost-effectiveness study that evaluates one of the recommended interventions and all relevant comparators;
- The recommend intervention is cost-effective at threshold of £30,000 per QALY and reports either incremental QALYs and costs or NMB.

The four included Cochrane reviews were:

|   |
|---|
| Review of anti-VEGF treatments for diabetic macular oedema (DMO); <sup>123</sup>                    |
| Review of interventions for preventing falls in older people living in the community; <sup>43</sup> |
| Review of statins for the primary prevention of cardiovascular disease (CVD); <sup>124</sup>        |
| Review of collaborative care for depression and anxiety problems. <sup>125</sup>                    |

To assess the impact of the Cochrane review, a model was run assuming an increase in utilisation upon publication of the Cochrane review. This allows the estimation of utilisation both with and without the Cochrane review. To calculate the value of the increased utilisation the authors considered the additional QALYs generated and their value to the NHS assuming a threshold of £30,000 per QALY (i.e. that we are willing to spend £30,000 for one additional QALY of health). The value of this increase in health was then compared with the cost of carrying out a Cochrane review.

Using the base-case assumption, the estimated health gains for the four case studies ranged from 116 QALYs from the review of anti-VEGF therapies for DMO to 15,816 QALYs from the review of statins for the primary prevention of CVD. The value in terms of net monetary benefit (NMB) which accounts for the value of the health gains and any additional costs of implementing the intervention ranged from a NMB of approximately £0.9 million for the anti-VEGF review to £0.4 billion in the Statins review.

Table 19: Impact of the Cochrane reviews to the NHS

| Cochrane reviews   | Assuming full implementation |                 | Base-case assumptions of the implementation |              |
|--|------------------------------|-----------------|---|--------------|
|  | QALYs gain                   | Net values      | QALYs gain                                  | Net values   |
| Review of anti-VEGF treatments for diabetic macular oedema <sup>123</sup>                          | 5,600                        | £48,444,564     | 116   | £877,048     |
| Review of Interventions for preventing falls in older people living in the community <sup>43</sup> | 23,910                       | £740,601,295    | 1,558                                       | £48,139,336  |
| Review of statins for the primary prevention of cardiovascular disease <sup>124</sup>              | 534,406                      | £13,832,171,646 | 15,816                                      | £409,227,452 |
| Review of collaborative care for depression and anxiety problems <sup>125</sup>                    | 58,254                       | £917,535,903    | 416   | £6,487,256   |

Source: Hodgson (2015)<sup>122</sup>

These significant benefits were observed assuming relatively modest increases in implementation resulting from the Cochrane reviews of just 1% in our base case. In scenario analyses conducted assuming just a 0.1% increase in utilisation, the value of the realised benefits remained positive in three of the cases (the exception being anti-VEGF therapy for DMO) with estimated health gains ranging between 12 QALYs from the review of anti-VEGF therapies for DMO to 1590 QALYs in the statins review and NMB ranging from -£10,816 for the anti-VEGF review to £41 million in the Statins review.

This study also highlights a number of drivers of value and the importance of considering the policy context. In particular the following factors are important when considering the potential value of any review or update:

- The size of the eligible population;
- Current and projected utilisation of the intervention;
- Current and future NICE guidelines and technology appraisals;
- Cost-effectiveness and resource implications of implementing the interventions.

The analysis also illustrates some of the challenges of evaluating the value of

The results of this study, while subject to a number of substantial caveats have shown that there is substantial value from implementing the recommended healthcare interventions both in terms of additional health benefits as well as net value to the NHS. A Cochrane recommendation regarding a cost-effective intervention needs only to lead to a fairly small change in practice to represent value for money. Further, these reviews can originate from any of Cochrane review groups including those based outside the UK. This comes however with a caveat to avoid cross-subsidisation of low impact reviews.

Cochrane outputs and in particular the difficulty of disentangling the influence of Cochrane from NICE guidance and other implementation activities. Due to these complexities it may be more appropriate for future research to consider how Cochrane is able to optimise their contribution to current processes of evaluation and implementation of interventions.

### Committee reflections

The Committee considered that what this work is primarily contributing is increased quantification of benefit; the value resides not so much in the numbers themselves as in the way the attempt at greater quantification highlights issues/challenges. The study quantifies the value of Cochrane reviews in a manner consistent with NICE methods. They use a dynamic model. They identify the potential benefits of increasing implementation of interventions and some of the drivers of the benefit of reviews.

The report distinguishes (at least initially) between helping to identify the most effective and cost-effective treatments, and promoting use by clinicians and policy makers. Just as many factors and different pieces of evidence influence decision makers in making a recommendation, many factors influence the timing and extent of implementation of recommendations. In principle a Cochrane review might influence the recommendation, and given a recommendation the Cochrane review might influence the implementation of the recommendation.

Taking the example of NICE technology appraisals, the manufacturer, and the ERG or AG, will generally systematically review evidence on treatment effect as a preliminary to estimating cost-effectiveness.<sup>126</sup> If this is going to happen to what extent does an existing Cochrane review mean that the job is done for them or is facilitated? If a new or updated review is undertaken, this raises questions regarding how much of the benefit of implementing an appropriate technology should be assigned to the Cochrane review as opposed to the NICE appraisal process.

Cochrane reviews will only occasionally match the decision problem facing decision makers. Moreover, given the NICE approach to reviewing literature the Cochrane review might possibly speed up the review or provide some sort of validation of any review undertaken as part of the NICE process. There may (very occasionally) be cases where the result of a review is in effect new information but generally reviews are quite different from trials in this respect. The NICE process would have uncovered the relevant information and thus it really isn't the case that the Cochrane review (even if cited) is influencing the recommendation. On the other hand, possibly the implementation of a recommendation may be faster/greater when there is a supporting Cochrane review.

Consider the example of aflibercept, an anti-vascular endothelial growth factor. The decision (by NICE) to recommend aflibercept for treatment of diabetic macular oedema (DMO) appears to have been driven by the combination of the VIVID and VISTA trial results and the economic modelling based on these trials. Reading the review of the evidence and the discussion of further considerations (and given the Committee's experience of participating

in many broadly similar decisions) it really is hard to see how the Cochrane review<sup>123</sup> made any difference to the decision making process.

The authors of the CRD/CHE report<sup>122</sup> have not given a justification for using £30,000 to value QALYs, and given recent York research and DH practice a value £15,000 might have been more appropriate. If the additional costs incurred due to the increased utilisation of anti-VEGF therapy are translated to QALYs using a more appropriate estimate of the opportunity cost in terms of displaced health benefits, implementation of a NICE recommendation of a technology with an ICER of £21,422 produces a net loss of QALYs. Use of a  $\lambda$  of £15,000 in the aflibercept case turns the net monetary benefit from £5,061 to -£3,789.

A key assumption is that 1% of any increased utilisation can be attributed to the Cochrane review. The authors argue (fairly reasonably) that they were unable to do other than make such an arbitrary assumption given the time available to complete the work. The estimates of the benefits attributable to Cochrane reviews would obtain greater credence if there were supporting evidence from empirical studies of the determinants of increasing utilisation. As the authors note they were particularly limited by lack of utilisation data.

Where there is a very large body of literature a reasonable assessment of the evidence would be much harder without a review, and it seems more plausible that a Cochrane review may be influential. Statins might seem to be such a case. However, since there was no uniform welcome from the clinical community to the lowering of the risk threshold for prescription of statins (down to risk >10%) and already evidence of considerable variation in response to the previous guidance (statins where risk >20%), questions remain about the likely impact of Cochrane reviews on GP prescribing behaviour.

The authors of the CRD/CHE study note that they haven't accounted for the many uncertainties regarding their estimates. As they note this would be a standard part of any economic evaluation but that in order to do this they need access to a fully executable model. But even with a fully executable model the problem of uncertainty would still be great in that different analysts frequently come up with different models and different results when confronting the same decision problem and the same body of data. It needs to be stressed that estimates of incremental costs and incremental QALYs are generally sensitive to parametric and structural assumptions.

The authors note that the study design is based on choosing studies with evidence of cost-effectiveness and of course many reviews do not have such evidence and thus cannot be assessed

Clearly some reviews are much more likely to bring large benefit than others. To what extent can these be identified in advance (for example, based on number of patients, extent of uncertainty, alternative treatments etc.)? Cross-subsidising reviews which do not have a reasonable prospect of producing a positive net benefit is not efficient unless it is impossible to distinguish in advance between those which are likely to be cost-effective and those which are not.

with this approach. Presumably a similar methodology could be used to identify the net loss of benefit when utilisation of a non-cost-effective intervention increases as a consequence of a Cochrane review. The Committee have no evidence regarding such net losses but perhaps it should be recognised that reviews could produce negative net monetary benefits. As the authors note, the four examples are necessarily unrepresentative because of the need for a reliable and fully reported cost-effectiveness analysis.

There is a temptation to point to one or two “blockbuster” reviews which by themselves justify the use of NIHR support for Cochrane reviews, that is, the estimated value of these reviews far exceeds the total cost of all of the Cochrane reviews. This might be appropriate if we are drilling for oil and no one site is a better prospect than any other. But perhaps the situation is more akin to a drug which is more effective in some sub-groups than in others. It is not a good use of resources to treat all because the total benefit exceeds the total cost, at least not if we can identify sub-groups where the costs exceed the benefits. Some Cochrane reviews such as one about “Chinese herbal medicine in the treatment of ectopic pregnancy” (DOI: 10.1002/14651858.CD006224.pub3) would be considered by many as inappropriate use of resources if prepared with support from NIHR funding.

A limitation (with respect to our broader purpose) is that there is no analysis or discussion regarding the NIHR infrastructure support for Cochrane activities. The emphasis is on the value of individual reviews versus an estimate of the cost of those reviews. This engages broader issues than were in their remit. Taking the overall resource for infrastructure, to what extent can it be or should it be allocated to different Cochrane groups or indeed different Cochrane reviews? It seems unlikely that costs are not to some extent variable rather than fixed. It should be possible to estimate what part of the infrastructure support is fixed (unrelated to whether one or twenty groups are supported) and what part varies by the number of groups supported. Is it feasible to identify the likely value of reviews produced by different groups and thus identify groups which merit NIHR support and ones that do not? Going further, it seems plausible to suggest that particular reviews are more likely to represent a good use of resources and others much less likely. If these could be identified it raises the question should the funding of individual groups reflect this anticipation? These questions raised by the committee upon reading the economic study will require further investigation.

## *Case studies of the economic impact of selected systematic reviews:*

### *Main points*

- *Very selective information was available for this exercise.*
- *For Cochrane to represent value for money Cochrane would only need to recommend a small number cost-effective interventions a year.*
- *However, Cochrane needs to avoid cross-subsidisation i.e. 'if one high impact review to save the NHS money, it makes all reviews worthwhile' is not the correct message to portray.*
- *It would be useful to see more Cochrane work incorporating economic evaluation to determine whether reviews lead to savings in the NHS.*
- *Cost savings are not the only possible outcome. Methods may show effective treatments which cost the NHS money.*
- *Reviews also exist to evaluate standard practice, which could result in savings to the NHS.*

## CHAPTER 5 - COCHRANE STRATEGY AND THE NHS

### *Overview*

*This chapter will discuss stakeholders' feedback, Cochrane's strategic plans and its relation to the NHS, and propose changes in reporting and monitoring processes between Cochrane UK and NIHR. Key points include:*

- *The findings from Stakeholder interviews*
- *The Cochrane Strategic Plan, and its relevance to the NHS*
- *The role of Cochrane UK in meeting key clinical and policy issues in the NHS*
- *Timeliness and up-to-dateness of reviews*
- *Centralisation or decentralisation in Cochrane*
- *Changes in reporting and monitoring processes between Cochrane UK and NIHR*

### Report from Stakeholder interviews

The themes from these interviews,<sup>2</sup> in most cases, added weight to existing findings of this committee report and were an interesting snapshot in time of how Cochrane and is perceived in the UK. Thirty-four interviews were conducted during November and December 2015 with a range of Cochrane review users and producers, many of whom have multiple roles and interests in evidence synthesis and how this is used in health care in the UK. An overarching theme from the interviews was that this NIHR investment in Cochrane had affected culture change in the NHS towards more evidence use in decision making. Most of the interview sample described the current NIHR spend on Cochrane therefore as good value for money.

Cochrane is a trusted and valued source of evidence for many NHS health professionals, technical experts developing clinical guidance and information producers and information intermediaries e.g. bloggers. It is also a trusted source of evidence for another group of people, but they find it more challenging to use in practice, namely health commissioners, policy developers, NHS managers and patients and the public and they value it less because of this.

Cochrane reviews are seen as a quality product with a robust process underpinning their production. The identity and brand is strong and visible to those who are research aware, but less so to those that are not. Relevance of Cochrane reviews is an issue for some of this sample, and despite the quality of the product Cochrane reviews will have limited value if they do not address questions of importance and relevance to the NHS.

Cochrane reviews are well received when they have clearly described interventions, are not too narrow in scope, address current and ongoing uncertainty, explain the treatment effect (or not) simply, and attempt to place the review in context.

It is encouraging to see Cochrane UK's efforts in using social media as a channel for communicating and providing context for the results and implications of Cochrane reviews,

especially for an NHS audience. Some UK review groups are perceived as risk averse in having a public conversation about their reviews, preferring to post a review and hope that there is interest.

There was no consensus about who the most important users of Cochrane Reviews were but interviewees were interested in having a dialogue with Cochrane about targeting users with Cochrane products that would be particularly useful in NHS decision making and policy development.

There was a certain amount of push back about Cochrane's policy of focussing on high quality randomised controlled trials for reviews ('gold standard'). Many were interested in exploring how to incorporate different types of primary research; pragmatic trials and realist evaluations of treatments, qualitative research, cohort studies and large data sets (such as the National Joint Registry).

Perhaps the biggest challenge for Cochrane is getting the balance right between prioritising reviews and review updates of high importance and relevance to the NHS, rapid reviews to assess critical and time sensitive questions, and managing the numbers of empty reviews.

Interviewees welcomed this review and the close analysis of value to the NHS and the exploration of how to measure this in the future. The full report<sup>2</sup> is included in the Appendix 11.

### [Cochrane's Strategic Plan](#)

The Strategy to 2020 establishes Cochrane's aspirations and priorities for the next five years and sets out how they plan to achieve their vision. Within the context of Cochrane's mission it is based around achieving four key goals.

### [Cochrane's key goals of the 2020 Strategy](#)

**GOAL 1: Producing evidence**

To produce high-quality, relevant, up-to-date systematic reviews and other synthesised research evidence to inform health decision making.

**GOAL 2: Making our evidence accessible**

To make Cochrane evidence accessible and useful to everybody, everywhere.

**GOAL 3: Advocating for evidence**

To make Cochrane the 'home of evidence' to inform health decision making, build greater recognition of our work, and become the leading advocate for evidence informed health care.

**GOAL 4: Building an effective and sustainable organisation**

To be a diverse, inclusive and transparent international organisation that effectively harnesses the enthusiasm and skills of our contributors, is guided by our principles, governed accountably, managed efficiently and makes optimal use of its resources.

These goals are structured as three interlocking areas of equal focus and priority (Goals 1-3), underpinned by a fourth foundational area (Goal 4) designed to strengthen Cochrane and support our mission.

As of Spring 2016, a number of the key issues identified in this report are being addressed in the 2020 Strategy, but others are not mentioned at all. The table below gives an overview of how the 2020 Strategy relates to the priorities of the NHS at this point in time. It will be a great opportunity for Cochrane to show any major progress that has been made since Spring 2016. The Committee recommends SRPAG should follow-up on these items in annual reporting, in their role to monitor contract compliance.

Table 20: Relationship between 2020 Strategy and NHS priorities; Committee’s interpretation in Spring 2016.

| <b>Priority for the NHS</b>                               | <b>What’s in 2020?</b>   | <b>What is unclear/less optimal?</b>  |
|---|--|---|
| <b><i>Patient involvement</i></b>                         | We will implement our new partnerships strategy, and develop new partnerships with consumer networks, technology providers, and other organisations hosting the Global Evidence Summit in 2017.<br>We will create a more inclusive organisation by launching the Cochrane Membership Scheme and re-developing the Cochrane Community website around it.  | Details as yet unclear.   |
| <b><i>Collaboration with NICE</i></b>                     |  | Not addressed.  |
| <b><i>UK NHS and public/patient frontline</i></b>         |  | Not addressed.  |
| <b><i>Prioritise to topics of greatest importance</i></b> | We will improve the Cochrane Review prioritisation list by increasing the transparency of each new entry, incorporating more priorities identified by external parties to ensure that it reflects global needs, and providing more opportunities for competent potential author teams and individuals. A paper explaining the rationale for revisions to list and proposed changes is published by March 2016. | Details as yet unclear. Cochrane Response and Cochrane Innovations: both new developments appear to be in their infancy. The requirements for a topic to be deemed as high importance remains opaque, and fundamentally the funder, NIHR, has an expectation that topics should relate to UK needs. |

| Priority for the NHS                                   | What's in 2020?   | What is unclear/less optimal?  |
|--|---|--|
| <b><i>Keep more reviews up-to-date</i></b>             | We will develop and begin to implement a comprehensive updating strategy for Cochrane content to ensure that high priority reviews are kept up-to-date.   | Talks about keeping priority reviews up-to-date. The challenge to keep all reviews up-to-date remains.                   |
| <b><i>Prepare reviews more rapidly</i></b>             | We will address the challenge of improving timeliness of review production by re-evaluating the Cochrane editorial process and supporting pilot projects that improve production efficiency, author and editor experience, and review quality.  | Details as yet unclear. Cochrane Response and Cochrane Innovations: both new developments appear to be in their infancy. |
| <b><i>Use best available evidence, beyond RCTs</i></b> |   | Not addressed.   |
| <b><i>Role and structure of CRGs and Editorial</i></b> | We will implement changes to Cochrane Groups' structure and functions to ensure our organisational structure is optimally aligned to Cochrane's mission and goals. New accountability, reporting and support structures and processes are in place between the Central Executive Team and Groups. New managerial, reporting and support structures and processes are working well to support Cochrane Group transformation and normal work targets. | Details as yet unclear.  |
| <b><i>Training</i></b>                                 | We will improve our training resources by establishing a new online learning environment. We will expand the support we provide to Cochrane editors by delivering a programme of training and accreditation for them.   | Details as yet unclear.  |

| Priority for the NHS       | What's in 2020?  | What is unclear/less optimal?   |
|----------------------------|--|---|
|                            | We will engage with our users to bring the concepts and methodologies of evidence synthesis into mainstream use beyond the research and medical communities, so that people know why and how evidence should be used to inform their health decision-making. |   |
| <b>Governance</b>          | We will improve the effectiveness of Cochrane's governance by finalising and implementing a new governance structure, including a newly re-formed Governing Board (formerly Steering Group).   | Needs to make sure that an adequate number of non-Cochrane stakeholders are included. |
| <b>Transparency</b>        | We will increase the transparency of the organisation's governance and improve the opportunities for any contributor to participate in governing the organisations and/or to be appointed to a leadership position.  | Details as yet unclear.   |
| <b>Financial stability</b> | We will strengthen Cochrane's financial position by diversifying and expanding our funding base, both at core and group level.   | Details as yet unclear.   |

### Meeting key clinical and policy issues in the NHS

Timeliness of review production is essential to ensure the relevant, rigorous evidence is available within an appropriate timeframe to meet the demands of the policy or decision-making cycle.<sup>127</sup> The topics of reviews not only need to match up with NHS and patient priorities, the timeline for delivery of complete and up-to-date evidence needs to align with policy and decision-making processes.<sup>127</sup> It is essential that Cochrane avoids being comfortable and complacent, as it needs to think about radical new ways to meet current demands as well as future challenges.<sup>10</sup> One of the challenges facing Cochrane in the future is how to adapt the mission of Archie Cochrane and NIHR in a compatible way; a re-think is needed to face the modern challenges, which are difficult.<sup>10</sup>

Time-to-publication and currency (up-to-dateness) of new reviews remain crucial matters faced by NIHR-funded CRGs, and Cochrane in general. The CEU assessed the median time-to-publication (TTP) of a sample of SRs produced by NIHR-funded CRGs. Time-to-publication was defined as meaning the period in months between protocol and publication of the completed SRs. Analysis of a sample of SRs completed in 2013 showed a median TTP of 30 months, which improved somewhat by the 2104 sample (median: 23). The overall median TTP for both samples was 23 months (range: 8 to 103).<sup>4</sup> Similarly the time-lag between the search date and publication of the completed SR was considerable; 24 weeks in 2013, 27 weeks in 2014, and 25 weeks overall. There was substantial variation between assessed reviews, with number of weeks between the date of searching and publication of the review ranging from two weeks right up to 195 weeks (2013 and 2014 combined).<sup>4</sup>

Table 21: Time between protocol and searching and publication of completed NIHR-CRG SRs

|   |
|---|
| CONFIDENTIAL CONTENT FROM COCHRANE – MADE AVAILABLE TO NIHR |
|---|

Source: Cochrane Collaboration (2015)<sup>4</sup>

Cochrane acknowledged the challenges of ensuring SRs are published in a timely manner, giving the following reasons:<sup>4</sup>

- *Reliance on a predominantly volunteer contributor base;*
- *A culture that prides itself on an inclusive approach to commissioning and the provision of extensive author support, leading to ‘bottle-necks’*
- *Reviews becoming more complex and challenging to produce as methodology advances*
- *Technology not keeping pace with needs<sup>4</sup>*

Reliance on contributors that often have other priorities, or have no grant for their salary to carry out the review may not be quite the same as a volunteer contributor base.

Despite delays in publication, exemplars of good practice exist, such as the review of bevacizumab for macular degeneration. This review produced by the NIHR-funded Eyes and Vision CRG, was completed three months after publication of the protocol.<sup>128</sup> An analysis of TTP from 2005-2014 across all UK-based CRGs<sup>†</sup> showed considerable variation between CRGs and within CRGs over the time period.

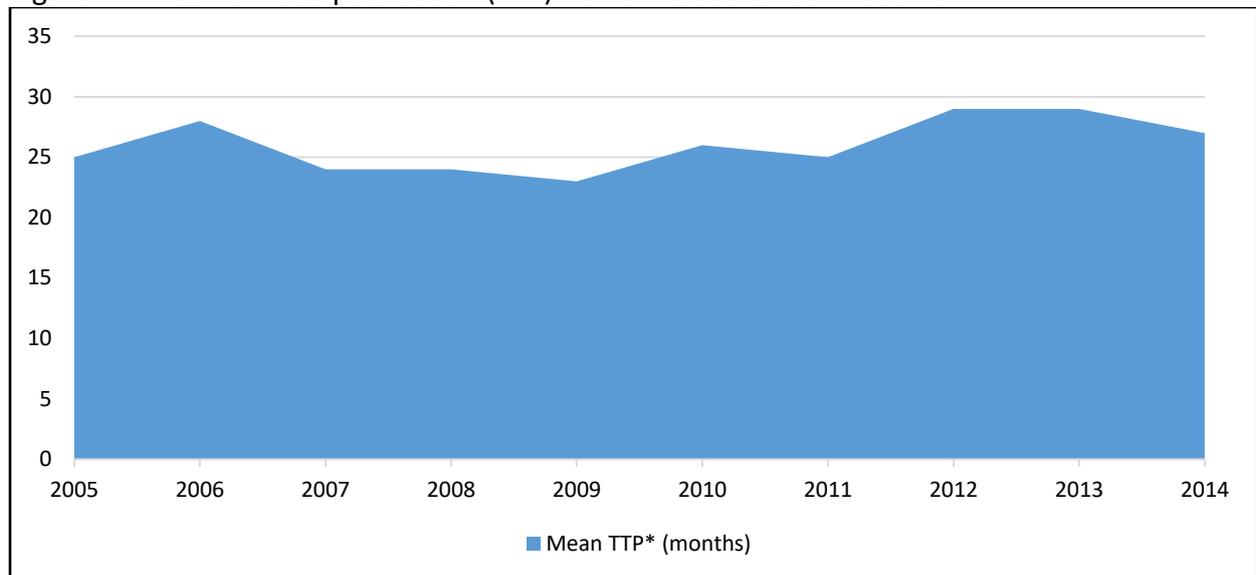
As the methodological requirements and quality assurance procedures involved have become more intensive, TTP for some groups has increased since 2005. Other show improvements in TTP, perhaps as a consequence of capacity building and increased expertise within the teams. Overall mean TTP for all UK-based CRGs and for all years was 24 months. While this represents a considerable time delay in review production, especially in meeting stakeholders' needs for timely evidence to inform policy and decision-making; it may also be indicative of increases in workload, increased

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<sup>†</sup> This included three non-NIHR-funded CRGs: Developmental, Psychosocial and Learning Problems; Stroke and Vascular CRGs. The analysis did not include the EPOC CRG, now funded by NIHR.

requirements for methodological rigour, greater complexity in review topics and scope, and an ongoing process of enrolment and training of volunteer review teams.

Figure 14: Mean time to publication (TTP)<sup>‡</sup> for UK-based CRGs<sup>§</sup>: 2005-2014



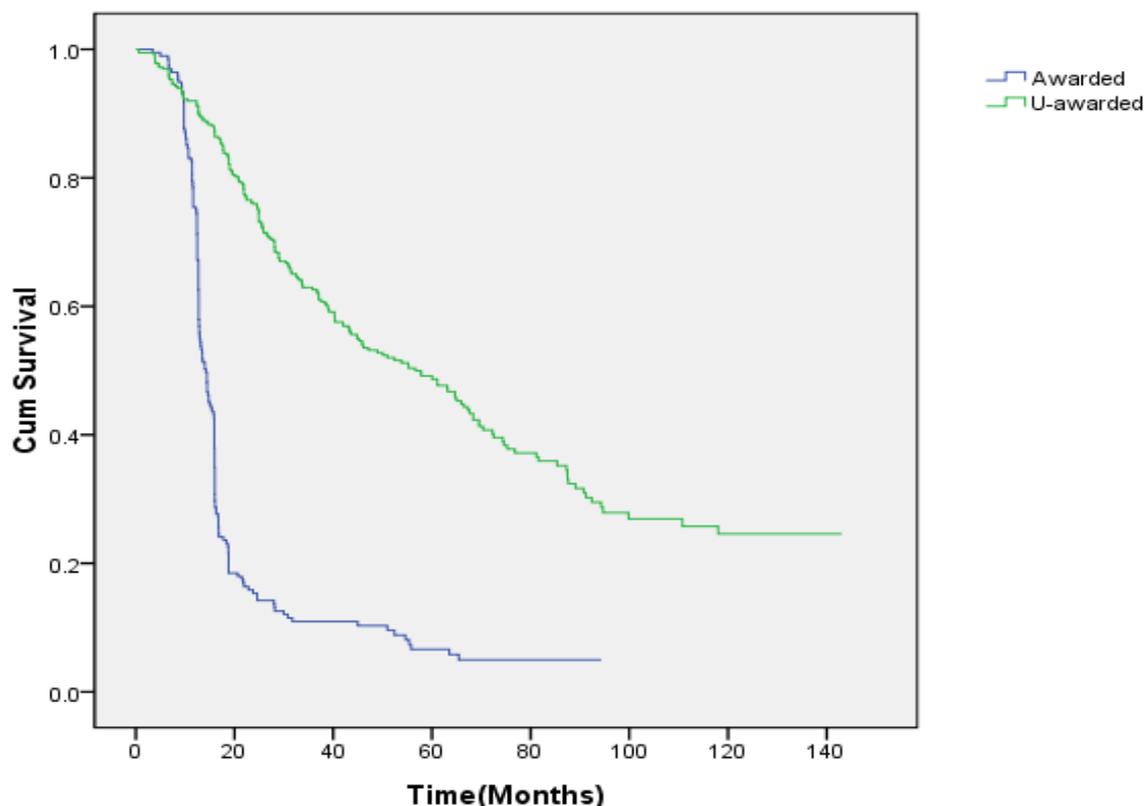
Source: Cochrane Collaboration (2015)<sup>4</sup>

A recent study was undertaken by NETS-CC in partnership with Queen's University, Belfast,<sup>129</sup> investigating the impact of NIHR Cochrane Incentive Scheme funding on TTP.<sup>129</sup> The figure below shows time-to-publication was up to 2.5 years faster for Incentive Award-funded reviews than non-awarded reviews.

<sup>‡</sup> TTP defined as elapsed time (months) between protocol and review publication.

<sup>§</sup> This included three non-NIHR-funded CRGs: Developmental, Psychosocial and Learning Problems; Stroke and Vascular CRGs. The analysis did not include the EPOC CRG, now funded by NIHR.

Figure 15: Time-to-publication (TTP) for Cochrane Incentive Award-funded reviews compared to non-awarded reviews



Source: Bailey S, Clarke M. & Zhang YG (2016) <sup>129</sup>

#### Publish when ready

In 2013, Cochrane launched a new continuous publishing model for CDSR, known as Publish When Ready" (PWR).<sup>130</sup> The PWR approach enabled immediately availability of new and updated reviews; alternatively, release of new publications could be scheduled by the CRG editorial team. This publication model allows continuous updating of CDSR and minimises the publication time lag which is inherent in resources published quarterly.

#### Priority list of titles

*"In January 2015 the Cochrane Priority Reviews List was launched, with approximately 300 reviews and updates. The list has become a 'living' record of Cochrane's attempt to identify titles that are of greatest importance to our stakeholders and are most likely to impact significantly on health outcomes worldwide. The list has evolved, with almost a 100 titles added, 28 new protocols published and 82 reviews and updates published between January 2015 and March 2016. The list is updated in real time by staff at the Cochrane Editorial Unit (CEU) and a version is published on Cochrane.org once every two months."*

*"The current process is reliant upon Cochrane Reviews Groups (CRGs) undertaking their own prioritisation exercises, with little or no input from the Cochrane Central Executive Team (CET) and no participation by other groups within Cochrane."*

*“To address the issues outlined above we are introducing a number of changes to the way the Cochrane Priority Reviews List is compiled, with a view to streamlining and focusing the list, ensuring that Cochrane priorities explicitly address the needs of global healthcare decision makers and promoting wide participation by appropriately skilled authors. We will:*

- 1. Actively seek referrals from other groups within Cochrane, such as Fields, Methods Groups and Centres.*
- 2. Reduce the size of the list overall and impose a maximum number of titles per group.*
- 3. Require that submissions to the Cochrane Priority Reviews List be accompanied by documentation that gives a rationale for inclusion, plus supporting evidence for the importance of the titles(s).*
- 4. Engage with external partners such as World Health Organisation (WHO) and Pan American Health Organization (PAHO) to improve our ability to reflect priorities that represent global.*
- 5. Encourage all groups to engage in a formal prioritisation process based on consultation with one or more external stakeholders groups such as funders, health professionals, consumers, guidelines agencies or healthcare policy makers.*
- 6. Encourage CRGs to propose submit titles that are open to new authors or author teams, conditional on them having the required skills and knowledge.*
- 7. An expectation that CRGs will 'fast track' titles on the Cochrane Priority Reviews List through their editorial processes.*
- 8. Support CRGs in creating impact plans for their priority reviews.*
- 9. Support CRGs by providing a screening service for priority reviews where appropriate.”*

The above text is from the CEU's outlined plans.<sup>131</sup>

It is unclear how the Priority Setting Methods Group has been involved in this prioritisation process. There is also no mention of taking NHS priorities into account, on the contrary, global organisations like WHO are likely to have very different priorities. Many CRGs may see this as a tick box exercise with little purpose and little practical help in strategic prioritisation of topics and reviews.

NIHR has funded Warwick Business School to do the project “Improving the capabilities of NHS organisations to use evidence” (Ref HS&DR - 12/5002/20). This project focuses on what forms of evidence are used by NHS commissioning groups, when it is used and how. It would be good if Cochrane and Cochrane UK note this project and take account of its findings.

#### [Centralisation or decentralisation? Cochrane's proposed plans for Group level change: Review of the structure and function of Cochrane Groups](#)

Cochrane has initiated a consultation about changing the structure and function of CRGs and their relation with the CEU.<sup>132</sup> The Committee welcomes that Cochrane has opened up the debate around centralisation versus decentralisation of the CEU. This will highlight the benefits and problems with both options. Decentralisation problems may include difficulties maintaining standards and quality, with no improvement on timeliness. Equally,

centralisation may improve the quality, but result in far less timeliness, delaying processes with greater central editorial steps. Prioritisation centrally may dramatically help CRGs in terms of workload, however potentially lacks the individual topic area expertise.

The Committee considered that economies of scale can be gained from CRGs working together, this is an important aspect and needs to be seriously explored. Centralisation versus decentralisation is a core consideration for Cochrane's future and should be transparently and swiftly discussed. A clear argument for why Cochrane is proposing splitting development and editorial functions as a key to solving the problems needs to be made. The Committee expects some intensive discussions within Cochrane about this, hopefully resulting in a sensible way forward with focus on maximising in-country impact of their reviews.

Furthermore, clarifying areas for consistency and areas for flexibility is critical to Cochrane's roles and functionality moving forward. Cochrane has to set definitions regarding where CRGs can have flexibility and where they have to behave in consistent way, e.g. with prioritisation.

The nature of funding sources will dictate where responsibilities lie and funding sources should be openly considered when thinking about future direction of travel, capacity and accountability. It seems currently unclear how infrastructure of fewer larger groups will be funded. Will it follow the (presumed) external grant income?

There appears to be a clear emphasis on doing fewer reviews than Cochrane have said in the past, but there is not an explicit decision to abandon comprehensiveness. Cochrane should clarify its strategy concerning coverage, so that funders and users know what to expect in the near future.

#### Planned developments in reporting and monitoring processes between Cochrane and NIHR

The UK NIHR-funded CRGs are currently monitored via annual reports submitted on 1 May each year to NETSCC. The reports contain qualitative reporting against the objectives set in the business plan agreed as part of the contracting process with the UK Department of Health, and quantitative data based on outputs. In order to monitor the performance of each group, a formula is used to calculate a score, which in turn is used to rank groups against each other.

The NIHR QQR Panel had previously made a recommendation to enhance these metrics with additional points aligned to the NIHR's "Adding Value in Research Framework", and this has been incorporated in to the CEU model, specifically the following.

1. Rating review groups should not be dominated by the volume of output alone, but should consider other aspects such as quality, relevance, utility and complexity
2. How groups are monitored should be transparent to all
3. The monitoring approach should encourage and reward groups that adhere to Cochrane's strategy

Cochrane are intending to undertake a governance review of CRGs in line with the parallel work in the rest of Cochrane. How Cochrane approach performance will inevitably form a part of this, but is likely to consider:

- Clear evidence that the title is a high priority to key end users: patients, health professionals, local policy makers and other international health systems
- High adherence to Cochrane standards and expectations (Methods Expectations of Cochrane Intervention Reviews – MECIR)
- Reviews that include a GRADE analysis and summary of findings table to facilitate incorporation into clinical practice and guidelines

In addition, there are other characteristics that are consistent with Cochrane Strategy and desirable to funders and decision makers:

- Reviews that include appropriate and useful enhanced features e.g. improved coverage of harms via inclusion of non-randomised studies, or multiple treatment meta-analyses
- Reviews of complex interventions e.g. health service delivery reviews
- Reviews that address different types of questions that are a high priority to end users
- Reviews that are produced in a timely and efficient manner
- Reviews that directly lead to new primary research
- Reviews that are accompanied by a clear dissemination/knowledge translation plan

The new model is currently being piloted within Cochrane and will hopefully be agreed in 2016. It has been agreed to run the current NIHR reporting mechanism in 2016.

The Committee feels that key performance indicators should focus on measures of impact; emphasising the need for groups to plan and think more strategically moving forward in order to maximise impact on the NHS.

Metrics need refinement to more precisely capture possible impact, quality, size and complexity of reviews. Although outputs, quality and activities remain important, more emphasis on measures of impact is advisable for future evaluations of NIHR Cochrane funding. Impact should be assessed in terms of impact on policies, practice change, culture change, and methodology change. For realising such impact, improving communication with the public, health professionals and policy makers will be key for Cochrane UK, individual review groups, and Cochrane worldwide.

The Committee also recommends public disclosure of CRG performance. A number of low quality Cochrane SRs exist and can be identified from existing and future MECIR and readability studies. Currently, although these exercises have provided invaluable insight into the CRGs who perform well consistently producing high quality reviews, the Committee notes a lack of transparency in disseminating the findings. It remains unclear what remedial action was put in place to support those CRGs performing less favourably.

### *Current and planned developments in Cochrane: Main points*

- *The Committee recommends that Cochrane maintains its focus on full, timely and relevant systematic reviews. Don't invent new products to cut down production time. This is echoed in stakeholder feedback; a new output is not required, just the existing product delivered quicker and with high relevance.*
- *Cochrane should continue work on developing expertise and processes, to get better and quicker at producing reviews.*
- *Cochrane should revisit some of its goals. There seem to be many different objectives in many areas. However, the Committee feels that an explicit focus is needed on topics relevant to decision making for patient care, as a primary goal.*
- *The strategy to 2020 should determine and highlight Cochrane's niche and unique selling points, and provide clear direction on/towards these.*
- *Centralisation vs decentralisation is a core consideration for Cochrane's future and should be transparently and swiftly discussed. Clarifying areas for consistency and areas for flexibility is critical to Cochrane's roles and functionality moving forward.*
- *The nature of funding dictates where responsibilities lie and funding sources should be openly considered when thinking about future direction of travel, capacity and accountability.*
- *Key performance indicators should focus on measures of impact; emphasising the need for groups to plan and think more strategically moving forward in order to maximise impact on the NHS*

## CHAPTER 6 - THE VALUE FOR MONEY OF NIHR COCHRANE INVESTMENT AND POINTS TO NOTE FOR THE FUTURE

### *Overview*

*This chapter deals with the question whether NIHR funding for Cochrane should be continued.*

- *Cochrane has been good value in the past, but could it have been better value?*
- *Cochrane has had value in the last five years, but was this as good value or as impactful as the previous ten years?*
- *Cochrane still represents good value for money when compared to its competitors, however does funding fit and is it effectively occupying a niche?*
- *Would less funding undermine the Cochrane product?*
- *Should other options, i.e. more targeted funding or re-distribution of funding be considered?*

### *Cochrane has been good value in the past, but could it have been better value?*

Impact is hard to demonstrate, but the Committee feels that NIHR investment in Cochrane infrastructure has made large (both direct and indirect) contributions to:

- A culture change in the use of evidence to support decision making
- Reviews in some areas of high importance to the NHS
- Synthesis methods development

However, the value of the investment has been limited to some extent by:

- The fact that Cochrane's ad-hoc responsive approach to review topics generated by authors interests has not secured, after 20 years, a comprehensive set of reviews, or a guarantee that NHS priorities are met
- Variable performance of CRGs in outputs, and variable processes
- Methods (focus on randomised trials) that exclude consideration of important aspects of decisions (harms, patient experience and economics, for example)
- Less secure infrastructure funding in other countries

CRGs and Cochrane UK have spent a lot of time training and building capacity within in CRGs, the wider research community, and the NHS. This has helped the culture change in the use of evidence to support decision making, and should continue to be encouraged and expanded.

Cochrane as an organisation has acted as a key driver of research synthesis methods development and actively promoted adoption of many aspects of systematic review methodology. Examples of innovations developed within Cochrane and adopted by reviewers on a global scale include:

- Cochrane tool for assessing risk of bias in randomised trials<sup>91</sup>

- Cochrane risk of bias assessment tool: for non-randomised studies of interventions (ACROBAT-NRSI)<sup>92</sup>
- Cochrane Highly Sensitive Search Strategy (HSSS) for identifying randomised controlled trials in Medline<sup>93</sup>

However, of concern are empty reviews with overly restrictive inclusion criteria concerning the types of studies, such as only RCTs, in situations where other types of studies addressing the question exist.

Furthermore, Cochrane has a number of resources, generated with support of NIHR funding, which are not fully accessible, such as specialised registers. The Committee recommends that Cochrane looks into ways to increase sharing of resources and collaboration.

[Cochrane has had value in the last five years, but was this as good value or as impactful as the previous 10 years?](#)

One evaluation discussed in this report showed that 88% of Cochrane reviews are rated to have a low risk of bias, compared to only 12% of non-Cochrane SRs. However, the group of non-Cochrane reviews is a very mixed bag, very likely to contain reviews from for example leading HTA and reimbursement agencies which have similar or even higher quality than Cochrane reviews. Another finding that 8% of Cochrane reviews in two topic areas were assessed at high risk of bias was in line with the findings of the CEU's MECIR Screening Project which found 5% of NIHR-funded SRs assessed required major amendments.

It is apparent that CRGs face challenges in review capacity to deal with large numbers of reviews assessed as in need of updating. During the 2014 assessment process, 1,250 reviews were assessed as requiring an update, which were either in-progress or awaiting sufficient resources to complete them.

There are tensions between CRG's and central editorial processes. It is for Cochrane to address these issues, with adequate attention paid to maintaining the motivation of CRG staff.

Although the Committee is aware of many expressions of positive experiences, there are also tensions between authors and CRGs, especially where prospective reviewers are dismissed because of CRG workload and where long delays occur in dealing with protocols and draft reviews; this means that NIHR investment is put at risk where reviews cannot get through the editorial pipeline in reasonable time. Data about workflow delays should be included in NIHR monitoring requirements.

Although Cochrane's MECIR screening project has provided invaluable insight into the CRGs who perform well consistently producing high quality reviews, the Committee notes a lack of transparency in disseminating the findings of these exercises. It remains unclear what remedial action was put in place to support those CRGs performing less favourably.

Cochrane should further explore ways of reaching wider audiences and interacting more. Groups should be encouraged to increase liaisons with social media and infomediaries.

Cochrane still represents good value for money when compared to its competitors, however does funding fit and is it effectively occupying a niche?

In the systematic review world, Cochrane is a highly respected player. Preparing systematic reviews is nowadays a highly competitive field.

People support Cochrane as the first port of call and do not want to see Cochrane go. Cochrane is seen as a trusted source by healthcare professionals, clinicians, guideline developers, information producers and infomediaries. Cochrane evidence is also valued by health commissioners, policy developers, NHS managers and the public, however they find it more challenging to use in a practical sense. Consequently, they value it less than could be the case, leaving room for additional improvement.

There are advantages of Cochrane being a reviewer-driven organisation and there are few alternatives. A key benefit of Cochrane's collaborative model of working alongside volunteer reviewers who are also healthcare professionals is that the voluntary review authors based within the healthcare system have in-depth and acute knowledge of their particular topic of interest that top-down researchers may not be aware of. The reviewer-driven approach enables insight and innovation at this level, increasing relevance to the NHS and impact on health care.

The Committee observes that Cochrane's terminology around 'volunteer' may be dated. A number of Cochrane processes don't entirely align with the idea of volunteerism. It is important to acknowledge that there are a number of full-time paid individuals working in Cochrane, and a number of academics gaining from Cochrane. Conversely, the true volunteer nature of consumers is perhaps being under-used, with varying levels of good practice across groups. Further focus on consumer value and use is recommended.

The NIHR invests a great deal of time and money into gaining patient and public involvement in its research. Cochrane do not necessarily always take advantage of this but should. For example, Cochrane could make greater use of horizon scanning and literature review rather than starting prioritisation exercises from scratch. NIHR could help with priority setting work using already existing resources, such as HTA PG that should be tapped into. The Committee recommends SRPAG should follow-up on these items in annual reporting, in their role to monitor contract compliance.

The Committee acknowledges that Cochrane is a worldwide organisation, and therefore focus on the NHS should not be exclusive. However, to justify considerable NIHR funding, the scope of Cochrane reviews should be optimised as much as possible to the NHS and commissioners' needs. Improving timeliness and hitting policy decision windows better will increase impact and use of reviews.

The Committee also felt that the relationship between Cochrane and NICE and similar agencies should be encouraged and emphasised further; strengthening links, routine collaboration, and utilising each other's products and sharing of information. This would strengthen Cochrane's position relative to its many competitors.

### Would less funding undermine the Cochrane product?

NIHR have committed £16 million funding for CRGs over the five year contract period (2015-2020); in addition Cochrane UK is funded by NIHR and there are Cochrane Incentive Awards and Cochrane Programme Grants available. This report discussed that there is substantial value from implementing some healthcare interventions recommended by Cochrane both in terms of additional health benefits as well as net value to the NHS. Clearly some reviews are much more likely to bring large benefit than others. If such reviews can be identified in advance, inefficient cross-subsidising of reviews which do not have a reasonable prospect of producing a positive net benefit could be avoided. However, currently there is no easy way to distinguish in advance between those which are likely to be cost-effective and those which are not.

Given that Cochrane is receiving protected non-competitive ring-fenced funding, the Committee recommends that it needs to be continually evaluated and justified. NIHR Infrastructure funding should be linked to key performance indicators.

The Committee welcomes Cochrane's steps towards open access, but thinks it is vital to see more clarity in relation to plans for open access and alternative funding models for Cochrane should revenue be lost from the library. Although this transformative initiative will enable freely available Cochrane SRs for all globally, there are concerns regarding possible impact of loss of Cochrane Library royalties on the financial stability of Cochrane. Funders and Cochrane need to work together, and transparency in proposed plans is encouraged.

This is also extended to the 2020 Strategy, with the Committee recommending that it should be reviewed carefully and individual points identified for clarification, where the vision of Cochrane at 2020 is still unclear.

### Should other options, i.e. more targeted funding or re-distribution of funding be considered?

The Committee felt that it is important to consider whether there are better ways to spend the NIHR funding in Cochrane, but equally it is vital to consider the wider cost and impact of not producing Cochrane reviews. Both questions are difficult to answer. To ensure responsiveness and coverage for the NHS, the Committee recommends to continue funding Cochrane and consider increased funding if it will guarantee better coverage. However, this funding should be linked to key performance indicators to ensure optimal value for money. If warranted, variation of funding be it either increase or decrease should be swiftly implementable.

The Committee is well aware that Cochrane is a worldwide organisation and that the activities of UK based CRGs have a worldwide focus. Funding UK based CRGs gives benefits worldwide, and simultaneously the NHS benefits from Cochrane work done elsewhere in the world.

Many NHS staff contribute to Cochrane. This is a good thing, but we need to be conscious of the opportunity costs of using clinicians, nurses and other health care professionals for

preparing systematic reviews. It will be reassuring if Cochrane can increasingly demonstrate impact.

The Committee recommends that key performance indicators should focus on measures of impact; emphasising the need for Cochrane to plan and think more strategically moving forward in order to maximise impact on the NHS. Key performance indicators include impact and prioritisation, and linked to these, relevance and timeliness. Impact can only happen if the quality of outputs is high.

Metrics need refinement to more precisely capture possible impact, quality, size and complexity of reviews. Although output numbers and activities remain important, more emphasis on measures of impact is advisable for future evaluations of NIHR Cochrane funding. Impact should be assessed in terms of impact on policies, practice change, culture change, and methodology change. For realising such impact, improving communication with the public, health professionals and policy makers will be key for Cochrane UK, individual review groups, and Cochrane worldwide.

The Committee recommends public disclosure of CRG performance. A number of low quality Cochrane SRs exist and can be identified from existing and future MECIR and readability studies. Currently, although these exercises have provided invaluable insight into the CRGs who perform well consistently producing high quality reviews, the Committee notes a lack of transparency in disseminating the findings. It remains unclear what remedial action was put in place to support those CRGs performing less favourably.

Cochrane UK functions as the "front door" contact for relationship building. A key area for expansion is to function as an interface between, and assist, groups and policy/decision makers e.g. NHS Commissioners in terms of deliverance – facilitating and enabling priority reviews to be completed and put mechanisms in place to deal with any delays.

The Committee was pleased to see the announcement about replacing the current Cochrane Steering Group structure with a new Board. The current structure does not involve non-Cochrane stakeholders and it is not quite clear who is in charge of what, also in respect of the chief executive officer and the editor. The Committee welcomes the intention to include more external stakeholders and thinks this is crucial, and recommends to increase transparency wherever feasible.

*The value for money of NIHR Cochrane investment and points to note for the future: Main points*

- 1) The Committee recommends to continue funding Cochrane. However, this funding should be linked to key performance indicators to ensure optimal value for money. If warranted, variation of funding be it either increase or decrease should be swiftly implementable.*
- 2) A revised structure of Groups could impact dramatically on efficiencies, outputs and future funding models, and should be explored, and pursued more proactively by Cochrane. E.g. fewer, larger groups could overhaul efficiencies.*
- 3) In the Committee's opinion, the past has shown good value, the present currently represents slightly reduced value than past time periods, and the future is currently unclear.*
- 4) Key performance indicators should be crucial in securing funding.*
- 5) Many recommendations may reflect or be in progress in line with the Cochrane strategy to 2020, however the Committee feel that progress needs to speed up, be more definite and more transparent.*

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