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The Dr Dorothea Sandars and Irene Lee Churchill Fellowship

Research and Training in the
Systematic Review of New Treatments for Eye Disease

Report by

Dr Sharon A. Haymes

2010 Churchill Fellow
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Signed: Sharon A. Haymes

Dated: 26th January 2011
ACKNOWLEDGEMENTS

I am deeply thankful to the Winston Churchill Memorial Trust of Australia for this life-changing experience. I am also exceedingly indebted to the late Dr Dorothea Sandars and to Irene Lee for their sponsorship. In addition, Irene Lee provided such helpful words of encouragement and motivational support through her continuing correspondence.

It was my honour and privilege to meet and learn from so many knowledgeable people. In particular, I would like to thank Professor Richard Wormald, Anupah Shah, Iris Gordon, and Dr Catey Bunce from the Cochrane Eyes and Vision Group, UK. From the Cochrane Eyes and Vision Group, US, I thank Professor Kay Dickersin, Dr Tianjing Li, Nancy Fitton, Jay Rubin and Tsung Yu. I am also grateful to Professor Gary Rubin and Dr Nick Smith at Moorfields Eye Hospital, UK, and Associate Professor Gislin Dagnelie, his assistants and Professor Hendrik Scholl at the Wilmer Eye Institute, US. I sincerely thank the bionic eye patient at Wilmer who so willing shared his experiences with me. These people taught me so much, helped make my stay comfortable and enjoyable, but more importantly were an enormous source of inspiration.

I thank Professors Jonathan Crowston and Jill Keeffe who supported my application and granted me the time away from my workplace to pursue this tremendous opportunity. I thank my colleagues at the Centre for Eye Research Australia, University of Melbourne and Royal Victorian Eye and Ear Hospital for covering for me while I was away, especially, Dr Trish O’Connor, Dr Lucy Busija, Natasha Tomic, Jennifer Hassell, and Betty Tellis. They are not only supportive colleagues but truly wonderful friends.

I am indebted to my parents, Richard and Sophia Bentley; and my family, Lisa Bentley, Michael Petrie, Dominique Petrie, Sam Lauriola, Chelsea and my boys Matthew and Nathan. I could not have achieved this without them. Also, I thank my nearest and dearest special friends who got me there and believed in me. They know who they are and why this was a challenging time in my life. This was most certainly the beginning of a new journey for me.

The greatest insights gained in travelling in search of information are those gained about oneself. Now it is time to take what I learnt and contribute back to the world in every way possible, in every encounter and with every opportunity. During my Fellowship, I heard Patricia Schroeder (former member of US House of Representatives, US Congress) speak about rolling up our sleeves, not wringing our wrists, to do the work required for health care policy to be based on evidence; that we
must get involved in the process not just the outcome, no matter how tedious. In going about it, she spoke of the 110 *Rules of Civility & Decent Behavior in Company and Conversation*, which George Washington copied out by hand by age sixteen, in particular,

“Labor to keep alive in your breast that little spark of celestial fire called conscience.”
ABOUT THIS REPORT

There is much written on systematic review. In this report I provide an overview of the process, advantages and disadvantages, case examples and applications in eye care, primarily from personal insights gained during my Fellowship visits to two centres of excellence and an international colloquium associated with the Cochrane Collaboration. Additionally, I was fortunate enough to visit clinical research centres involved in the implantation of retinal prostheses (bionic eye) and report on my insights concerning how to measure the functional outcomes of this technology and other upcoming ground-breaking interventions.
# Table of Contents

Acknowledgements .................................................................................................................. iii
About this Report ....................................................................................................................... v

1  Introduction ............................................................................................................................. 2
2  Executive Summary .................................................................................................................. 4
3  Fellowship Program ............................................................................................................... 6
4  Main Report ............................................................................................................................. 8
   4.1  Systematic Reviews and Meta-Analyses of Health Research ........................................ 8
       4.1.1  Introduction and Rationale of Systematic Reviews and Meta-Analysis ............ 10
       4.1.2  Formulating the Research Question ................................................................. 11
       4.1.3  Searching for Relevant Studies ......................................................................... 12
       4.1.4  Deciding Which Studies to Include ................................................................. 13
       4.1.5  Assessing Study Quality .................................................................................... 13
       4.1.6  Publication and Outcome Reporting Bias ........................................................... 14
       4.1.7  Synthesising Results and Meta-Analysis ............................................................. 15
       4.1.8  From Evidence to Recommendations ................................................................ 16
       4.1.9  Systematic Reviews in Context ......................................................................... 19
       4.1.10 Involving Consumers .......................................................................................... 21
       4.1.11 Systematic Reviews in Eye Care ........................................................................ 22
       4.1.12 How to Become Involved .................................................................................... 22

4.2  Outcome Measures of Functional Performance in Bionic Eye Research .............. 23

5  Conclusions and Future Plans .............................................................................................. 26
6  Recommendations .................................................................................................................. 27
7  References ............................................................................................................................... 28
1 INTRODUCTION

Almost half a million Australians have vision loss or are blind. In the fight to avoid blindness, many clinical trials of new eye treatments and interventions are underway, for example the retinal prosthesis or ‘bionic eye’. The best evidence for and against the effectiveness of such interventions should come from the combined analysis and systematic review of relevant high quality clinical trials.

A systematic review is a comprehensive summary of the medical literature on a particular research question, which uses explicit methods to identify, appraise, select and synthesise all high quality research evidence relevant to that question. An objective and transparent approach is used, with the aim of minimising bias. For clinical questions about intervention effectiveness, systematic reviews of high-quality randomised controlled trials (RCTs) are generally considered the highest level of evidence and crucial to evidence-based medicine. However, systematic reviews need not be limited to RCTs.

Good reviews begin with a clear question or hypothesis to be tested, which is developed in consultation with users. Second, a thorough search is conducted to find all relevant published and unpublished studies, thereby limiting the impact of publication and other biases. The databases and citation indexes searched (e.g. PubMed and Web of Science), and any individual journals searched, are fully documented. Third, explicit criteria for the types of studies to be included are established (so as to limit selection bias on behalf of the reviewer). Studies are selected on the basis of meeting the eligibility criteria and relevance to the specific research question. Fourth, the quality of the selected studies is examined systematically; in particular, for potential biases and heterogeneity. Each article may be assigned an objective assessment of methodological quality using a rating system. Finally, study results are synthesised, sometimes using statistical techniques (meta-analysis), and interpreted.

The Cochrane Collaboration, established in 1993, leads the world in evidence-based health care and systematic review (http://www.cochrane.org/). The Collaboration is an international, independent, not-for-profit organisation comprising more than 50 review groups covering various health disciplines, with over 28,000 contributors from more than 100 countries, dedicated to making up-to-date accurate information about the effects of health care readily available worldwide. Contributors work together to produce systematic reviews of health care interventions (over 4000 so far), known as Cochrane Reviews, which are published online in The Cochrane Library.
Cochrane Reviews are intended to help providers, practitioners and patients make informed decisions about health care, and are arguably the most comprehensive, reliable and relevant source of evidence on which to base these decisions.

Systematic review in eye care is a relatively small field compared with systematic review in other health care disciplines. The Cochrane Eyes and Vision Group (CEVG) was registered with the Cochrane Collaboration in April 1997. It has just over 200 members who are coordinated and supported by an editorial team based at the London School of Hygiene & Tropical Medicine in the UK, with a US satellite base at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. The over-arching objective of the CEVG is to prepare systematic reviews of all the interventions used to prevent or treat eye diseases and/or vision impairment. Additionally, the group prepares reviews of the evidence for interventions that aim to help people adjust to vision impairment or blindness. Systematic reviews that emphasise the major causes of blindness in the world and geographic areas where there are wide variations in clinical practice and outcomes are a priority. CEVG reviews focus on RCTs or quasi-RCTs and provide descriptive syntheses where such data are lacking. The main outcome for CEVG reviews is visual function, which can be assessed in a variety of ways including measurement of visual acuity, assessment of visual fields, assessment of real-world task performance, and assessment of vision-related quality of life.

To date, the CEVG has produced 150 reviews, the majority on glaucoma and retinal degenerations, where there have been many RCTs in the past decade or so evaluating the effectiveness of new treatments. With new interventions in all areas of eye care and ophthalmology on the horizon, there is a growing need for more RCTs and for unbiased systematic reviews. This is of fundamental necessity in continuously improving clinical care and decision-making. To achieve this, there is a need to increase the number of vision researchers and practitioners who are trained in preparing and using systematic reviews. The main objective of the CEVG Baltimore satellite group is to develop a critical mass do this in the US. With few Australian vision researchers and practitioners trained in Cochrane systematic review methodology, I believe there is also a need to do so in Australia. Thus, the primary purpose of my Churchill Fellowship was to undertake training in the rigorous Cochrane methodologies and work with the CEVG in conducting systematic reviews on new and upcoming eye care interventions in future, including glaucoma and the bionic eye. The secondary purpose was to learn more about how to measure the clinical effectiveness of the bionic eye. Ultimately, it is my hope to increase Australia’s capacity to make substantial contributions to evidence-based eye care, and subsequently, to help providers, practitioners, patients and policy makers decide on the most appropriate interventions.
2 EXECUTIVE SUMMARY

The Dr Dorothea Sandars and Irene Lee Churchill Fellowship to Undertake Research and Training in the Systematic Review of New Treatments for Eye Disease

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The primary purpose of my Fellowship project was to undertake training in the rigorous Cochrane methodologies in order to conduct systematic reviews on new and upcoming eye care interventions, including glaucoma and the bionic eye. The secondary purpose was to learn more about how to measure the clinical effectiveness of the bionic eye.

Highlights of the Fellowship included: a course on systematic reviews at the London School of Hygiene & Tropical Medicine (LSHTM), London, UK; working with members of the Cochrane Eyes and Vision Group editorial team, London, UK (Professor Richard Wormald, Anupa Shah, Iris Gordon, Dr Catey Bunce); working with members of the CEVG team, Baltimore, US (Professor Kay Dickersin, Dr Tianjing Li, Nancy Fitton, Jay Rubin and Tsung Yu); discussions with Professor Gary Rubin and Dr Nicholas Smith at Moorfields Eye Hospital, London, UK; discussions with Associate Professor Gislin Dagnelie, Professor Hendrik Scholl and a bionic eye patient at Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, US; the Consumers United for Evidence-Based Healthcare International Summit, Keystone, US; and the Joint Colloquium of Cochrane & Campbell Collaborations, Keystone, US.

Systematic reviews are considered one of the highest levels of evidence and are essential in making health care decisions. Although Australia is strong in evidence-based health care and systematic review, having several established Cochrane Groups in the region, I suggest that evidence-based care should be further promoted among Australian eye care professionals.
specifically, and that the number trained in using and preparing systematic reviews should be increased. Stakeholders should work together on these systematic reviews, with consumers and patients involved from the outset. Furthermore, systematic reviews need to be put in context with patient values and we need to better understand how those values affect decision making in eye care.

With new technological interventions in eye care comes the need for new outcome measures. International consensus on a standardised set of bionic eye outcome measures is required and should include clinical measures of rudimentary vision, orientation and mobility performance, activities of daily living, and the patient perspective. In addition, psychosocial measures should be devised for selecting suitable candidates.

I plan to implement, disseminate and promote the knowledge I gained about systematic review and outcome measures during this Fellowship in the following ways:

i. Contribute to systematic reviews, clinical guidelines and policy, so that all concerned may make the most appropriate choices regarding eye care. Specifically, I will contribute to updating a Cochrane systematic review on reading aids for adults with low vision through the CEVG, UK and continue to contribute to a new Cochrane systematic review on the comparative effectiveness of types of medical interventions for primary open angle glaucoma through the CEVG, US.

ii. Develop a short training workshop on conducting a systematic review for eye care professionals and researchers in Victoria.

iii. Assist the CEVG with promoting systematic review and conducting training workshops at local and international vision conferences.

iv. Collaborate with other Cochrane Review Groups in Australasia.

v. Encourage the application of mobile phone strategies, ‘mHealth’, in local eye care projects. Specifically, the development of a mobile phone application for teaching communication skills to medical staff, as part of a project in which I am involved at the Royal Victorian Eye & Ear Hospital.

vi. Discuss and devise strategies for measuring bionic eye outcomes with Centre for Eye Research Australia and other Bionic Vision Australia team members.
3 FELLOWSHIP PROGRAM

September 6 – 10, 2010: London, UK
London School of Hygiene and Tropical Medicine
Systematic Reviews and Meta-Analyses in Health Research
Course Coordinators: Dr Pablo Perel and Katharine Ker

September 13 – 17, 2010: London, UK
London School of Hygiene and Tropical Medicine
Cochrane Eyes and Vision Group
Main contacts: Prof. Richard Wormald, Anupa Shah, Iris Gordon, Dr Catey Bunce

September 15, 2010: London, UK
Institute of Ophthalmology and Moorfields Eye Hospital
Main contact: Professor Gary Rubin

September 27 – October 15, 2010: Baltimore, Maryland, US
Johns Hopkins School of Public Health
Cochrane Eye and Vision Group (US satellite)
Main contacts: Professor Kay Dickersin, Dr Tianjing Li
October 4 - 5, 2010:  Baltimore, Maryland, US
Lions Vision Research and Rehabilitation Center
Wilmer Eye Institute
Johns Hopkins University School of Medicine
Main contacts: Assoc. Prof. Gislin Dagnelie, Professor Hendrick Scholl

October 17, 2010:  Keystone, Colorado, US
Advocacy in the Era of Evidence: An International Summit for Consumer Advocates
Consumers United for Evidence-Based Healthcare (CUE)

Joint Colloquium of Cochrane & Campbell Collaborations
4 MAIN REPORT

There were two principal components to my Fellowship that I will cover in this report: i) systematic reviews and meta-analyses of health research, and ii) the measurement of clinical outcomes of the bionic eye.

4.1 SYSTEMATIC REVIEWS AND META-ANALYSES OF HEALTH RESEARCH

My Fellowship commenced with a most stimulating learning experience – a course on systematic reviews at the renowned London School of Hygiene & Tropical Medicine (LSHTM), UK. The LSHTM has an internationally excellent reputation in public health and tropical medicine. The five day course was the first of its kind offered by the School and one of the few face-to-face courses covering all aspects of systematic review, including design, analysis and interpretation, with an opportunity to gain interactive and practical experience of the tasks involved. Delivered by eminent researchers from a variety of disciplines, the opportunity to listen to and discuss their ideas was invaluable. Also beneficial, was the opportunity to discuss issues with the other 40 or so course participants, who brought insights from diverse cultural and professional backgrounds. I highly recommend the course to other health care researchers and practitioners interested in learning to conduct systematic reviews and who prefer or require a short but comprehensive, and thus, intensive course.

The course followed the principles of the Cochrane Collaboration methodologies for systematic reviews, as outlined in the Cochrane Handbook for Systematic Reviews of Interventions (available at http://www.cochrane.org/training/cochrane-handbook).³ The course content comprised: introduction and rationale of systematic reviews and meta-analyses; question formulation and protocol development; conducting searches; study selection; critical appraisal; statistical methods and software for meta-analysis; publication and outcome reporting bias; dealing with missing data; reviews of complex interventions; from evidence to recommendations and systematic reviews in context. I will briefly describe and highlight issues that I thought were especially important and useful.

Throughout this section on systematic review, I will integrate the knowledge and experience from the LSHTM course with that gained from my visits to the Cochrane Eyes and Vision Groups (CEVGs) in the UK and US and attendance at the Consumers United for Evidence-Based
Healthcare (CUE) International Summit for Consumer Advocates and Joint Colloquium of Cochrane & Campbell Collaborations.

I spent one week with the main CEVG based at the LSHTM, led by Coordinating Editor and Ophthalmologist, Dr Richard Wormald. Under the guidance of Managing Editor Anupa Shah, Information Specialist Iris Gordon and Statistical Editor Dr Catey Bunce, I edited reviews in preparation, learnt to use the management software developed by the Cochrane Collaboration to support the systematic review process and gained practical experience in hand searching. Following that, I spent three weeks with the CEVG US satellite, at the US Cochrane Center, Johns Hopkins School of Public Health (JHSPH). Under the guidance of Director and Project Investigator Professor Kay Dickersin and Methodologist Dr Tianjing Li, I assisted with a systematic review on the comparative effectiveness of types of medical interventions (eye drops) for primary open angle glaucoma (NB. Glaucoma, of which primary open angle is one form, describes a group of eye diseases in which there is progressive damage to the optic nerve characterised by specific structural abnormalities of the optic nerve head and associated patterns of visual field loss; it is the second leading cause of blindness worldwide with an estimated prevalence between 1-4%)

In addition, I assisted with the development of a framework for prioritising comparative effectiveness research questions related to primary angle closure glaucoma, listened to presentations on the group’s most recent research work (to be presented at the Joint Colloquium) and assisted with preparations for the CUE Summit.

The CUE is a national US coalition of health and consumer advocacy organisations committed to empowering consumers to make the best use of evidence-based health care; it is a consumer advocate-scientist partnership. The CUE Summit incorporated a day of presentations and workshops in Keystone, Colorado, attended by 88 participants from the US and 10 additional countries. Keynote speeches were delivered on, “How do we fight to get the consumer voice front and center in healthcare decision-making?” (Cornelius Baker, Senior Communications Advisor, Academy for Educational Development and National Policy Advisor, National Black Gay Men’s Advocacy Coalition) and “Communicating evidence: Lessons learned from USPSTF’s recommendations on screening young women for breast cancer,” (Assoc. Prof. Ned Calonge, President and CEO of The Colorado Trust, a philanthropic foundation dedicated to advancing the health of the people of Colorado, Associate Professor of Family Medicine at the University of Colorado, Denver, and of Epidemiology at the Colorado School of Public Health), with a panel discussion on, “Global Consumer Action,” (including a presentation by Janet Wale from Australia, convener of the Cochrane Consumer Network) to conclude the day.
Finally, I attended the Joint Colloquium of Cochrane & Campbell Collaborations, immediately following the CUE Summit, in Keystone, Colorado, where there were over 900 delegates and presenters from leading research and policy-making organisations around the world. The program featured more than 100 workshops and 30 oral sessions on statistical methods and meta-analysis, education and training, information retrieval, editorial process, investigating bias, knowledge translation, consumer issues, and global health and equity. Keynote speeches were delivered on, “Can democracy survive?” (Patricia Schroeder, former member of the US House of Representatives), “Beyond Bounds: Care and Research in a Mobile World,” (Assoc. Prof. Ida Sim, University of California, San Francisco; international leader in informatics for clinical research and evidence-based medicine) and “Sex, lies, and pharmaceuticals,” (Australian Ray Moynihan, Investigative Journalist; award-winning health journalist, author, documentary-maker and academic researcher with a global reputation).

4.1.1 INTRODUCTION AND RATIONALE OF SYSTEMATIC REVIEWS AND META-ANALYSIS

Reviews should be treated as scientific studies, using strict methodologies that can be replicated by others to arrive at similar conclusions. Reviews should involve a multidisciplinary team (experts in the field, information specialist, statistician and consumer), value multiple viewpoints, encourage deliberation and provide an audit trail. The team approach helps to reduce the bias a single reviewer might introduce. In addition, rigorous methodologies and accountability not only help to reduce bias but potentially improve reliability and accuracy of conclusions. Further strengths of systematic review are that large quantities of information can be synthesised (essential given the number of studies published on a topic and time demands in today’s world) and they can establish whether or not scientific findings are consistent and generalisable across populations, settings, and treatment variations. Moreover, meta-analyses can increase power and precision of estimates of treatment effects and risks. As well as assisting practitioners and patients to make informed decisions, systematic reviews can be used by researchers to identify, justify and refine hypotheses, recognise and avoid the problems of previous work, estimate sample sizes, identify adverse effects and covariates that warrant consideration in future studies. As they are widely published and accessible, they become an authoritative summary of the body of evidence thereby reducing the need for traditional narrative reviews that tend to be produced over and over again. Also, they can be used to formulate guidelines and legislation concerning what interventions work, where and for whom. However, a valid criticism is that systematic reviews can quickly become out of date, and require regular updating. Cochrane currently recommends updating reviews every two years.
4.1.2 FORMULATING THE RESEARCH QUESTION

Formulating a good research question is critical in producing a good review. A review should be based on an important, well-focused and answerable question that is relevant to patient care. Questions that have been answered by common sense or strong empirical evidence are of little use and wasteful of resources. The most useful reviews are those that can improve clinical practice and change is more likely to occur where collective uncertainty exists, which is often reflected in variations in practice.\(^7\)

A structured approach to formulating a good clear research question, ‘PECOS’, was advocated in the course as follows:

- **Population**: Disease / condition, personal characteristics (e.g. age, sex) and setting (e.g. community, hospital)
- **Exposure**: Treatment or intervention (including intensity, dose, timing, duration, method of delivery)
- **Comparisons**: Type of control (e.g. no treatment, standard treatment)
- **Outcomes**: Primary and secondary types (should be defined, few, relevant to patients, include adverse as well as beneficial effects), measures (how and when), and economic cost
- **Studies**: Design (e.g. experimental vs. observational, RCT vs. non-RCT, masked vs. open), where the double-masked RCT is the gold standard for assessing effectiveness (although, situations exist where this is not possible)

There should be a balance between each of these aspects being too specific to be workable and too broad to be useful.\(^7\) Most Cochrane systematic reviews focus on RCTs. Although this is the gold standard, it should be noted that studies of lesser methodological quality nonetheless may have important information to offer.

An example of a well formulated question based on a published Cochrane review\(^4\) is: Do medical interventions (eye drops) compared with placebo, no treatment or other treatments for patients with primary open angle glaucoma prevent progression or onset of visual field damage? In this case, the population is patients with primary open angle glaucoma; the exposure is eye drop medication; the comparisons are placebo, no treatment or other treatments; the outcome is visual field progression; and studies are RCTs.
The research question then guides the review, clarifying the criteria that primary studies should meet in order to be included, the search strategy required to find those studies and the data that need to be extracted. Although the question should be proposed before initiating the full review, it need not be so rigid that exploration of other issues is not undertaken. Indeed, some knowledge of studies on the topic of interest, and thus, a scoping search, is usually required to formulate the question in the first instance. Furthermore, it may become evident that the question needs to be modified based on the information collected during the review process. However, caution should be exercised to ensure that any modifications to the question do not create bias and that modifications are reported along with an explanation.

4.1.3 SEARCHING FOR RELEVANT STUDIES

To maximise available data and reduce the risk of bias, as many relevant studies as possible need to be identified, regardless of publication status or language. Multiple overlapping and carefully planned search strategies should be used. Strategies include searching the numerous electronic databases available (with careful consideration of search terms), hand searching journals and conference proceedings, searching bibliographies of articles, existing registers of studies, grey literature (i.e. literature not published in books or journals, such as government reports and dissertations), the internet, and contacting experts, companies and researchers. The search strategy should be recorded and provided explicitly, including the number of hits.

Practical laboratory sessions on searching electronic databases facilitated by a Cochrane Information Specialist during the LSHTM course were very helpful. Furthermore, it was clear that Information Specialists have much to contribute to producing a high quality review, even with experienced researchers on the team. Information Specialist Iris Gordon (CEVG UK) taught me much about hand searching. Electronic searching cannot be relied upon to find all relevant published studies, since less than one-third of the world’s medical journals are routinely indexed in the major electronic databases (e.g. MEDLINE and EMBASE) and indexing errors do occur. Hand searching involves manually searching through medical journals and conference proceedings for accounts of controlled trials which are not yet indexed in the major electronic databases. Hand searching is laborious. Ideally, two people search journal issues or conference proceedings looking for relevant studies. A third person checks consistency and agreement. Most Cochrane Review Groups and Centres seek volunteer hand searchers and provide the necessary training and support.
4.1.4 Deciding Which Studies to Include

The search output is merged and duplicates removed. The titles and abstracts are examined for potentially eligible studies and full texts retrieved. Full texts are examined against the inclusion criteria and those eligible are selected. To minimise bias and error, examination of records and full text articles should be undertaken by at least two review authors independently, with discrepancies resolved through discussion or referral to an additional review author. It is helpful to develop an ‘eligibility assessment form’ for the review. Reviewers should be alert for missing study information and multiple reports of a single study. Decisions about which studies to include can be greatly influential. The selection process and decisions should be documented, see for example the ‘preferred reporting items for systematic reviews and meta-analyses’ (PRISMA) statement.\(^8\)

Data of interest to the review question are then extracted, again, by at least two authors. As for assessment of eligibility, it is useful to develop a ‘data extraction form’ for the review. This further minimises bias and error and yields a concise, permanent record. It is important to be aware that data may not be reported where expected, adequately or at all, and may require conversion to an appropriate format.

During my visit to the CEVG satellite at JHSPH, I gained practical training in determining eligibility of full text articles obtained following literature search and abstract review. An eligibility assessment form was developed for the particular review being prepared. This was accompanied by a comprehensive codebook explaining meaning and possible responses to all questions on the form. Both were available to all review authors online, with several example articles. The form included questions on study registration, study design (RCT vs non-RCT), group assignment sequence, results/data reported, comparisons made, number of participants in each study arm, proportion with confirmed primary open angle glaucoma, and length of follow-up. I found that the required information was often missing (e.g. clinical trial registration number) and decisions were sometimes difficult. This experience made clear to me the need for explicit instructions, training and practice, and the usefulness of a structured form for documenting the selection process and decisions.

4.1.5 Assessing Study Quality

Systematic reviews should provide an assessment of the quality of the studies included, so that the reader may appraise the extent to which the conclusions should be believed. Cochrane recommends that such an assessment of individual studies should emphasise the risk of bias in the
results (risk of overestimation or underestimation of the true intervention effect), rather than the methodological quality of the study, since the former is really the critical issue. They discourage the use of scales yielding a summary score and instead recommend the use of a tool comprising a description and judgement (yes, no, unclear risk of bias) for each entry in a ‘risk of bias’ table, where each entry addresses a specific study feature. For parallel group RCTs, the study features or domains of interest in such a table are: allocation to intervention sequence generation; sequence concealment; masking of participants and research personnel; incomplete outcome data; selective outcome reporting; and other potential sources of bias. Review authors should then summarise assessments of risk of bias across the domains, again using a description and judgement (yes, no, unclear risk of bias), both within and across studies, upon which an overall risk of bias assessment might be made. I was able to obtain invaluable practice in judging risk of bias by examining and discussing articles from the scientific literature on glaucoma RCTs with LSHTM course facilitators and participants.

4.1.6 Publication and Outcome Reporting Bias

Publication bias refers to studies with positive findings being more likely to be published than studies with negative findings. Outcome reporting bias refers to the selection, on the basis of the results, of a subset of the original recorded outcome variables to be reported. Authors should evaluate individual studies for these specific biases. The Outcome Reporting Bias in Trials (ORBIT) 9-level classification system is a useful tool for this, identifying whether there is evidence that the outcome was measured and analysed but only partially reported, whether the outcome was measured but not necessarily analysed, if it is unclear whether the outcome was measured, or if it is clear the outcome was not measured. Also, reporting biases should be guarded against in systematic review by creating a protocol and adhering to pre-determined outcome measures. As with formulating the research question, if it becomes necessary to deviate from the protocol, the changes and explanations should be fully documented.

I discussed the problem of outcome reporting biases in industry-sponsored clinical trials with researchers during my visit to JHSPH. They recently conducted a study comparing clinical trial information contained in internal company documents with publications. The trials assessing off-label uses of gabapentin (prophylaxis against migraine and treatment of bipolar disorders, neuropathic pain, and nociceptive pain), had been sponsored by Parke-Davis/Pfizer. For 8 of the 12 reported trials, the primary outcome defined in the protocol differed from that in the published report. Furthermore, reporting of key analysis information was inconsistent, incomplete, and possibly incorrect. The researchers recommended that trial protocols should be made publicly available, and
both protocols and published reports should specify the primary type of analysis and criteria used to include participants in the analysis.

4.1.7 SYNTHESISING RESULTS AND META-ANALYSIS

In synthesising the data, reviewers should consider: the direction of the treatment or intervention effect; the magnitude of the effect; the consistency of the effect across studies; and the strength of evidence for the effect. This can be done descriptively and/or statistically.\textsuperscript{3} Statistically, meta-analysis is the technique of unique value in systematic review, where results (e.g. risk ratio, odds ratio, absolute risk difference, mean difference) from two or more studies addressing similar research questions are combined. It yields an estimate of the average intervention effect and tests an overall hypothesis. A forest plot can be generated, showing individual study effects together with the overall average effect. Advantages of meta-analysis include increase in power, increase in precision, the ability to investigate the consistency of studies, to answer questions not addressed by individual studies, and the potential to settle controversies arising from conflicting studies. However, meta-analysis can be misleading, especially if study designs, within-study biases and variation across studies are not considered. Indeed, meta-analysis may be no better than the studies it combines, except with regard to the number of patients included, and may misinform if biases are larger than the real effects.

It is important to select the appropriate type of meta-analysis and make suitable adjustments depending on the study designs and nature of data. This can be complex and best managed by a statistician in some cases. I gained experience using two computer software programs during LSHTM practical laboratory sessions facilitated by statisticians - \textit{Stata} (Version 11. College Station, Texas: StataCorp LP; 2009) and \textit{Review Manager (RevMan) - Version 5.0. Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration; 2010). \textit{Stata} is a comprehensive, yet relatively affordable program. \textit{RevMan} is the software used for preparing and maintaining Cochrane Reviews, facilitating preparation of text, assessment of risk of bias, entry of study data, and meta-analysis, in a single document that can be shared by authors and editors. It is available free to registered authors for preparing Cochrane reviews or for academic use, but for commercial use a license must be purchased. I acquired additional experience using this software whilst assisting with editing an update on the use of antibiotics to treat trachoma.\textsuperscript{12} Trachoma is one of the most common causes of preventable vision loss and is particularly prevalent among children living in poor communities. Repeated episodes of conjunctivitis (inflammation of the membranes of the eyes caused by chlamydia infection), lead to scarring and inturning of the eyelid. The eyelashes then rub on the cornea, causing opacification and blindness. Antibiotics can be used to treat the infection.
This review is important in Australia as trachoma remains endemic in Australian Aboriginal communities and indeed, studies conducted in Australia have contributed to this review. The original systematic review was conducted in 2005, and found supporting evidence that antibiotics do reduce active trachoma.

As many judgments are required in systematic review and meta-analysis, sensitivity analyses should be conducted to determine whether or not various decisions influence the findings, where the primary analysis is repeated substituting alternative ranges of values for subjective decisions, in order to examine the robustness of the findings. Additionally, consideration must be given as to the most appropriate methods for the case in point, and caution exercised in simply assuming that previously used methods are appropriate. For example, Dr Li and colleagues from the JHSPH group presented work on the perpetuation of inappropriate meta-analysis methods in systematic reviews of prostaglandin analogue eye drops for glaucoma. One or more inappropriate statistical methods were used in 8 of 16 reviews analysed. Six described pooling data from similar treatment arms across studies, resulting in a non-random comparison; three described an incorrect formula to calculate the variance of the effect estimate. A critical assessment of previous systematic reviews on a given topic and the statistical analyses therein is imperative before initiating another.

4.1.8 FROM EVIDENCE TO RECOMMENDATIONS

A concise statement of findings, a considered discussion and clear conclusions in systematic reviews are important for facilitating health care decision making. The Cochrane Collaboration suggest review authors might consider summarising findings in a table. They also suggest that the discussion incorporate five areas: summary of main results (benefits and harms); overall completeness and applicability of evidence; quality of the evidence; potential biases in the review process; and agreements or disagreements with other studies or reviews. Conclusions should cover implications for clinical practice and implications for research. The review should assist people to understand the implications of the evidence and apply the results to their specific situation.

To assess quality of a body of evidence, the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) Working Group, a widely representative group of international guideline developers, has produced a useful system. Over 20 organisations have adopted it, including the Cochrane Collaboration, World Health Organization, BMJ Clinical Evidence, National Institutes of Health and Clinical Excellence and the American College of Physicians (http://www.gradeworkinggroup.org/index.htm. Accessed October 26, 2010). Within the GRADE system, the quality of a body of evidence involves consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and
risk of publication bias.\textsuperscript{13, 14} Four levels of quality of evidence are specified: \textit{high}, when it is considered that further research is very unlikely to change health care provider confidence in the estimate of effect; \textit{moderate}, when further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate; \textit{low}, when further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and \textit{very low}, when any estimate of effect obtained from existing clinical trials is very uncertain.\textsuperscript{14} As part of this, RCTs begin as high quality evidence and observational studies begin as low. Quality may be downgraded as a result of limitations in study design or implementation, imprecision of estimates (wide confidence intervals), variability in results, indirectness of evidence, or publication bias. Quality may be upgraded because of very large magnitude of effect, a dose-response gradient, and if all plausible biases would reduce an apparent effect. Critical outcomes determine the overall quality of evidence. GRADE principles are currently being phased into Cochrane reviews. GRADE is not only useful for systematic reviews, but for assessment of health technology (e.g. the bionic eye in future) and development of clinical practice guidelines. A similar system, tailored to the local health care context, is used for clinical guideline development in Australia.\textsuperscript{15}

During my visit to JHSPH, I assisted with a project on the development of a framework for prioritising comparative effectiveness research questions based on glaucoma clinical practice guidelines - the American Academy of Ophthalmology \textit{Primary Angle Closure Preferred Practice Patterns}.\textsuperscript{16} This was similar to a recently published study conducted by the Cochrane team at JHSPH on \textit{Primary Open Angle Glaucoma}.\textsuperscript{17} Because clinical practice guidelines are typically developed by professional societies aiming to assist health care practitioners with decision-making, the clinical questions derived from them reflect key issues and dilemmas facing clinicians at the time of guideline development. Thus, practice guidelines can provide a reasonable starting point for setting research priorities. The framework developed by the team at JHSPH involved restating the guideline recommendations as answerable clinical questions that could be addressed by either clinical trials or systematic reviews and having members of a specialist clinician group (American Glaucoma Society) rate the importance of having an answer to each question for providing effective clinical care. This was done as a two-round Delphi survey. The most important clinical questions were related to eye drop therapy and surgical intervention. The team recommend the following systematic, transparent and participatory approach for filling the evidence gaps in subspecialty areas:

- work with guideline developers in a particular area to develop answerable clinical questions from existing guidelines;
- survey members of one or more professional organisations to assess individual and consensus rankings of the clinical questions;
• determine evidence needs and research priorities by matching the ranked questions with existing evidence; and
• partner with funders, evidence producers, and evidence synthesisers (e.g. Cochrane Collaboration Groups) to fill the information gaps.¹⁷

This method potentially lessens the gap between evidence generation and translation to clinical care when used in conjunction with guideline developers, research funders, evidence producers, and consumers. However, it should be noted that clinical practice guidelines may not cover all important issues.

In proceeding from evidence to recommendations, the Collaboration advises that authors should avoid making specific recommendations that depend on assumptions about available resources and values.³ Often the findings of the individual studies and thus, the review, cannot be generalised to anymore than a small proportion of the population with the condition for which the treatment was developed, and specific circumstances. It is for this reason Guyatt et al. suggest that the N of 1 RCT provides the highest level of evidence for treatment decisions,¹⁸ (where patients undertake pairs of treatment periods in which they receive a target treatment in one period of each pair and a placebo or alternative in the other, with masking of allocation). Further, conclusions about the practical usefulness of an intervention entails weighing the pros and cons of benefits and harms and costs, which requires additional, informed information beyond the scope of the systematic review. Thus, the current position of the Collaboration is that specific clinical recommendations are more the domain of clinical guideline developers. Instead, they suggest review authors highlight different actions that might be consistent with particular patterns of values and preferences.³ Indeed, of considerable interest and importance is how patients’ values actually impact on their decisions about the available treatment options. In spite of obtaining and weighing the best available evidence, value judgements underlie every clinical decision and every clinical decision demands attention to the particular circumstances of the patient and their values.¹⁸

However, the conclusions of some Cochrane systematic reviews have attracted criticism of their repeated findings of insufficient evidence to make conclusions and their lack of definitive clinical recommendations. For example, in a recent review, ‘Neuroprotection for Treatment of Glaucoma’, the authors conclude,

“...In accordance with the selection criteria for inclusion, we identified no studies relevant for this review... Although neuroprotective agents are intended to act as pharmacological antagonists to prevent cell death, the evidence that they are effective in preventing retinal ganglion cell death, and thus preserving vision in patients with open angle glaucoma, has
not been demonstrated. Long-term RCTs are needed to determine whether or not neuroprotective agents may be beneficial for individuals with open angle glaucoma.”

While this may seem of no use to some, others argue that the finding of insufficient evidence is imperative for identifying and encouraging much needed research. Also, while the Cochrane Collaboration argues against making specific clinical recommendations, stakeholders may want such recommendations in spite of biases and questionable validity external to the populations and circumstances of the studies included in the review.

Systematic reviews themselves can be a little too long, complex and difficult to understand, with many pages dedicated to methodological rigor, particularly for active clinicians and some consumers. Reviews need to condense evidence into messages that stakeholders can absorb reasonably quickly and understand. Cochrane reviews include a useful plain language summary, specifically aimed at lay people.

4.1.9 Systematic Reviews in Context

Conflict of interest in medical research was raised frequently at the Colloquium. We need to be mindful of the issues involved. As part of the keynote address, Ray Moynihan spoke on the merging of marketing and medicine. He questioned the existence of some medical conditions as serving only the financial gain of some pharmaceutical companies. His book with co-author Barbara Mintzes, Sex, Lies and Pharmaceuticals, details how drug industry employees worked with paid key opinion leaders to help develop the disease entity known as ‘female sexual dysfunction’, running surveys to portray it as widespread and helping to design diagnostic tools to persuade women that their sexual difficulties deserve a medical label and treatment. He believes that this is just one of several instances where some pharmaceutical companies have misled the public in order to build global markets for new drugs. He called for more evidence in definitions of medical conditions and their epidemiology. In the discussion at the end of this presentation, some suggested that research should be publicly funded and not industry funded. Others suggested it would be best to have objective monitoring panels. However, it was pointed out that finding experts with no conflict of interest can be somewhat difficult!

Dr Fiona Godlee, Editor-in-Chief of the British Medical Journal, provided similar thoughts in her plenary presentation on “The H1N1 Experience”, which related to a Cochrane systematic review on the benefits and safety of the drug Tamiflu (osetalmivir) for the treatment and prevention of infections due to influenza A and B virus. The analysis showed Tamiflu offered mild benefits in terms of duration of symptoms for healthy adults if taken within 24 hours of onset of symptoms, but
there was no clear evidence it prevented lower respiratory tract infections or other complications.\textsuperscript{22}

The findings relate only to use in healthy adults with influenza, not in patients judged to be at high risk of complications. Furthermore, the use of Tamiflu for reducing the duration of symptoms, has yet to be compared with non-steroidal anti-inflammatory drugs or paracetamol.\textsuperscript{21} Peer comments on published papers exposed misconduct and conflicts of interest with pharmaceutical companies. Licensing by the FDA was political and not evidence-based. In an editorial, Dr Godlee advised, “…it is a legitimate scientific concern that data used to support important health policy strategies are held only by a commercial organisation and have not been subject to full external scrutiny and review. It can’t be right that the public should have to rely on detective work by academics and journalists to patch together the evidence for such a widely prescribed drug. Individual patient data from all trials of drugs should be readily available for scientific scrutiny.”\textsuperscript{23} She highlighted the usefulness of post-publication peer review and comments on articles and recommended that trial data should be published. Dr Godlee reiterated the need to build groups who have no conflicts of interest.

Professor Gordon Guyatt gave a presentation entitled, “Evidence to Action: Dealing with Conflict of Interest in Moving from Systematic Reviews to Guidelines”, primarily on challenges arising during the development of the American College of Chest Physicians guidelines for antithrombotic therapy. He described conflict of interest as being primary, i.e. financial and or intellectual (where guideline panel members promote their own research), or secondary (where panel members have previous involvement with guidelines). To minimise the problem, he suggested: having a methodologist chapter editor with no important conflicts of interest; and a committee of academic physicians reviewing a potential panel member’s financial conflicts who decides if they are acceptable, unacceptable, or acceptable provided future industry involvement is restricted. Furthermore, experts who are approved as panel members during this review but judged to have important financial or intellectual conflict of interest should be allowed to participate in collecting and interpreting evidence. However, only panel members without important conflicts should participate in deliberations and the development of guidelines. A conflict of interest grid of panel members should be submitted with the guidelines. Such approaches may facilitate optimal use of Cochrane and other systematic reviews in guiding clinical practice.

As indicated by the Tamiflu example given by Dr Godlee, systematic reviews and guideline recommendations can attract considerable public interest and controversy. Indeed, this was a key lecture in the LSHTM course. Two systematic reviews were cited and discussed in depth as case examples: “Male circumcision and risk of HIV infection in sub-Saharan Africa,”\textsuperscript{24} in which male circumcision was found to be associated with significantly reduced risk of HIV, and “Nutritional quality of organic foods,”\textsuperscript{25} in which no differences in nutritional quality were found between organically and conventionally produced foods. The messages delivered by the main authors of
these papers who delivered the lectures were clear - to use rigorous methodologies, to keep meticulous records, to be transparent, take great care with recommendations, to be prepared for controversy, and able to respond to the media. These points were reinforced by Assoc. Prof. Ned Calonge (Chair, US Preventative Services Task Force [USPSTF]), who gave a keynote address at the CUE Summit on, “Communicating evidence: Lessons learned from USPSTF’s recommendations on screening young women for breast cancer.” The guidelines developed suggested that there was insufficient evidence to support mammography screening in women 40-49 years. This was not at all well received. Assoc. Prof. Calonge explained that communication is critical and that great care must be taken with messaging and wording of guideline recommendations. In this example, it was important to put screening and testing in context with the individual. He urged guideline developers to distinguish between what is recommended for a group and the individual.

4.1.10 INVOLVING CONSUMERS

The Cochrane Collaboration believes that effective health care is created through equal partnerships between provider, practitioner and patient. Cochrane Reviews are unique because they are both produced by, and are relevant to, everyone interested in the effects of health care. Based on the best available evidence, health care providers can decide if they should fund production of a particular drug. Practitioners can find out if an intervention is effective in a specific clinical context. Patients and other health care consumers can assess the potential risks and benefits of their treatment.

The one day CUE Summit I attended in Keystone, Colorado, gave me the opportunity to hear thoughts and concerns directly from consumers and consumer advocates. Some of the issues made clear to me during this meeting were that: consumers would like to challenge policy and decisions not based on scientific evidence; as a matter of social justice, minority diseases should not be overlooked in terms of research and funding; consumers should be included on decision-making panels, yet it is not always clear who should be chosen (e.g. patients, advocates, families, carers, or the public) and for what reasons; it is imperative to involve consumers in research from the outset, as their preferred outcomes may not be that of providers and researchers; consumers want to know about conditions that are painful, distressing, disabling, life threatening and common; they want information, including statistics, in plain language that they can understand; and they want to know how to identify ‘good’ studies. Furthermore, concerns were raised by consumers about the ethics of RCTs and whether or not consumers should have a choice about their treatment. The importance of considering individual cases and unique circumstances in health care decision making was raised repeatedly.
Every Cochrane Review Group aims to have members who will represent the consumer viewpoint in deciding which reviews should be done, the questions that should be asked, and how the results should be presented. The Cochrane Consumer Network (CCNET) coordinates the involvement of consumers within the Collaboration (http://consumers.cochrane.org/, Accessed October 12, 2010).

4.1.11 SYSTEMATIC REVIEWS IN EYE CARE

After visiting the main CEVG at LSHTM, UK and the satellite group at JHSPH, US, I was fortunate enough to attend a face-to-face meeting of key members from both groups at the Joint Colloquium of Cochrane & Campbell Collaborations in Keystone, Colorado. This really provided me with an opportunity to establish a relationship with the core editorial team. Although the CEVG has been highly productive, we discussed the need for greater involvement by potential authors and consumers, and the need for a policy on prioritising the many updates that are currently required. Additionally, a key issue is whether or not to have potential review questions on the website under ‘reviews required’. There can be problems. For example, if potential review questions are posted, the right people with the right expertise may not take up a particular title. On the contrary, if they are not posted, the opportunity to engage those who are willing to contribute but who have difficulty coming up with a title may be missed. The group felt it is important to obtain input from core advocacy groups (e.g. Macular Society), experts (e.g. American Academy Ophthalmology) and consumers on topics requiring urgent review.

4.1.12 HOW TO BECOME INVOLVED

Researchers, practitioners, providers and consumers can contribute by becoming involved in the Cochrane Collaboration in a number of ways, depending on interests and skills - as a review author, editor, methodologist / statistician, consumer representative, hand searcher, translator, or funder. Persons should contact the review group (health care area) of interest http://www.cochrane.org/about-us/get-involved; Accessed December 8, 2010).
4.2 Outcome Measures of Functional Performance in Bionic Eye Research

During my visit to London, UK, I had stimulating discussions with Professor Gary Rubin from the Institute of Ophthalmology and Moorfields Eye Hospital, who is a world expert on outcome measures for vision research. In particular we discussed how to measure orientation and mobility performance and activities of daily living, both key factors in evaluating the benefits of the bionic eye. This is currently a pressing topic of discussion among bionic eye researchers around the world, including Australia. Professor Rubin is establishing a clinical assessment centre dedicated to this, as are we at the Centre for Eye Research Australia (CERA).

CERA is a key research partner in Bionic Vision Australia (BVA), a consortium of world-leading Australian researchers, collaborating to develop an advanced bionic eye (http://www.cera.org.au/index.php?nodeld=109. Accessed December 2, 2010). A bionic eye uses a retinal implant connected to a video camera that is built into a pair of glasses. The camera converts images into electrical impulses which activate remaining retinal cells. The cells then send visual information along the optic nerve to the brain, where the image is interpreted. In this way the bionic eye mimics the function of the retina and restores sight. The BVA aims to implant an advanced bionic eye in 2013. As part of the project we are developing clinical measures to assess performance with the new device, which will be in accordance with US Food and Drug Administration (FDA) guidelines,27 and perspectives from the field.28-30 New interventions often require new measures. Most clinical measures that have been developed to date are for use with patients who have slight to severe vision loss. We need to be able to measure changes in those with severe to profound vision loss, at least in the early phases of the project. While timed performance is objective and reliable (e.g. walking speed),31-36 there are nuances in performance that are important to capture more directly (e.g. hesitations, hand / foot searching and fatigue). We discussed the pros and cons of measuring mobility in a controlled indoor laboratory setting versus the real world (e.g. control of lighting and obstacles versus realism), and the need to involve expert orientation and mobility instructors in the development of improved measures that are valid for this particular population. In addition, the patient perspective on quality of life with the new device is imperative and requires a novel measurement instrument. A consistent and joint approach to all of these measures, by all groups undertaking similar research, would augment submissions to the FDA for standardised tests and enable comparisons between studies. Valid comparisons across clinical trials are important because, at this stage, the pool of potential recipients is small and
comparisons across studies would expedite the accumulation of evidence to further advance bionic eye development in future.

In addition to this discussion, I was extraordinarily fortunate to spend time with Assoc. Prof. Gislin Dagnelie, a principal investigator in the 60-electrode Argus II retinal prosthesis (bionic eye) clinical trial sponsored by Second Sight Medical Products (Sylmar, California), and colleagues at the Lions Vision Research and Rehabilitation Center, Wilmer Eye Institute, Johns Hopkins University School of Medicine. Upon arrival at Wilmer, I sensed I was in the right place and that the experience would be a highlight. The plaque on the wall of the new building was inscribed with a quote from Churchill, made in 1943 in regard to re-building the Houses of Parliament after destruction in World War II,

“We shape our buildings. Thereafter, they shape us.”

I was able to interview and observe the clinical testing of a patient who had received a bionic eye. For reasons of privacy and confidentiality, I will limit my report to broad comments and not disclose any personal or clinical information. I am indebted this person for many insights shared and lessons learned. As both a clinician and researcher, I have come to realise that no amount of reading the literature or second-hand information can replace listening to the patient, if one really wants to understand the issues. As there are no bionic eye recipients in Australia to date, the knowledge I was able to acquire and bring back to share with colleagues was invaluable.

It was clear the patient was dedicated to contributing to science for the benefit of others, spending many hours every week undergoing clinical tests and discussing his experiences with others. He was extremely tolerant of the long and tedious testing protocol and well-supported by family and friends. He wears the device for approximately 5 hours per day. When asked about his experience, he was exceedingly positive. The only disadvantages mentioned were that the power pack became a little heavy after a while and that the wires sometimes caught on objects, emphasising the importance of device design.

To obtain accurate and sensitive measures of profoundly low levels of vision, one method used by the group at Wilmer was scotopic sensitivity threshold testing. Also, several clinical tests had been devised to measure performance, with comparisons being made between the device off versus on. I observed the patient performing a sock-sorting task and mobility tasks. In the former, the patient was required to identify the colour of socks (black, white or grey) and the percentage of correct responses out of 40 trials was determined. Both indoor laboratory and outdoor real world mobility performances were assessed. Outdoor performance was video recorded for later analysis. For the
level of vision, the path was appropriately short (less than 10 m) and simple with few obstacles. Comparison with other mobility devices, such as the long cane or sonic aids, would be interesting.

Comprehensive articles have been written on what might be measured post-implantation.\textsuperscript{28-30} However, the literature presents the ideal; the current reality is that this is not necessary or achievable. In practice, levels of vision likely to be attained will be rudimentary and at this stage we need very simple clinical tests of function and performance to measure outcomes. Also apparent to me was the need to carefully devise a psychosocial evaluation for identifying suitable candidates and the need to build the evidence in this area.
5 CONCLUSIONS AND FUTURE PLANS

Altman advocated that, “We need less research, better research and research done for the right reasons.” Toward this end, I suggest that conducting systematic reviews and safeguarding against conflicts of interest are essential in health research. However, while systematic reviews are considered one of the highest levels of evidence for making treatment decisions, there is a place for expert opinion and traditional review. Indeed, there is also a place for public and consumer opinion. Furthermore, knowing the tools of evidence-based medicine, such as systematic review, while necessary, is not sufficient for delivery of the highest quality patient care. Guyatt et al. explain that in addition to clinical expertise, the clinician requires compassion, sensitive listening skills, and broad perspectives from the humanities and social sciences, in order to cultivate an understanding of the patient’s health care needs in the context of their experiences, personalities and cultures.

I plan to implement, disseminate and promote the knowledge I gained about systematic review and outcome measures during my Dr Dorothea Sandars and Irene Lee Churchill Fellowship in the following ways:

i. Contribute to systematic reviews, clinical guidelines and policy, so that all concerned may make the most appropriate choices regarding eye care. Specifically, I will contribute to updating a Cochrane systematic review on reading aids for adults with low vision through the CEVG, UK and continue to contribute to a new Cochrane systematic review on the comparative effectiveness of types of medical interventions for primary open angle glaucoma through the CEVG, US.

ii. Develop a short training workshop for eye care professionals and researchers in Victoria.

iii. Assist the CEVG with promoting systematic review and conducting training workshops at local and international vision conferences.

iv. Collaborate with other Cochrane Review Groups in Australasia.

v. Encourage the application of mobile phone strategies, ‘mHealth’, in local eye care projects. Specifically, the development of a mobile phone application for teaching communication skills to medical staff, as part of a project in which I am involved at the Royal Victorian Eye & Ear Hospital. This modality for delivering an educational tool may have greater impact among busy eye care clinicians than traditional methods, given its growing popularity and accessibility among the broader medical community.

vi. Discuss and devise strategies for measuring bionic eye outcomes with CERA and other BVA team members.
6 RECOMMENDATIONS

I would like to make the following recommendations based on my Dr Dorothea Sandars and Irene Lee Churchill Fellowship experience:

i. Although Australia is strong in evidence-based health care and systematic review, having established several Cochrane Groups in the region, I recommend that evidence-based care should be further promoted among Australian eye care professionals and that the number trained in using and preparing systematic reviews should be increased.

ii. Stakeholders should be working together on systematic reviews, and, consumers should be involved from the outset.

iii. We must continue to be mindful and open concerning conflicts of interest in eye care research and clinical guideline development.

iv. International consensus on a standardised set of bionic eye outcome measures is required. The set should comprise clinical measures of rudimentary vision, orientation and mobility performance, activities of daily living, and the patient perspective. Measures should be relatively simple at this stage. In addition, I recommend that a set of psychosocial measures should be devised for selecting suitable candidates.

v. My final recommendation is that we study patients' values, how they affect decision making in eye care currently and the best ways to incorporate them into clinical care in future.
7 REFERENCES

15. National Health and Medical Research Council (NHMRC). NHMRC additional levels of evidence and grades for recommendations for developers of guidelines - Stage 2 Pilot Canberra, ACT: Australian Government; 2009.