Evidence Building and Synthesis Research Effective Health Care Research Consortium

Annual Report

Implementation Year 2: 15 May 2012 to 14 May 2013

Version: 24 June 2013 (revised)







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1. PROGRAMME DESCRIPTION

Title of RPC: Effective Health Care Research Consortium

Reference number: PO 5242

Period covered: Implementation Year 2: April 2012 to March 2013

Name of lead institution Liverpool School of Tropical Medicine (LSTM)

and RPC Director: Paul Garner (Professor)

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This Consortium exists to increase evidence-informed decisions to improve health and health care for the poor in low- and middle-income countries.

The Consortium synthesises relevant and reliable research to contribute to a global evidence-base to make health care more effective, improve health, reduce illness and death and avoid the public and providers wasting money on ineffective health care. At the same time, the Consortium builds capacity of groups worldwide, but particularly in low- and middle-income countries to carry out these reviews, interpret and use them.

The contributors are embedded in The Cochrane Collaboration: three lead large research networks in Africa, South Asia, and China; and two lead global teams synthesising research in infectious diseases and health service organization and financing. All have track records in preparing high quality, systematic reviews relevant to low- and middle-income countries; all are skilled in effective dissemination and know how to influence policy; and all have highly effective working relationships with each other.

The focus of the Cochrane reviews are in infectious diseases, particularly malaria, tuberculosis (TB), and diarrhoea; HIV; mental health; reproductive health; and a wide range of other conditions and problems relevant to low and middle-income countries. However, the Consortium is but one contribution to the global effort and global funding in preparing and updating Cochrane Reviews, so its portfolio reflects the direct support to running the Cochrane Infectious Diseases Group (CIDG), and to the interests and specialities of the Cochrane Centres and their authors. Nevertheless, the entire Consortium prioritises topics for review that are likely to be relevant to the health of the poor, particularly women, in low- and middle-income countries. The investment builds on DFID support since 1992 in building the science, the reviews, the networks, and the influence of The Cochrane Collaboration in Africa, Asia, China and globally, through the World Health Organization (WHO).

Lead and partner organisations

UK Lead: LSTM. Includes CIDG and Liverpool Co-ordination Team.

Africa Lead: South Africa Cochrane Centre/Stellenbosch Centre for Evidence Based Policy

Includes African partners in: Nigeria, Kenya, Cameroon, The Gambia and Uganda.

India Lead: South Asian Cochrane Centre

China Lead: Chongqing Medical University

Includes a Chinese partner in Shanghai

Norway Lead: Effective Practice and Organization of Care Group

Budget

Budget approved for DFID financial year 2 was £1,072,669. Actual expenditure by end-DFID financial year 2 was £1,072,444. All quarterly claims submitted to DFID as required within the financial year.

2. OVERVIEW OF THE YEAR

Progress and achievements

On decision making globally

This has been a very good year with demonstrable impact. Three Cochrane reviews had substantive impact on global policies, and one an important review to underpin an existing recent global recommendation:

Primaguine for transmission of malaria (New Cochrane Review)

The new Cochrane Review of **primaquine for reducing malaria transmission** was used by the most senior WHO malaria policy committee to restrain enthusiasm for a global recommendation for universal use of single dose primaquine with malaria treatment to prevent transmission. "Speaking of Medicine" ran a blog on this topic, and the policy debate continues.

Impacts: This 'old' recommendation is being resurrected despite potential safety concerns in people with G6PD deficiency where the drug could potentially cause haemolysis. The review is slowing the push for a rapid up-scaling of this intervention, and there is now time for more critical analysis of existing data.

Rotavirus vaccines (Cochrane Review update plus commissioned review)

The 2012 update Cochrane review of **rotavirus vaccines** was used by the WHO's Strategic Advisory Group of Experts (SAGE), alongside another commissioned systematic review that we were part of, in deciding to recommend purchase of these vaccines for routine use in Africa. The first edition of this review was in 2003. We reported on this last year.

Impacts: Cochrane Review and associated output central to the WHO-SAGE decision to recommend the vaccine in low- and middle-income countries. The SAGE meeting was in April 2012, and then WHO published a position paper in <u>January 2013</u>. This draws extensively on the Cochrane Review and the unpublished systematic review that we contributed to.

Routine deworming programmes (Cochrane Review update)

The 2012 update Cochrane Review of **routine deworming programmes** used new analytical methods and GRADE provided a much clearer analysis. The first edition of this review was published in 1997. "Speaking of Medicine" ran a <u>blog</u> on this topic, with an avalanche of debate on websites and in policy communities globally.

Impacts: Debate and true engagement, with some evidence of disinvestment. The potential for savings are large. For example, Kenya is planning to <u>deworm 5 million children</u> every year for 5 years. In 2012, 3.6 million were dewormed at a cost of \$0.36 per child, a total cost of \$1296K = £857K per year. Five million will cost \$1800K per year (£1191K) or \$9000K (£5955K) over five years. Costs are generally estimated by the advocates based on the drug costs, so delivery needs to be factored in; and scaling up the calculations across whole continents means the potential saving is large.

Xpert® MTB/RIF for drug resistant TB (Cochrane Diagnostic Test Accuracy Review)

We completed a methodologically challenging and innovative review examining the diagnostic test accuracy of Xpert for drug resistant TB.

Impacts: This is unlikely to change policy but is strong evidence to underpin the current WHO recommendation for rapid scale-up, and the UNITAID commitment of US\$30 million, although implementation <u>questions clearly remain.</u>

In addition, we have been successful in applying a logic framework to a number of our Cochrane Reviews.

On regional decision making

• Ghana Essential Medicines Committee: In 2011-2, the Consortium partnered with the Ministry of Health (MOH) and WHO in Ghana to use reliable evidence to inform adoption of new drugs in the national essential medicines approval process. In the past, this has depended on expert opinion. The

Consortium partnered with the committee and provided training and support in using GRADE and summarising the reliable evidence from systematic reviews to consider several new drugs for adoption. We learnt that this translation was by no means straightforward, and the learning lessons from this will be published in <u>PLOS Medicine</u> in May 2013.

- **Kenya Paediatric Association:** the Consortium partnered with the Kenyan Paediatric Association in approaching an update of the national guidelines. Consortium staff (Sinclair and Garner) worked with Kenya Consortium partners (Opioyo, English) to synthesise reliable evidence for guideline development (fluid management in severely unwell children, umbilical cord care in hospitals, use of hydroxyurea in sickle cell disease). This meeting went really well, with high level of engagement and discussion. It provides a platform and model for evidence-informed decision making in clinical and public health in Africa.
- Regional courses in applying evidence: The Consortium developed a course, jointly accredited by LSTM and Stellenbosch University, entitled "Primer in Systematic Reviews & Research Synthesis", which we ran in Tanzania and Namibia for researchers and policy makers in the latest advances in systematic reviews. The South Asian Cochrane Centre has developed a similar course and run this in partner institutions in India too.
- **Establishing toxicology network in India:** Partners in India have developed a network of researchers but with engagement with policy makers to highlight priorities in a wide variety of toxicology issues in public health, including self-poisoning, agricultural poisons, and snake bite.

Evidence of demand

We identified various indicators of demand:

- The Heart and Stroke Foundation commissioned the Centre for Evidence Based Health Care at Stellenbosch to evaluate the health effects of widely promoted low carbohydrate diets.
- **The WHO malaria guidelines panel** indicated they wanted eight Cochrane Reviews to inform the next guideline update.

Influence on Cochrane

The Consortium, particularly CIDG, continues to play an active role in shaping strategy within The Cochrane Collaboration. This includes:

- Using GRADE evidence quality to guide the wording in abstracts which improves clarity. For example, for an outcome such as mortality with moderate quality evidence we say "the intervention *probably* reduces mortality".
- Our review specific dissemination strategy, welcomed by the Editor in Chief as good practice.

In addition:

With Cochrane Editors, we have developed further the review classification system where updates not needed; and have highlighted the problem of readability of Cochrane reviews;

China partners have explored whether machine translation was a feasible option for translating to Chinese;

Cameroon partners have developed French translations and are disseminating these.

Multimedia and access

The Cochrane Collaboration and Wiley have agreed a new publishing contract which facilitates Open Access publishing, with Gold Access (with a cost) and Green Access (no cost, free at 12 months).

The **India Council for Medical Research** (ICMR) renewed the India national licence for The Cochrane Library.

South Asia partners have adopted multimedia for disseminating their work in many different ways; their ground breaking project with medical students in India received some attention; and Prathap Tharyan has a highly successful blog.

South Africa explored use of blogs and multimedia; and CIDG were successful in disseminating important reviews through blogs (both with "Speaking of Medicine").

Other projects and impacts

WHO Guidelines evaluation: The Liverpool Office, in partnership with the Stellenbosch Centre for Evidence Based Health Policy and the Director General's Office of WHO, carried out an evaluation of the quality of WHO Guidelines Development Processes. The Consortium presented the results as a seminar to WHO, and the WHO have presented the results to the Director General's Senior Management team, and was published in May 2013.

India snake bite project: India partners have successfully brought together specialists who want to examine the burden of this health problem in India, potential effective solutions, and how best to deliver them.

African INDABA: The South African Cochrane Centre and the Centre for Evidence Based Health Care ran a highly successful Indaba for Cochrane author training, to celebrate 20 years of the Cochrane Collaboration, and to discuss the future. This was tremendously successful event, reported on "Speaking of Medicine".

Challenges and disappointments

- The Consortium was not able to identify candidates for the Consortium fellowship programme which aimed to develop existing authors in the first period from China and India partners, but has been highly successful in countries of Africa, with one from South Africa, and two from Kenya.
- There was a lack of co-ordination with the Nigeria partner, who held a national Cochrane meeting without engaging the South African Cochrane Centre, but this has been rectified.
- We put in a bid to follow up on earlier Conflict and Stabilisation work. The company managing the bid split it into two stages, suggested we do most of the work for one third of the money and they would make a decision at that point, so we declined.
- The China partnership has not been successful in identifying author teams and topics to carry out Cochrane Reviews.

Other observations

Researchers and policy makers now accept systematic reviews methods. This is positive in relation to their use in decision making, but for academia brings with it particular drivers that need to be actively managed.

With academic recognition of systematic reviews, there follows academic competition and a reward structure that could **generate disincentives to collaboration**, **encourage duplication**, and **reward one off publications that are not updated**. It may also water down the strong mentorship philosophy in the Collaboration of enabling and supporting young researchers.

We are keeping this in mind as we generate strategies to avoid these negative influences in developing the new generation of researchers and authors. DFID and other funders will be important influences on this process.

3. LOGFRAME OUTPUTS

OUTPUT 1: High quality, up to date Cochrane or related systematic reviews relevant to improving health outcomes in the poor

Output indicator 1.1: Number of systematic reviews relevant to the content and delivery of poverty-related health programmes: new Cochrane Reviews (target 10; quantity 10).

Output indicator 1.2: Number of systematic reviews relevant to the content and delivery of poverty-related health programmes: updated Cochrane Reviews (target 5; quantity 6).

Output indicator 1.3: Number of systematic reviews relevant to the content and delivery of poverty-related health programmes: qualitative reviews, scoping reviews, overviews (target 2; quantity 2).

Progress to date

- We performed on target for new and updated Cochrane Reviews relevant to developing countries, as well as other reviews (see verifiable indicators, below).
- Please note the reviews below are only those that we returned in our performance against indicators, but we actually produced far more. In total the Consortium produced 44 published research outputs, and these were mostly Cochrane Reviews. See Annex 4.
- Three reviews also impacted at outcome level (see section 1).

Commentary

Cochrane reviews (1.1 & 1.2)

CIDG, the Cochrane Centres in Africa and India, and the Cochrane Effective Practice and Organization of Care Group all worked hard in achieving this target. Performance with the partner in Chongqing has been more limited.

CIDG has a strategy that prioritises high impact reviews, and these principles are being rolled out throughout the Consortium, and this is being demonstrated in the topic coverage (see below).

As the quality and complexity of reviewing increases, we are faced with the challenges of training new people in what is becoming a much more specialist and complex task. It appears that the initial Cochrane dissemination strategy of engaging everyone in the process of preparing a review is becoming impractical. Within the Consortium, we have observed this and are leading the way in trying to address this but it is not easy.

Other reviews (1.3)

We have carried out a scoping review to guide our TB reviews (this maps out what has been done and develops a conceptual framework about what needs to be done); and a systematic review of qualitative research. Whilst we met our targets, we had some disappointments with reviews in progress:

- a) An overview (reviewing all relevant systematic reviews) of food supplementation has been delayed;
- b) Plans for an overview in TB adherence with China partner fell through;
- c) The team in Nigeria carrying out a scoping review related to reproductive health are still bringing the review up to current expected standards.

Verifiable indicators

Diarrhoea		
Granados CE, Reveiz L, Uribe LG, Criollo CP. Drugs for treating giardiasis. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD007787. DOI: 10.1002/14651858.CD007787.pub2	NEW (1.1)	
Lazzerini M, Ronfani L. Oral zinc for treating diarrhoea in children. Cochrane Database of Systematic Reviews 2012, Issue 6. Art. No.: CD005436. DOI: 10.1002/14651858.CD005436.pub3	UPDATE (1.2)	
Soares-Weiser K, MacLehose H, Bergman H, Ben-Aharon I, Nagpal S, Goldberg E, Pitan F, Cunliffe N. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD008521. doi: 10.1002/14651858.CD008521.pub3	UPDATE (1.2)	
Note also contributes to Outcome indicator 1		
HIV		
Grobler L, Siegfried N, Visser ME, Mahlungulu SSN, Volmink J. Nutritional interventions for reducing morbidity and mortality in people with HIV. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD004536. doi: 10.1002/14651858.CD004536.pub3	UPDATE (1.2)	
Mbuagbaw L, Ye C, Thabane L. Motivational interviewing for improving outcomes in youth living with HIV. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD009748. DOI: 10.1002/14651858.CD009748.pub2	NEW (1.1)	
Omeje I, Okwundu CI. Effectiveness and safety of first-line tenofovir + emtricitabine + efavirenz for patients with HIV. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD007276. DOI: 10.1002/14651858.CD007276.pub3	NEW 1.1)	
Okwundu CI, Uthman OA, Okoromah CAN. Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD007189. DOI: 10.1002/14651858.CD007189.pub3	UPDATE (1.2)	
Infectious		
Danso-Appiah A, Olliaro PL, Donegan S, Sinclair D, Utzinger J. Drugs for treating <i>Schistosoma mansoni</i> infection. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD000528. doi: 10.1002/14651858.CD000528.pub2	UPDATE (1.2)	
Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S, Garner P. Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD000371. doi: 10.1002/14651858.CD000371.pub5		
Note also contributes to Outcome indicator 1		
Wall ECB, Ajdukiewicz KMB, Heyderman RS, Garner P. Osmotic therapies added to antibiotics for acute bacterial meningitis. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD008806. DOI: 10.1002/14651858.CD008806.pub2	NEW (1.1)	
Colvin C, Smith H, Swartz A, Ahs J, de Heer J, Opiyo N, Kim J, Marraccini T, George A. Household recognition and response to child diarrhoea, pneumonia and malaria in Sub-Saharan Africa: A systematic review of qualitative research. Social Science & Medicine 86 (2013) 66-78		
Malaria		
Graves PM, Gelband H, Garner P. Primaquine for reducing Plasmodium falciparum transmission. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD008152. DOI: 10.1002/14651858.CD008152.pub2	NEW (1.1)	
Note also contributes to Outcome indicator 1		
Reproductive		
Rohwer AC, Khondowe O, Young T. Antispasmodics for labour. Cochrane Database Syst Rev 2012, Issue 8. Art. No.: CD009243. DOI: 10.1002/14651858.CD009243.pub2	NEW (1.1)	
Systems		
Pande S, Hiller JE, Nkansah N, Bero L. The effect of pharmacist-provided non-dispensing services on patient outcomes, health service utilisation and costs in low- and middle-income countries. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD010398. DOI: 10.1002/14651858.CD010398	NEW (1.1)	
ТВ		
Cuello-García CA, Pérez-Gaxiola G, Jiménez Gutiérrez C. Treating BCG-induced disease in children. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD008300. DOI: 10.1002/14651858.CD008300.pub2	NEW (1.1)	
M'Imunya JM, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD006591. DOI: 10.1002/14651858.CD006591.pub2	NEW (1.1)	
Steingart KR, Sohn H, Schiller I, Kloda LA, Boehme CC, Pai M, Dendukuri N. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD009593. DOI: 10.1002/14651858.CD009593.pub2		
Ryan H, Sinclair D. Scoping review of TB. Unpublished document.	OTHER (1.3)	

OUTPUT 2: Accessible products for knowledge uptake

Output indicator 2.1: Number of "push" products (summary series) (target 1; quantity 1).

Output indicator 2.2: Number of reviews, training or synthetic technical products commissioned by national decision makers or intermediary organizations or networks ("pull" products) (target 2; quantity 2).

Output indicator 2.3: Stakeholder satisfaction.

Progress to date

We have met our indicators of performance in the log frame (see verifiable indicators).

The indicators are quite limited and do not encompass the full range of our work in this output, around making reviews accessible, in summarising them, and in preparing them for guidelines groups.

Output indicator 2.3 will be evaluated through a survey sometime in years 3 or 4.

Commentary

Making Cochrane Reviews more accessible

One component of our strategy is to make Cochrane Reviews, our base product, more accessible. This is not currently captured in our indicators.

- To improve readability by better structuring the results section, including working with authors to use the summary of findings table to help with this. We are leading the way in the Collaboration.
- To improve the clarity of the abstract and plain language summary by structuring the language around the GRADE evidence quality assessment.
- To use logic frameworks to express the theory of change that is being tested with a review.
- Our China partner has explored use of machine translation of Cochrane Reviews.
- We have been advocating for Open Access. An Open Access route has now been agreed with the
 publisher (March 2013) for all Cochrane Reviews. Whilst this is good, gold access will be at high cost
 and we do not have these funds currently.

We intend to work on simplified English approaches in CIDG reviews that will enhance machine translation but have not started this.

Summaries of reviews

We continue to prepare "Evidence Update", and have improved the format and now use this only for important CIDG reviews. The summaries are put on the website, published in "Africa Health" and used by partners.

The South Asian Cochrane Centre and the Centre for Evidence Based Health Care in Stellenbosch both summarise reviews in relation to specific demand projects, where organizations ask for help in particular topic areas. This was also the case for the Ghana Essential Medicines Initiative. This seems likely to be the approach the Consortium takes as a whole, rather than generating a large number of generic dissemination products, and we intend to provide guidance in generation of these products, and a variety of formats to allow people to design project-specific summaries.

Articles discussing our reviews

We continue the series in the International Journal of Epidemiology, with one in press; we are starting to work with Shally Awasthi from Lucknow on a dissemination series for a new journal in India. In addition, *The Cochrane Library* have published an <u>editorial about the deworming review</u>, one about the <u>XPERT</u> review, and have made a <u>special collection of reviews in TB</u>.

Preparation for Guidelines groups

We have assisted WHO guidelines groups with reviews in TB and TB and nutrition with GRADE summaries and methodological advice.

Wikipedia project

This is a new project that the Consortium is carrying out with the Cochrane Editor in Chief's office. The aim is to ensure Wikipedia entries are accurate and evidence informed, using reliable evidence where appropriate. The recent Consortium Planning meeting at the Indaba allowed us to set out the details of engagement.

Capacity building - internal and external

Between May and August 2012 the Communications Specialist ran two-day workshops at our three Partner Centres in China, South Africa and India titled 'Developing Communications Delivery Plans to support the translation and use of research into policy and practice'. The sessions covered both theory and practice and looked at understanding the decision-making environment, how to influence change within that environment, and how to utilise effective communications to connect research with end users.

A cross-consortium team from Stellenbosch University, the South African Cochrane Centre and LSTM delivered a four-day course titled 'Primer in Systematic Reviews & Research', to staff from the University of Namibia and the PolyTechnic of Namibia, on finding, appraising, interpreting, and considering application of findings of reviews. The host institutions organized all aspects of the course, apart from the teaching and materials. The course is now accredited with LSTM and Stellenbosch University.

We provided a structured short course in evidence synthesis for a DFID senior adviser, Malcolm McNeil.

Verifiable indicators

2.1	South Asia – India: New or Updated Cochrane Systematic Reviews of Public Health Importance, Issue 10, 2012, <i>The Cochrane Library</i> . A newsletter sent to Partners by email to promote reviews to targeted stakeholders within their Networks, post-publication in <i>The Cochrane Library</i> .	
2.2	 Rotavirus vaccine systematic reviews commissioned by WHO (update of Cochrane Review; safety review; and review of dosing schedules). Charles I, Okwundu CI, Nagpal S, Musekiwa A. Home or community programmes for treating malaria: a systematic review commissioned by WHO (in press). 	
2.3	To be measured by survey years 4-5. Some anecdotal information. For example, we ran webinars for USAID and for Gates Foundation when the deworming review was published, and had positive feedback on this by email.	

OUTPUT 3: RPC partner institutions and researchers in the South have increased competence for research

Output indicator 3.1: Number of institutions with a developed strategy and code of conduct to promote research integrity (target 1; quantity 2).

Output indicator 3.2: Number of new Cochrane editors appointed or new authors completing reviews from Southern Institutions (new editors target 1; quantity 2; new first authors target 8; quantity 6).

Output indicator 3.3: Number of Partners with multiplier funding at least matching DFID investment (target 1; quantity 4).

Progress to date

Good progress on approximating to the targets (see verifiable indicators).

Commentary

Integrity and publishing policy

- Development of institutional code of conduct to promote research integrity has been slow. A consultant carried out a baseline needs assessment. This was an extremely informative piece of work that we will follow up on.
- One action from this survey was to prioritise establishing a publishing policy for the Consortium, and in 2012 at the Executive Meeting we developed this publishing policy for the Consortium which members could use to influence their own institutions.
- South Africa and India partners continue to be major contributors to establishing trials registration in these countries; and CIDG have lobbied for the biggest drug trial in the world to be published (DEVTA), and were eventually successful.

Cochrane authors and editors

In last year's report we reported five new editors appointed from developing countries following the Consortium Editors' training and advocacy initiative in 2010. This year we report one editor, consistent with our target.

For authors, there is an ambiguity in the indicator, "number of authors completing Cochrane reviews from Southern Institutions". The target of eight is straightforward to achieve; we report on a much stricter indicator, that is, the number of new first authors from a developing country. This is a good indicator of capacity development, but probably a little ambitious. This year, six first authors from low- and middle-income countries completed their first Cochrane review and we would like to discuss with DFID a) making the indicator stricter; and b) reducing the target by half.

Matched funding

Partners in South Africa and India have made great strides with matching funding, with numerous government and international grants; see below.

Verifiable indicators

3.1	Indicators of progress			
	Effective Health Care Research Consortium. Consortium Publication Policy. 20 February 2013. For all Consortium partners, contractors and authors, CIDG authors. Available from CIDG home page: http://cidg.cochrane.org/sites/cidg.cochrane.org/files/uploads/EHCRC_Publication%20policy_final%2020Feb2013_0.pdf			
	Practical considerations in designing, conducting and reporting clinical trials. Held at VI Conference of the Indian Association of Public Health Dentistry; SS College of Dental Surgery, Vikarabad, Andhra Pradesh, India.			
	Scientific Misconduct and Inducement to participation. Workshop on Research ethics & good practice (GCP) guidelines; CMC Vellore,			
3.2 (editor)	New Cochrane editors from developing country: Newton Opioyo, Nairobi, new editor with the EPOC Group			
3.2	Colombia:	1 Woman ¹		
(authors)	Mexico:	1 Man ²		
	Kenya:	1 Man ³		
	South Africa:	2 Women ^{4 5}		
	Nigeria:	1 Man ⁶		
3.3	Grants			
	Chongqing 80,000 RMB. Effects of vitamin A supplementation on children's health: a series of Me analyses. Chinese Nutrition Society Nutrition research fund special research fund of the DSM: South Africa US\$272,205. Policy BUDDIES – BUilding Demand for evidence in Decision making through Interaction and Enhancing Skills of policymakers. World Health Organization			
	South Africa R697,125. EVISAT: EVidence to Inform South African Tuberculosis policies. World Health Organization			
	South Africa \$US 23,000 SU. To conduct two Cochrane Reviews to inform new WHO guideline reviews on HIV health services delivery. University of California			

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¹ Granados CE, Reveiz L, Uribe LG, Criollo CP. Drugs for treating giardiasis. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD007787. DOI: 10.1002/14651858.CD007787.pub2

² Cuello-García CA, Pérez-Gaxiola G, Jiménez Gutiérrez C. Treating BCG-induced disease in children. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD008300. DOI: 10.1002/14651858.CD008300.pub2

³ M Imunya JM, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD006591. DOI: 10.1002/14651858.CD006591.pub2

⁴ Rohwer AC, Khondowe O, Young T. Antispasmodics for labour. Cochrane Database Syst Rev 2012, Issue 8. Art. No.: CD009243. DOI: 10.1002/14651858.CD009243.pub2

⁵ Adeniyi FB, Young T. Weight loss interventions for chronic asthma. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD009339. DOI: 10.1002/14651858.CD009339.pub2.

⁶ Onwuezobe IA, Oshun PO, Odigwe CC. Antimicrobials for treating symptomatic non-typhoidal Salmonella infection. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD001167. DOI: 10.1002/14651858.CD001167.pub2.

4. RESEARCH OUTPUTS IN BRIEF

Published research outputs

Published research outputs

Ind	icators and definitions	N	Notes
Α.	Published research outputs	45	New Cochrane Reviews (16) Updated Cochrane Reviews (18) Other systematic Reviews (3) Other publications (8)
В.	Peer reviewed publications	45	
C.	Peer reviewed publications which comply with DFID Open Access policy	2	1 Cochrane Review and 1 Journal Review Note all Cochrane Reviews published (n=33) have totally free access in all <u>low-income countries</u>
D.	Peer reviewed publications with a Southern researcher as the primary author	6 women, 22 men Total 28	
E.	Peer-reviewed publications explicitly addressing gender issues or women/girls	6	Mainly reproductive health Cochrane Reviews
F.	Data sets made openly and freely available to external researchers	None	

Technologies

Indicators and definitions	N	Notes
New technologies/products released or, where required, achieving regulatory approval	None	
Technologies halted during development stages	None	

Highlight(s)

We outline some highlights in section 1, and list these below:

Four important Cochrane Reviews:

- Cochrane Review of primaquine for reducing transmission of malaria.
- Cochrane Review of rotavirus vaccines.
- Cochrane Review of routine deworming programmes.
- Cochrane Review of Xpert for drug resistant TB.

Regional decision making:

- Ghana Essential Medicines Project.
- Kenya Paediatric Association Guidelines Project.
- Regional courses in applying evidence.
- Toxicology network in India.

Other Outputs

WHO Guidelines evaluation

The Liverpool Office, in partnership with the Stellenbosch Centre for Evidence Based Health Policy and the Director General's Office of WHO, carried out an evaluation of the quality of WHO Guidelines Development Processes. This included an Appraisal of Guidelines for Research and Evaluation (AGREE) of the quality of guidelines since the Guidelines Review Committee had been formed; and interviews with Programme Directors. This study showed progress had been made, but some departments were actively avoiding the central quality assurance process. The Consortium presented the results as a seminar to WHO, and the WHO have presented the results to the Director General's Senior Management team.

Other publications to report

Three important systematic reviews were published:

- A review examining prevalence of diabetic eye diseases in Africa;
- A review of malaria in pregnancy, adapting and extending part of the current Cochrane Review update;
- A review about steroids in tuberculosis, drawing on several Cochrane Reviews.

Methods

We also added a systematic review of economic evaluations in the Cochrane Review, 'Artesunate versus quinine for treating severe malaria'.

Sarah Donegan the statistician helped advance the field with papers about individual patient data (IPD) analysis.

Policies

Consortium publishing policy (discussed above).

Other reviews

Burgess PI, Maccormick IJ, Harding SP, Bastawrous A, Beare NA, Garner P. Epidemiology of diabetic retinopathy and maculopathy in Africa: a systematic review. Diabet Med 2012 Jul 21. doi: 10.1111/j.1464-5491.2012.03756.x

Critchley, J. A., F. Young, et al. (2013). "Corticosteroids for prevention of mortality in people with tuberculosis: a systematic review and meta-analysis." <u>The Lancet Infectious Diseases</u> **13**(3): 223-237.

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Methodology

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Donegan S, Williamson P, D Alessandro U, Garner P, Smith CT. Combining individual patient data and aggregate data in mixed treatment comparison meta-analysis: Individual patient data may be beneficial if only for a subset of trials. Stat Med 2012 Sep 17. doi: 10.1002/sim.5584.

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Policies

EHCRC. Consortium Publication Policy. 20 February 2013. Aimed at: All Consortium partners, contractors and authors, CIDG authors. Available from CIDG home page:

http://cidg.cochrane.org/sites/cidg.cochrane.org/files/uploads/EHCRC_Publication%20policy_final%2020Feb20 13_0.pdf

5. UPTAKE / ENGAGEMENT WITH BENEFICIARIES

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CIDG, South African Cochrane Centre	WHO	 In malaria, we have been in consultation about their information needs, and are responding by prioritising reviews in mass drug administration and strategies to eradicate larvae (Garner, Graves).
		In TB, we have been contributing to the guidelines panels; one panel in nutrition; and one in TB diagnosis (Sinclair, Steingart).
		In diarrhoea, by responding to SAGE making recommendations about rotavirus vaccine (Soares).
		 In HIV, in preparing a review of decentralisation in HIV treatment (Kredo).
Centre for Evidence Based Health Care, Stellenbosch	Heart and Stroke Foundation, South Africa	The Centre for Evidence Based Health Care in Stellenbosch was approached by this body for advice on low carbohydrate diets. The "Noakes diet" is being widely promoted, somewhat similar to the Atkins diet, but promotes high fat, particularly saturated fat, to promote cardiovascular health. The Heart and Stroke Foundation was concerned that the diets may be harmful, and that the interpretation of the diet by the population may also do harm, in that it appears to promote saturated fats as health promoting. As a Consortium activity we decided to respond to this. The
		Consortium set up a team that wrote a protocol, sought existing systematic reviews initially; these appeared to be insufficient, so we embarked on a rapid systematic review which is nearing completion.
Wellcome/KEMRI	Paediatric Association, Kenya	KEMRI/Wellcome Trust helped the Kenyan Paediatric Association in the last revisions to the Paediatric Clinical Guidelines. In partnership with the Consortium, we aimed on the current round of revisions to use best practice as set out by GRADE and the AGREE standards. The Kenyan team prepared systematic reviews on three main topics (fluid management in shocked, septic children; cord care in hospitals; and hydroxyurea in Sickle Cell Disease); set up panels to discuss this. The Liverpool team helped with the training of the panels in GRADE, the interpretation of the reviews, and facilitating the transparent, consensus building for the recommendations in March 2013.
Calabar, Nigeria	Cross River State MOH	The main interaction is at State Level in Cross River, mainly around promotion of malaria control activities in the State; and with journalists.
South Asian Cochrane Network and Centre	Multiple national and state partnerships	The South Asia Cochrane Centre stays closely in touch with the ICMR in relation to their information needs, particularly in relationship to adoption of new vaccines; with the TB Research Institute in Chennai, examining what reviews would be useful to them and how the results of existing reviews are important; with State policy makers, particularly in the light of the deworming review, but also in examining how to use evidence in decision making.
	Toxicology	South Asian Cochrane Network and Centre have facilitated the development and implementation of a national study involving clinicians, herpetologists, laboratory scientists, snake anti-venom manufacturers, government agencies and civil society to describe the pattern and correlation between snake species and the clinical syndromes; management and outcomes after snake envenomation in

		different parts of India; and the laboratory techniques to develop venom detection kits. ⁷
Chongqing Public Health Department	Chongqing TB Bureau	Chongqing have had some consultation with regional TB partners to explore their information needs.
CIDG	The Cochrane Collaboration	CIDG continues play an active role in shaping strategy within The Cochrane Collaboration. Resources from DFID have helped us to contribute (see section 2, "influence on Cochrane).
	Wellcome Trust	Paul Garner met with Sir Mark Walport early in 2013. The discussion was about whether systematic reviews could offer anything to infectious diseases policy, and whether thorough reviews done by experts where as good as Cochrane reviews.
South Asian Cochrane Network and Centre	Cochrane Collaboration	Has multiple interactions with the Cochrane Collaboration, and then next International Cochrane Colloquium will be in Hyderabad in 2014.

6. OUTCOMES AND IMPACTS

Shaken the belief that investment in deworming is a best buy

The updated Cochrane Review had very substantive impacts. The <u>Speaking of Medicine Blog</u> authored by Paul Garner stimulated <u>discussion from the advocates</u>; there was an early rebuttal of their comments; various NGOs such as 'Givewell' which advise organizations on the effectiveness of aid, formed a view on the debate, and published this; and Nigel Hawkes, a journalist, wrote a <u>4-page feature for the British Medical Journal</u> on the debate.

Influencing how the WHO develops guidelines

A 2007 Lancet paper criticised the WHO's guideline development processes. Whilst the deficiencies had been well known for years, this paper was critical in inducing change, and the organization responded rapidly and effectively. Nevertheless, change is always slow, and there are others - not least the experts advising WHO - that preferthe status quo.

The Consortium has worked closely with the Global Malaria Programme in maintaining standards for evidence-informed decision making.

This year, we approached the Director General's office to evaluate progress of implementing change, to help the organization progress this further. We presented the results of the report to the WHO, and the paper from the report has been discussed by the WHO Senior Management Team.

Working with countries to identify models of evidence-informed decision making

We believe the Ghana and Kenya projects are important models to achieve our outcomes:

• In the Ghana project, with Essential Medicines Committee, that developed approaches for using evidence in national decision making processes. This is complete, and the paper published.

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⁷ The team aim to complete the study and disseminate the results by early 2016. It will help provide observational data on outcomes associated with snake envenomation and the relationship with different management protocols. This could aid decision making by bilateral agencies, the WHO and national organisations to supplement insufficient evidence from Randomized Controlled Trials (RCTs) of anti-snake venin (ASV) dosing. If attempts at developing venom detection kits are successful, this could aid the roll out of RCTs that compare individually titrated dosing of ASV versus high-dose ASV for snake envenomation. The improvements in health delivery and common protocols evolving from this study could improve health outcomes and save lives of people from resource-poor settings in India and the region

• In the Kenya project, with the Kenya Paediatric Association, national clinical guidelines were developed using international best practice effectively. This is on-going and documentation will be available soon.

Specific reviews

We have already mentioned Cochrane Reviews that have made an impact in section 1.

Other impacts

Community umbilical cord care

The Cochrane Review of umbilical cord care supported by DFID and published in 2004 identified this research priority. Community trials indicate a 30% reduction in mortality. This is a very important effect and very important impact of DFID funding (see verifiable indicators below: Lancet editorial).

Publication of DEVTA

DEVTA was the biggest drug trial ever carried out in the world. It tested Vitamin A and deworming, analysis was complete by 2007, but the results had never been published. CIDG and authors of the deworming review resulted in the trial authors eventually being cajoled into publication, as described by Bert Keller (see verifiable indicators below).

Verifiable indicators

Lancet editorial 2012

"...Research evidence on topical cord care is, however, scarce: most studies included in a 2004 Cochrane review were from high-income countries, and the review could not address the effect of topical care on systemic infections or mortality. The investigators called for trials in low-income settings, suggesting that "where the risk of bacterial infection appears high it might be prudent to use topical antiseptics". The choice of antiseptic and regimen of application was unclear: "it would seem sensible, in situations where packages of care around improving umbilical cord sepsis are introduced, to conduct randomized comparisons to identify the best agents and regimens".

Two large trials in *The Lancet*—both of which record encouraging reductions in neonatal mortality after application of a topical antiseptic, chlorhexidine, to the umbilicus—now improve the knowledge base. The trials build on the findings of a cluster-randomised controlled trial in Nepal, which compared chlorhexidine application with education on dry cord care and showed an apparent effect on neonatal mortality of chlorhexidine application in a subgroup enrolled within 24 h of birth (relative risk 0·66; 95% CI 0·46—0·95)." Osrin D, Hill ZE. Chlorhexidine cord cleansing to reduce neonatal mortality (editorial). The Lancet. 2012; **379**(9820): 984-6

* Zupan J, Garner P, Omari AAA. Topical umbilical cord care at birth. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD001057. DOI: 10.1002/14651858.CD001057.pub2.

2013 Cochrane review identifies unpublished study

"One million children were randomized in a deworming trial from India with mortality as the primary outcome. This was completed in 2005 but the authors have not published the results." Taylor-Robinson DC, Maayan N, Soares-Weiser K, Donegan S, Garner P. Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance. Cochrane Database of Systematic Reviews 2012, Issue 11

Blogger

"Data collection was completed in 2006, but the results were just published in The Lancet. Why the massive delay? According to the accompanying <u>discussion paper</u>, it sounds like the delay was rooted in very strong resistance to the results after preliminary outcomes were presented at a conference in 2007. If it weren't for the repeated and very public shaming by the authors of <u>recent Cochrane Collaboration reviews</u>, we might not have the results even today. (Bravo again, Cochrane). "

Bert Keller, Blog: http://www.bdkeller.com/2013/03/massive-trial/

The Cochrane Collaboration has released a series of 24 videos about The Cochrane Collaboration to celebrate the 20th anniversary, interviewing some of its leaders and contributors. Interviewed are a number of people who are part of the Consortium, or have been supported by the Consortium in the past, so these people clearly had something to say: They included: Godwin Aja (1), Paul Garner (5), Joseph Okebe (2), Prathap Tharyan (4), Vasumathi Sriganesh (2), Karla Soares Weiser (4), Jimmy Volmink (5). Videos can be found here: http://anniversary.cochrane.org/cochrane20-video-series-and-other-multimedia

7. COSTS, VALUE FOR MONEY AND MANAGEMENT

The aim of our management systems is good financial control and being able to assure value for money (VfM). This year we have made three important advances:

- We have established an across-Consortium online output monitoring system for partners, to allow identifying work for dissemination, and for us to harvest outcomes for the report (outcomes above, and see Annex 4).
- We have provided six monthly feedback on performance to partners, and a two year assessment of value for money.
- We have changed the balance of DFID investment based on partner performance for years 3+.

Details are in the narrative below the box.

Is the project / programme on-track against financial year budgets?	The Consortium is currently on track with the initial financial year budgets.
How did your forecasting of the programme expenditure during the year compare against the actual expenditure claimed?	Forecasting of the year changed very slightly throughout the quarterly forecasting and mainly in relation to partnership payments expected within a period. Due to delays in submitting invoices they were then transferred to the following period.
Have there been any large (in excess of 5%) budget variations during the period?	We have overspent on consultancy and travel. When we were required to cut the budget by 20% initially, it was not possible to cut salary positions so we trimmed our running costs excessively, and we will need to adjust this.
Are future costs on or off track against the last full budget / forecasting profile?	All future costs are on track in relation to the current work plans. Now <i>The Cochrane Library</i> is open access, we intend to pay for this for all our reviews relevant to the programme outcome. We do not have a budget line for this and request this.
Are there any changes in the cost structures (eg exchange rates)?	There are no changes in the cost structure as all work plans are calculated in sterling and within the initial approved budget.

Work plans (years 1-2)

Detailed work plans approved for all partners with expected delivery dates, and this forms the basis for the contract for the first two years. Further contracts beyond two years are nominally agreed, but the contract states explicitly this depends on performance in the first two years.

The partner plans and our assessment of them allow an early consideration of VfM issues. After the inception phase, for example, after considerable investment of time from our side and the partners themselves, we declined to enter into a contract with one partner because we judged the proposal was not VfM.

We also examine individual cost items in the budget, with particular attention to travel costs and workshop costs, and ask for a budgeted breakdown where appropriate. Budgets are nominally allocated to outputs.

Progress reports

Partners then report on progress against the work plans every six months and the Liverpool office provide feedback reports. This includes formative assessment and advice, and brings in information from meetings and visits. Where there are indications a partner is not delivering, the Liverpool office indicates that

remedial action is required. If there is an absolute failure to deliver on a substantive number of outcomes, then we can withhold 20% of the final payment for that year. We have had to consider this twice, and only completed payment once a revised down budget had been received for the subsequent year.

Although we have principles of "trust based financing", the system allows us to intervene when a partner appears to be consistently delivering below the contracted outputs. This is currently happening with one partner: we pointed out the problems that required remedial action at the 1 year and 18 month reports. Their dean became involved, plus an international team of advisers. Nevertheless, performance remained poor and we have asked for their year 3 plans to be downscaled by 2/3 to something that is achievable.

We have used external consultants to assess the partner reports but we have found this generally not very helpful. What is more use are internal assessments by staff that understand the technical side to what the partner is expected to deliver.

Online reporting and monitoring

Partners submit activities and outputs according to the headings of previous DFID annual reports through a bespoke online system. This we use to monitor progress, identify topics for dissemination, and compile annual reports.

Value for money assessment for each partner

All regional partners had a VfM assessment based on their 18 month reports of the programme (effectively 2 years given the inception phase of 6-months). This examined their outputs and their likelihood of contributing to the **outcome** of the programme, in a short summary of a few sentences. We then ask if the partner is on track for demonstrable impact by year 3, and by year 5. This provides the partner with a steer for their planning processes.

Then an overall value for money assessment is given categorised as either: Poor, Reasonable, Good, or Very Good, with very clear recommendations for the team in their planning and future work.

Improvements to planning and management for year 3+

The contract and planning document has been improved. Previously a number of outputs were really activities and partners have been given feedback on their work plans.

There is a nominal budget by output to allow assessment of VfM and to guide claw-back with failure to deliver.

CIDG has a separate budget for year 3 onwards (previously this was conflated with the management budget as many of the staff have dual roles). CIDG has not had a VfM assessment but it is pretty clear that it is performing well at outcome level.

Other VfM issues

International air travel is minimised by use of electronic communications. Air travel is by economy, in line with DFID procedures. We aim for each partner to have internal assessment processes on going to conferences, so that perhaps one person can represent the team at a meeting, rather than have several travelling.

Monitoring and VfM assessments (see above)

We manage partners through 6-monthly progress reports against their contracts and deliverables, and site visits. We have used both highly skilled external consultants and internal consultants but have found that the Director, Communications Specialist and Programme Manager all then have to rewrite the reports, and thus the external assessments lengthen and complicate the deliverables and VfM assessment. We have therefore decided to use expert peer review on some of the scientific outputs, and specialists to carry out ad hoc evaluation of case studies of impact, but will continue the monitoring and VfM assessments internally.

Staff - Communication specialist

The Communications Specialist is leaving in May 2013. We are carrying out an analysis of partner and consortium needs in communication, have committed to a part-time contracted post with LSTM for a service level contract, and intend to use contractors for any other specialist needs.

Staff - Statistician

The brilliant statistician in Liverpool who works for 2 days a week is moving on to a research fellowship. We are currently recruiting for a new post. A new statistician has been appointed in Cape Town.

Staff - tenured post

LSTM and Warwick University have appointed a tenured Associate Professor in research synthesis. This person will be based in Warwick, with 20% of their time allocated to the Liverpool Team. The successful incumbent is a trainee from the Reviews for Africa Programme and an editor with CIDG.

8. WORK PLAN & TIMETABLE

CIDG has a strategic plan with clear indicators of annual performance, which is available on: http://cidg.cochrane.org/sites/cidg.cochrane.org/files/uploads/CIDG Strategic-plan 2011-6.pdf

Annex 4 contains Cochrane protocols, which should mainly be completed in the next two years. Partners in India, South Africa, Nigeria, Cameroon, Kenya and China have their own strategic plans, and have their own contracts with the Consortium. These include a summary of their approach, their deliverables and, an associated activity plan and budget. These contracts are currently being renegotiated for years 3-5, and are available on request.

For reviews, we aim to deliver on malaria reviews for the WHO Guideline Group and in relation to the current emphasis on eradication. We intend to build capacity with partners, particularly TB in India, and nutrition with South Africa. With funding, we want to publish using Gold Open Access.

For research uptake, we aim to engage with Wikipedia through the pilot Cochrane project; we intend to move some of the global communication activities to India and South Africa

For capacity development, we are extremely keen to:

- Roll out the research uptake course.
- Extend the model of the National Guidelines work with Kenya.

The summary by partner is below:

Liverpool management office

- Put in place effective staffing configurations and contracting to fulfil our mandate in research uptake, including communications.
- Actively manage the consortium to maximise outcome and impact. This will include increasing funding to some partners and decreasing funding to others.
- Be instrumental in assuring the Wikipedia project is successful with partners.

CIDG

- Complete malaria reviews requested by the WHO malaria chemoprevention and therapy guidelines panel.
- Seek funding for malaria safety review of primaquine.
- Focus on TB diagnostic and diagnostic strategies.
- Obtain funds for Neglected Tropical Diseases reviews, particularly filariasis.

South Africa

- To develop further its regional leadership role.
- To set up and deliver on the policy engagement (BUDDIES) project.
- To set up and deliver on new TB response mode grant.
- To further develop capacity for high level author support.

Nigeria

- To increase the number of high quality reviews and updates.
- To establish better national communication about Cochrane and its outputs.

India

- To strengthen mechanisms to ensure production of high quality reviews.
- To develop state engagement.
- To successfully plan the next Cochrane Colloquium.

China

- To successfully complete at least two Cochrane reviews.
- To develop policy interface with Fudan University.

9. RISK

The risk register was updated in September 2012 and all partners have their own risk registers which the Liverpool Office view and discuss with partners.

The register is organized around the outcome and outputs in the log frame, see Annex 1.

10. MONITORING AND EVALUATION

This is covered in the value for money section.

We have collected case studies of impact. Partners have pro-formas for this to aid the Consortium to think at outcome, rather than output level.