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Using reliable evidence to inform healthcare decisions: Case studies from India and the South Asian region

Prathap Tharyan

Director, South Asian Cochrane Network & Centre

Prof BV Moses Centre for Evidence-Informed Healthcare & Health Policy

Christian Medical College, Vellore, Tamil Nadu, India

NICE/DFID/World Bank/MOHFW workshop; on HTA:
New Delhi, 10 October 2014

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Shingles vaccine can help prevent the disease in older adults

More than half of US drug safety studies never see the light of day

Cranberry juice 'offers little protection against cystitis'

Exercise can boost the odds of beating cancer by making patients feel less tired after treatment

Soothing tunes may help reduce stress in heart patients

Can Logging On Help You Lose Pounds?

Gold-standard review finds rotavirus vaccines are effective

Mammogram Benefit Seen for Women in Their 40s

CONVERSATIONS CAN HELP IMPROVE MEMORY, SAYS STUDY

Ginkgo Biloba Ineffective Against Dementia, Researchers Find

New drug hope for common form of dementia: review

Driver health checks fail OAPs

Fish Oil Supplement Research Remains Murky

The Truth About Alternative Medicine

Cultural sensitivity may improve diabetes outcomes

CAN THERE BE TOO MUCH BREAST-CANCER TREATMENT?

No need for pregnant women to fast during labour

Acupuncture 'helps women have babies'

A Cochrane review concluded that only Echinacea purpurea products showed any promise in treating colds and only when they contained the above-ground parts of the plant - not the root.

Cochrane in the news

Negative findings often buried

Electric Fans May Do More Harm Than Good In A Heat Wave

Laughing Gas Safe For Use During Delivery

General health check-ups 'offer no benefit'

Research has suggested certain vitamin supplements do not extend life and could even lead to a premature death

EXERCISES TO HONE STRENGTH AND CHALLENGE THE SENSORY SYSTEM CAN REDUCE RISK OF FALLS

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New doubts over Tamiflu

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BLACK COHOSH FOUND TO HAVE NO EFFECT ON MENOPAUSAL SYMPTOMS

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Issue 6 of 12, Jun 2011

- Anaesthesia & pain control (164)
- Blood disorders (101)
- Cancer (346)
- Child health (1268)
- Consumer & communication strategies (50)
- Dentistry & oral health (124)

SPECIAL COLLECTIONS

International Clinical Trials Day 2011

World No Tobacco Day

World Asthma Day

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EDITORIAL

VIEWPOINT: Randomised controlled trials using invasive 'placebo' controls are unethical and should be excluded from Cochrane Reviews

Placebo controls are frequently used to 'blind' participants, trial personnel and outcome assessors to intervention and control in clinical trials. Effective

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The best single source of evidence of the effects of interventions

The Cochrane Library is a collection of EBM databases

Database	Issue 6 2014
The Cochrane Database of Systematic Reviews (CDSR; Cochrane Reviews)	8492
The Cochrane Database of Reviews of Effects (DARE; Other Reviews)	30,299
The Cochrane Central Register of Controlled Trials (CENTRAL; Clinical Trials)	7,92,135
The Cochrane Methodology Register (CMR; Methods studies)	15,764
Health Technology Assessment Database (HTA)	13,638
NHS Economic Evaluation Database (NHSEED)	16,096

What **have** we done over the last decade?

1. We provided **training and mentoring**
   - In undertaking systematic reviews of relevance to regional priority health questions
2. We **disseminated** the results of these systematic reviews
   - Through advocating for wider access to *The Cochrane Library*
   - Through evidence summaries
3. We **advocated and inform healthcare and policy**
   - We worked with health policy makers and clinicians
4. We worked strategically towards **improving primary research and the culture of research**
   - By influencing the research agenda and advocating for better design, conduct and reporting of primary research

Funding

- ICMR Advanced Centre: 2007-2012
- Effective Health Care Research Consortium
  - Liverpool School Of Tropical Medicine / DFID (UKaid)
  - 2008-2012 and 2012-2016
- CMC Vellore
  - Core Research Position: 2008-2012
  - Sabbatical: 2012-2014

Summary of training activities (2008 -2012)

- In 90 introductory sessions lasting one hour to one full day:
  - **8314 health professionals from all over the country were trained about the importance of systematic reviews and meta-analysis and how to use them in providing reliable evidence to inform health decisions.**

- Through 17 five-day protocol development workshops and 9 five-day review completion workshops:
  - **559 health professionals were trained to conduct systematic reviews and meta-analysis and to summarize findings using the GRADE approach.**

Summary of training activities

- As a result of the training:
  - **68 new protocols for Cochrane Systematic Reviews and 58 full Cochrane Systematic reviews were published.**

- The trained pool of systematic review authors in India has increased:
  - **from 78 in 2007 to 420 in 2012; a more than five-fold increase over the five years.**

Growth of contributors to Cochrane from South Asia: From 2000 to 2014 (January end)

DFID funding----------

	2000	2002	2003	2004	2005	2006	2007	2009	2010	2011	2014
Authors	11	15	20	31	42	80	78	248	324	381	594
Editors	2	1	2	5	5	5	5	7	9	9	11
Others	2	15	18	28	19	35	43	284	187	234	380
Total	19	31	40	64	76	120	126	413	520	624	986

SACN formed ---------ICMR funding--------

838 Cochrane contributors in 2014 from India (17 in 2005)

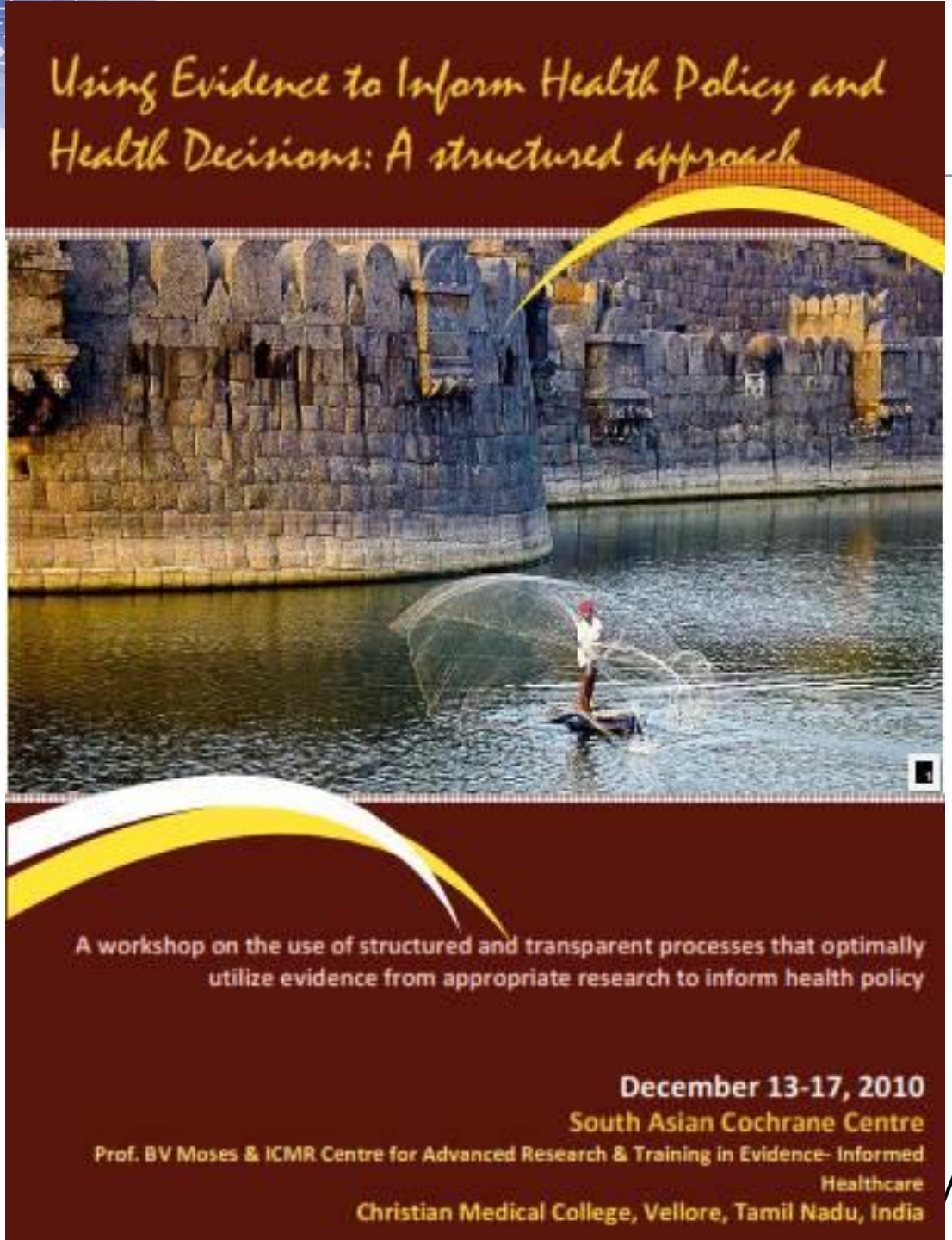
420 Cochrane Authors in 2014 from India (12 in 2005)

10 Editors in 2014 from India (5 in 2005)

309 Cochrane reviews, protocols, titles with Authors living in India in 2014 (11 in 2005)

272 reviews or protocols from India (173 full reviews; 99 protocols) in 2014

PRODUCING EVIDENCE TO INFORM HEALTH POLICY IN INDIA



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Intervention Review

Primaquine for preventing relapses in people with Plasmodium vivax malaria

Gawrie NL Galappaththy[1,*], Aika AA Omari[2], Prathap Tharyan[3]

Database Title: The Cochrane Library

Editorial Group: Cochrane Infectious Diseases Group

Published Online: 16 JUL 2008

Assessed as up-to-date: 30 OCT 2006

DOI: 10.1002/14651858.CD004389.pub2

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5 days *versus* 14 days of primaquine to prevent relapses due to *P. vivax* Malaria?

Abstract

Jump to...

Background

Plasmodium vivax infections contribute to a significant proportion of the malaria infections in many countries. Primaquine is the most widely used drug for treating the dormant liver stage. Different primaquine dosing regimens are in use.

Objectives

Changing Health Policy:

Primaquine for preventing relapses in people with Malaria due to *Plasmodium vivax*

Primaquine for preventing relapses in people with Plasmodium vivax malaria (Review)

Galappaththy GNL, Omari AAA, Tharyan P

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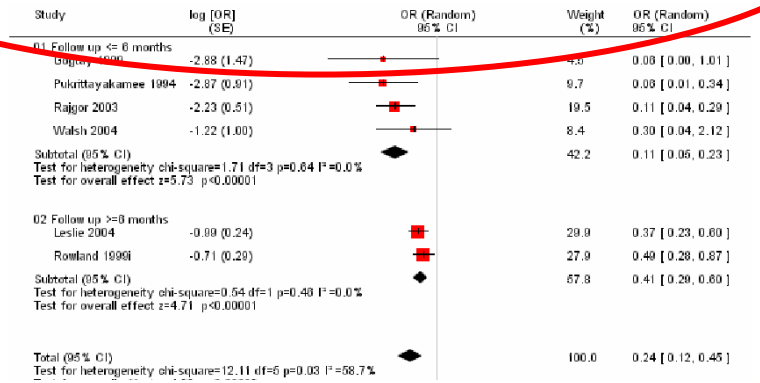
Evidence Update

Malaria Series

Does primaquine prevent relapses in people with *Plasmodium vivax* malaria?

Evidence supports the World Health Organization's recommended course of primaquine (15 mg/kg/day for 14 days) plus chloroquine.

Primaquine 14 days plus chloroquine versus chloroquine: *P. vivax* detected more than 30 days after starting primaquine



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Adobe Reader - [National Drug Policy Malaria revised.pdf]

MALARIA DRUG POLICY (2007)

Adobe Reader - [National Drug Policy Malaria revised.pdf]

(b) *P. vivax*

Age in year	Primaquine 2.5 mg base	
	Daily dose for 14 days*	
	mg base	No. of Tablets
< 1	Nil	Nil
1-4	[illegible]	[illegible]
5-8	5.0	2
9-14	10.0	4
15 & Above	15.0	6

- *Primaquine for 14 days should be given under medical supervision only*

PRIMAQUINE IS CONTRAINDICATED IN INFANTS AND PREGNANT WOMEN

Directorate of National Vector Borne Disease Control Programme
(Directorate General of Health Services)
Ministry of Health and Family Welfare
22-Shamnath Marg, Delhi-110054.

1

Review Published Jan 2007

Policy Changed May 2007

Park & Park *Text Book of Preventive and Social Medicine* changed recommendation in 2008

ho

Gawrie Galappaththy: Ministry of Health, Govt of Sri Lanka Wins the Kenneth Warren Prize at the XV Cochrane Colloquium at Sao Paulo, Brazil in October 2007

The Kenneth Warren Prize

This prize has been offered since 2000 and honours people in developing countries who are authors of reviews judged to be of high methodological quality and relevant to the developing world.

This year's recipient is Gawrie Galappaththy from the Ministry of Health, Sri Lanka for the review *Primaquine for preventing relapse in people with Plasmodium vivax malaria*.

A few words from Ms Galappaththy

Thomas C. Chalmers Award

This award is presented to the principal authors of the best oral and poster presentations at the Colloquium addressing methodological issues related to systematic review

The two recipients of this year's award are:

ry.wiley.com/doi/10.1002/14651858.CD008492.pub2/abstract

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Intervention Review

Artemisinin-based combination therapy for treating uncomplicated *Plasmodium vivax* malaria

David Sinclair[1,*], Nithya Gogtay[2], Felicity Brand[3], Piero L Olliaro[4]

Database Title

The Cochrane Library

Editorial Group: Cochrane Infectious Diseases Group

Published Online: 6 JUL 2011

Assessed as up-to-date: 28 FEB 2011

DOI: 10.1002/14651858.CD008492.pub2

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Abstract

Jump to...

Background

Plasmodium vivax is an important cause of malaria in many parts of Asia and South America, and resistance to the standard treatment (chloroquine) is now high in some parts of Oceania. This review aims to assess the current treatment options in the light of rising chloroquine resistance.

Informed WHO Malaria guidelines

y.wiley.com/doi/10.1002/14651858.CD006086.pub3/abstract

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Economic Evaluations

Intervention Review

Nutritional supplements for people being treated for active tuberculosis

David Sinclair[1,*], Katharine Abba[1], Liesl Grobler[2], Thambu D Sudarsanam[3]

Database Title
The Cochrane Library

Editorial Group: Cochrane Infectious Diseases Group

Published Online: 9 NOV 2011

Assessed as up-to-date: 1 JUL 2011

DOI: 10.1002/14651858.CD006086.pub3

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Abstract

Jump to...

Background

Tuberculosis and malnutrition are linked in a complex relationship. The infection may cause undernutrition through increased metabolic demands and decreased intake, and nutritional deficiencies may worsen the disease, or delay recovery by depressing important immune functions. At present, there are no evidence-based nutritional guidance for adults and children being treated for tuberculosis

Informed discussions of Govt. of India

COCHRANE COLLABORATION AWARDS KENNETH WARREN PRIZE TO DR. PRINCE CHRISTOPHER

Antibiotic therapy for Shigella dysentery (Review)

R.H. PC, David KV, John SM, Sankarapandian V

Dr. Prince Christopher, from the Family Medicine Unit, Christian Medical College, Vellore, Tamil Nadu, India, has been awarded the Kenneth Warren Prize for 2010. Dr. Prince led a team of authors from the Family Medicine Unit (**Drs. Kirubah David and Venkatesh Sankarapandian**) and the Low Cost Effective Care Unit (**Dr. Sushil John**) that evaluated the efficacy and safety of antibiotics used to treat Shigella dysentery.

The Kenneth Warren Prize is awarded each year by the Cochrane Collaboration to the principal author, living in a low or middle income country, of a Cochrane Systematic Review published in the previous year that is judged to be of high methodological quality and addresses a question of relevance to the developing world. Shigella dysentery affects the lives of millions of people

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Kenneth Warren Prize 2011

Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes (Review)

Lassi ZS, Haider BA, Bhutta ZA

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Zohra Lassi

Aga Khan University Pakistan

Ayurveda interventions for rheumatoid arthritis (Protocol)

Tillu GS, Chopra AA, Sarmukaddam SB, Tharyan P

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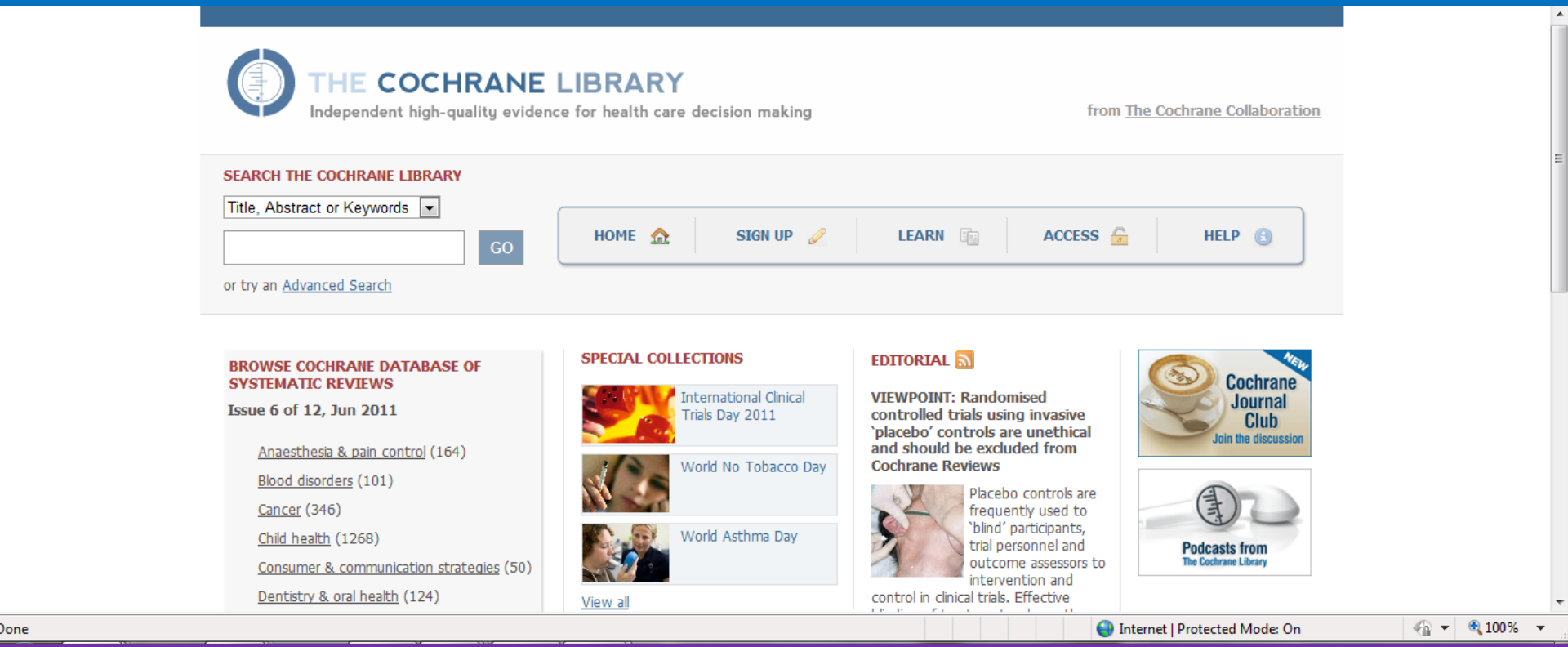

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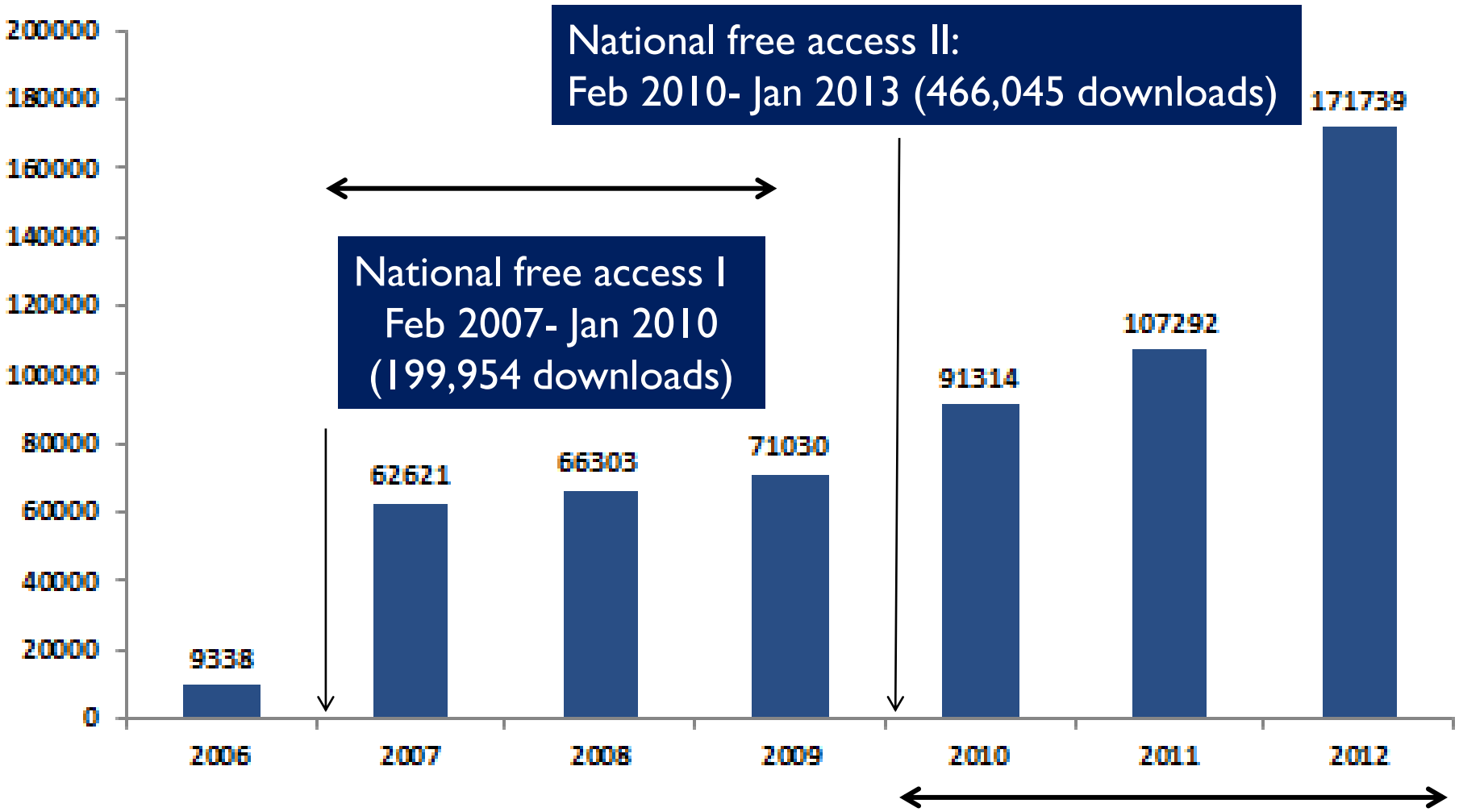

Impact of the National Provision

1. Increased awareness among clinicians, health policy makers, the media and the public
2. Increased use of Cochrane Systematic Reviews in clinical work and teaching
3. Increased number of Cochrane Systematic Review Authors from India contributing evidence to the global pool of reliable information to inform health decisions
4. Increased uptake of Cochrane Evidence in health policy decisions in India and globally (using evidence generated by review teams with Indian authors)
5. Enormous respect across the world for the example that the ICMR has shown in providing inspiring and responsible leadership in health care

SUMMARIZING THE EVIDENCE

Evide

Child Health Series

Is reduced osmolari
standard solution fo

In children admitted to hosp
with fewer unschedu
and less vomi

Inclusion criteria

Types of studies:

Randomized controlled trials, defined
the subjects followed were assigned p
one of two or more interventions by ra
This excludes quasi-randomized desig

Types of participants:

Children with acute diarrhoea (history of l

Types of intervention:

Experimental: Reduced osmolarity ora
solution (total osmolarity 250 mmol/L
reduced sodium).

Control: World Health Organization s
rehydration solution (90 mmol/L sodi
glucose, total osmolarity 311 mmol/L

Types of outcome measures:

Primary: need for unscheduled intrav
infusion during the course of treatmer

Secondary: stool output; children vomit
rehydration; and asymptomatic hypona
serum sodium less than 130mmol/L) du

Review: Reduced osmolarity oral rehydration solution for treating dehydration caused by acute diarrhoea in children
Comparison: 01 Reduced osmolarity ORS compared to WHO standard ORS
Outcome: 01 Need for unscheduled intravenous fluid infusion

Study	Treatment n/N	Control n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
Bangladesh 1995a	4 / 19	5 / 19		3.1	0.75 [0.17, 3.36]
x Bangladesh 1996a	0 / 18	0 / 18		0.0	Not estimable
CHOICE 2001	34 / 341	50 / 334		35.6	0.63 [0.40, 1.00]
Colombia 2000	7 / 71	16 / 69		11.5	0.36 [0.14, 0.95]
Egypt 1996b	1 / 94	8 / 96		6.1	0.12 [0.01, 0.97]
x India 1984a	0 / 22	0 / 22		0.0	Not estimable
India 2000b	11 / 88	12 / 82		8.5	0.83 [0.35, 2.01]
Mexico 1990a	2 / 82	7 / 84		5.3	0.28 [0.06, 1.37]
x Panama 1982	0 / 33	0 / 30		0.0	Not estimable
USA 1982	0 / 15	1 / 20		1.0	0.42 [0.02, 11.03]
WHO 1995	33 / 221	43 / 218		28.9	0.71 [0.43, 1.18]
Total (95% CI)	92 / 1004	142 / 992		100.0	0.59 [0.45, 0.79]

Test for heterogeneity chi-square=5.47 df=7 p=0.6025
Test for overall effect=-3.64 p=0.0003

.01 .1 1 10 100
Favours treatment Favours control

Reviewer's conclusions

Implications for practice:

Based on this review WHO and UNICEF now recommend reduced osmolarity ORS (total osmolarity 250 mmol/L or less with reduced sodium) be adopted as standard in primary care.

Implications for research:

We found insufficient data on cholera in children to make recommendations for this condition.

Evidence summaries: contextualized

CLINICAL EPIDEMIOLOGY AND GLOBAL HEALTH 2 (2014) 28–36

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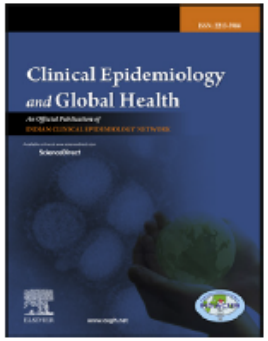

Evidence Summaries

Rifampicin compared to isoniazid for preventing active TB in HIV-negative people at risk of developing active TB: Implications for public health

CrossMark

Thambu David Sudarsanam [a,*], *Prathap Tharyan* [b]

[a] *Professor of Medicine, Christian Medical College, Vellore 632002, Tamil Nadu, India*

[b] *Professor of Psychiatry, Director, South Asian Cochrane Centre, Prof BV Moses & ICMR Centre for Research and Training in Evidence-Informed Healthcare and Health Policy, Christian Medical College, Vellore 632002, Tamil Nadu, India*

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Keywords:
Rifampicin
Isoniazid
Preventing TB
HIV-negative

ABSTRACT

A Cochrane systematic review summarized the evidence for the effects of four regimens containing short courses of rifampicin or rifamycin-combinations compared to isoniazid (INH) given for six to nine months on the development of active tuberculosis (TB), adherence, treatment-limiting adverse events, and hepatotoxicity in HIV-negative people with latent TB infection (LTBI) or at risk of developing active TB. The review included 10 randomized controlled trials that enrolled 10,717 HIV-negative (2% HIV-positive) adults and children (older than two years) that were conducted in Brazil, Canada, Germany, Hong Kong, Saudi Arabia, Spain, Taiwan, and USA. Participants were recruited from clinics in general hospitals or university-affiliated hospitals, pneumoconiosis clinics, homeless shelters, or in prison. The regimens compared were: rifampicin mono-therapy (three to four months) versus isoniazid (INH) mono-therapy (six months); rifampicin plus INH (three months) versus INH (six months); rifampicin plus pyrazinamide (two months) versus INH (six months); and rifapentine (900 mg) plus INH (900 mg) combination therapy, once-weekly, directly-observed (DOT) for three months versus self-administered INH (300 mg) for nine months. Follow-up ranged from two to five years.

The review concluded that four months of rifampicin and the standard INH treatment for six or nine months may not differ in the incidence of active TB in HIV-negative people at risk of active TB. Rifampicin probably increases treatment completion compared to INH in adults. While it is uncertain if treatment-limiting adverse events are any different, rifampicin probably results in significantly less hepatotoxicity in adults than INH. No instances of rifampicin resistance were observed in people who developed active TB while on rifampicin in the included trials. The review also concluded that two months of rifampicin plus INH may offer no advantage over longer INH treatment, and rifampicin combined with pyrazinamide is associated with more liver toxicity and treatment-limiting adverse events with uncertain benefits for TB incidence, or adherence compared to INH. A weekly regimen

1. The evidence

A Cochrane systematic review of 10 randomized controlled trials that enrolled 10,717 mostly HIV-negative (2% HIV-positive) adults and children at risk of developing TB and followed-up for two to five years concluded that:

- Rates of active TB were not higher with rifampicin mono-therapy (three to four months) compared to isoniazid (INH) mono-therapy (six months). Treatment completion was probably higher and adverse events, particularly liver toxicity, may be fewer with shorter regimens of rifampicin compared to INH (1781 participants, five trials).
- Rifampicin plus INH (three months) may offer no advantage over INH mono-therapy (six months) since rates of active TB, adherence, serious adverse events and hepatotoxicity did not significantly differ between the two regimens (536 participants, two trials).
- Rifampicin plus pyrazinamide (two months) is associated with more treatment-limiting adverse events compared to INH mono-therapy (six months), and probably more liver toxicity, and may have no significant benefits in the incidence of active TB or for adherence rates (661 participants, four trials).
- Rifapentine (900 mg) plus INH (900 mg) combination therapy, once-weekly, directly-observed (DOT) for three months, has higher completion rates, and less liver toxicity compared with nine months of self-administered daily INH (300 mg), though treatment discontinuation due to adverse events is probably more likely with the rifapentine-INH combination than with INH (7799 participants, one non-inferiority trial).

Review on which this evidence summary is based: Sharma SK, Sharma A, Kadhiravan T, Tharyan P. Rifamycins (rifampicin, rifabutin and rifapentine) compared to isoniazid for preventing tuberculosis in HIV-negative people at risk of active TB. *Cochrane Database of Systematic Reviews* 2013, Issue 7. Art. No.: CD007545. http://dx.doi.org/10.1002/14651858.CD007545.pub2.

This evidence summary presents an overview of the findings and the implications for low- and middle-income countries. For further details, please read the latest version of the full review that can be downloaded, free of charge (through various funded provisions) in most parts of the world, from the *Cochrane Database of Systematic Reviews* that is published in *The Cochrane Library* (www.thecochranelibrary.com).

Table 1 – Rifampicin (3–4 months) compared to isoniazid (6–9 months) for preventing active tuberculosis (TB) in HIV-negative people at risk of TB infection: summary of effects – follow-up 2 years to 5 years.

Outcomes	Illustrative comparative risks[a] (95% CI)		Relative risk (RR) (95% CI)	No of participants (studies)	Overall evidence quality
	Assumed risk	Corresponding risk			
	Isoniazid	Rifampicin			
Active TB Follow-up: 5 years	150 per 1000	121 per 1000 (70 to 210)	RR 0.81 (0.47–1.4)	332 (1) [b, c]	Very low (due to serious indirectness and very serious imprecision)
Adherence	690 per 1000	822 per 1000 (697 to 884)	RR 1.19 (1.01–1.3)	1768 (5)	Moderate (due to serious inconsistency)
Treatment-limiting adverse events	93 per 1000	45 per 1000 (21 to 93)	RR 0.48 (0.23–1)	1674 (4)	Very low (due to serious study limitations, inconsistency, and imprecision)
Hepatotoxicity: Grade 3 and 4 toxicity	46 per 1000	7 per 1000 (3 to 16)	RR 0.15 (0.07–0.4)	1774 (5)	Moderate (due to serious study limitations)

[a] The basis for the assumed risk is the control group risk in single studies, and the median risk in the control group for pooled data. The corresponding risk (and its 95% CI) is based on the assumed risk in the control group and the relative effect of the intervention (and its 95% CI). CI: confidence interval.

[b] In the placebo arm of this four-arm trial of adults with silicosis, 36/159 (23%) developed active TB.

[c] In another trial in children, data for comparative effectiveness could not be used for the outcome of developing active TB (no cases detected in 100 children over two years of follow-up).

What are the implications of the review for public health?

1. **Summary of the evidence from this Cochrane review:**
   a. Four months of rifampicin and the standard INH treatment of six or nine months may not differ in preventing progression to active TB in HIV-negative people with LTBI. Rifampicin probably increases adherence and treatment completion compared to INH in adults. While it is uncertain if treatment-limiting adverse events are any different, rifampicin probably results in significantly less hepatotoxicity in adults (0.2%–1.5%) than INH (5%). No instances of rifampicin resistance were observed in 40 people who developed active TB while on rifampicin in the included trials.
   b. No benefit in preventing progression to active TB, increasing adherence, or reducing the frequency of treatment-limiting adverse events and hepatotoxicity was detected when INH was added to rifampicin for three months compared to treatment with INH alone for six to nine months. This indicates that rifampicin plus INH combination treatment may not be a better alternative to INH alone (or rifampicin alone) for people with LTBI.
   c. Rifampicin plus pyrazinamide for two months may not differ from INH for six months in preventing active TB in HIV-negative people with LTBI, or in treatment completion compared to INH, in spite of the shorter treatment duration. This drug combination also probably increases the risk of hepatotoxicity in adults, and increases the incidence of treatment-limiting adverse events. These attributes are not consistent with those required of a public health intervention for preventing active TB in people with LTBI.
   d. Twelve doses of rifapentine plus INH administered weekly by DOT over three months is probably an effective and safer alternative to INH given for nine months in HIV-negative people at risk, though more data on the safety of the combination in adults (particularly the risk of hepatotoxicity in women), as well as in children are needed. One case of rifapentine resistance was observed in an HIV-positive individual who had low CD4 counts, though none were observed in HIV-negative people who developed active TB. The effects of this intermittent regimen in high TB burden countries need to be evaluated before its widespread use outside low TB burden countries commences.
2. **Implications for resource-constrained settings:**
   a. The results from the trials in this Cochrane review that were conducted in high- and middle-income countries may not yield the same effect estimates in high TB burden countries in Africa and Asia (particularly China and India) where re-infection rates are likely to be higher and co-morbid conditions that impair effectiveness such as nutritional and micronutrient deficiencies, are also higher.
   b. Another barrier to the uptake of four months of rifampicin in treating LTBI is the fear of inadvertent treatment of active TB leading to the development of rifampicin resistance, or the emergence of rifampicin resistance if rifampicin were to be more widely used for treating LTBI. The diagnosis of TB and of rifampicin resistance in adults may be accurately done using molecular techniques, though this may not be as accurate in children.[7] While the trials in this review did not reveal that anyone given rifampicin developed resistance, rifampicin resistance does occasionally occur in the context of LTBI prophylaxis particularly in immuno-compromised people; thus, careful selection of people

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   c. Ensuring compliance would also be important if four months of rifampicin were to become standard treatment for LTBI, as interrupted courses of treatment would increase the potential for the emergence of widespread resistance to rifampicin.
   d. The included trials differed regarding health systems arrangements and the delivery of care, such as the availability of resources to provide DOT effectively, that may differ from those in low-income countries where treatment of active TB is a priority; and the availability of adequate resources that can be diverted, or the political will to ensure DOT for LTBI prophylaxis, is likely to be low. While the relative advantage in treatment completion and safety with the shorter rifampicin regimen over INH is likely to be seen even in low-income countries, these pragmatic concerns may limit the applicability of the evidence from this review to resource-constrained countries with a high TB burden.

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Commentary on Evidence Summaries

Rifamycin drugs as alternati isoniazid treatment to preve (TB) in HIV-negative people active TB

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ABSTRACT

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1. The importance of this Cochrane review for global and national tuberculosis control strategies

Isoniazid preventive therapy (IPT) is the mainstay of the WHO recommendations for treatment of LTBI. Apart from concerns of hepatotoxicity the major drawback of isoniazid monotherapy is the long duration of treatment. Poor treatment adherence in persons who have no symptoms is a natural consequence. A regimen of shorter duration is therefore desirable.

This Cochrane systematic review summarizes the evidence from 10 randomized clinical trials that studied four interventions comprising of rifampicin alone or rifamycin in combination with other drugs for two to four months against the standard isoniazid monotherapy of six or nine months in 10,717 predominantly HIV-negative participants.[4,5]

All four interventions studied, viz., rifampicin monotherapy for three or four months, rifampicin plus isoniazid for three months, rifampicin plus pyrazinamide for two months and rifapentine plus isoniazid once a week by DOT for three months, were not different from isoniazid given alone for six or nine months in terms of preventing active TB. Adherence to treatment was significantly better in the shorter rifampicin monotherapy regimen and the weekly rifapentine–INH combination regimens. Hepatotoxicity was higher in the rifampicin plus pyrazinamide regimen, but lower in the rifampicin monotherapy and rifapentine plus isoniazid weekly regimen compared to isoniazid monotherapy.

2. Challenges and unanswered questions

In terms of the primary objective of shortening the duration of treatment all the regimens included in this review seem to achieve this goal, though the strength of the evidence leaves much to be desired. Most of the trials included in this review are from the developed countries. It is a moot point whether these results would be generalizable to the developing countries which bear the major TB burden. Apart from the high risk of reinfection, the duration of protection offered by a single course of chemoprophylaxis is unknown. While TB preventive therapy should be prioritized in high-risk groups, the feasibility of implementing it in a wider context needs careful consideration. In settings where exclusion of active TB can be problematic, TB chemoprophylaxis (especially with rifampicin-containing regimens) needs to be used with great caution.

The basic biology of *Mycobacterium tuberculosis* latency is not well understood and we do not have reliable biomarkers to predict which individuals with LTBI will progress to active disease (likely in only 5%–20%). Research is urgently required into understanding the pathogenesis of latent TB disease, biomarkers to predict progression, improved diagnostics for LTBI and effective treatment regimens for latent infection with drug resistant TB. Before initiating LTBI treatment, it is essential that active TB is effectively ruled out and the diagnosis of LBTI reliably established. The tuberculin skin test (TST) and interferon-gamma release assays (IGRA) are designed to detect cellular immune response to *M. tuberculosis*, but do not differentiate between latent infection and active disease and, if negative, do not allow TB infection to be ruled out.

Several ongoing clinical trials are testing the efficacy of shorter and/or intermittent regimens to treat LTBI, and of supervised versus self-administered treatment. These trials should provide more data to inform health policy decisions.

3. Conclusion

For LTBI treatment to become a reality in high TB burden countries, in addition to answering these basic scientific questions, cost-effectiveness and implementation research will be required to determine the best strategies to scale-up LTBI treatment at a population level.

Conflicts of interest

All authors have none to declare.

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CAN EVIDENCE INFORM LOCAL DECISIONS?

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सत्यमेव जयते

MINISTRY OF HEALTH & FAMILY WELFARE
NIRMAN BHAVAN, NEW DELHI - 110108

D.O.No. Z-28020/77/2006-CH(Part)
Dated the May, 2009

2778 (R04)
9.6.09

Dear Sir,

A Technical Committee under the chairpersonship of Dr. M.K.Bhan, Secretary, Department of Bio-technology was established to develop national guidelines on deworming.

The recommendations of the Technical Committee on deworming are being forwarded to you for necessary action at your end.

Table1. Recommended Deworming Treatment Strategy

Category	Prevalence*	Action for deworming
High	≥ 70%	Preschool and school-age children 2-3 times each year
Moderate	≥ 50% (50% - 70%)	Preschool and school-age children at least once each year
Low	< 50%	Only symptomatic individuals (i.e. those who pass worms in their stools)

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Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance

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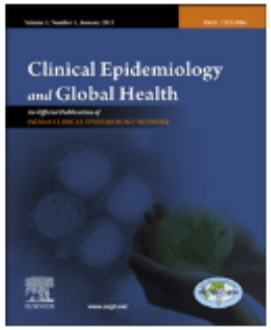

Evidence Update

Does regular deworming of school children in areas endemic for intestinal worms improve their physical health and school performance? Summary of the evidence and implications for public health programmes

- Many countries have adopted routine periodic targeted deworming of school children and this policy has many advocates, including the World Bank and many other organisations that consider it one of the most cost-effective interventions for global health. Consequently, a considerable amount of public money is invested in achieving the postulated benefits.
- Others question these estimates and argue that the apparent benefits may apply to some helminthic infections such as schistosomiasis, but not necessarily to all helminthic infections.

Review objectives: To summarise the effects on nutritional indicators, haemoglobin, cognition, school attendance; and the impacts on school performance and mortality of deworming programmes for soil-transmitted intestinal worms (nematode geohelminths) in children.

An update of a Cochrane systematic review of 41 community-based clinical trials that randomised 65,168 children below 17 years from 23 countries in Africa, China, South Asia, and South East Asia found that:

- In children identified as infected after screening, a single dose of deworming drugs probably increased weight and may have increased haemoglobin, compared to no deworming, but its effects on school performance were uncertain.
- Single or multiple doses of deworming drugs given to all school children in endemic areas without screening had inconsistent or uncertain benefit, or little evidence of benefit, on their physical health or school attendance.

Results and conclusions

- Our interpretation of this data is that it is probably misleading to justify contemporary deworming programmes based on evidence of consistent benefit on nutrition, haemoglobin, school attendance or school performance as there is simply insufficient reliable information to know whether this is so.

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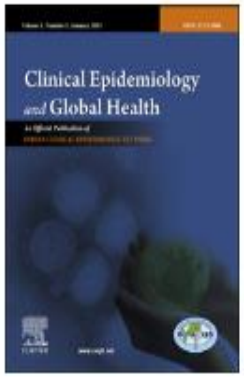

Commentary on Evidence Summaries

Does regular deworming of schoolchildren in areas endemic for intestinal worms improve their physical health and school performance? Commentary on an Evidence Summary

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Christian Medical College, Vellore 632002, Tamil Nadu, India

1. Commentary

The findings of this Cochrane systematic review may at first glance appear counter intuitive and invite controversy. However, when one focuses on the patterns that emerge, it becomes clear that the findings are consistent with biological expectations.[1]

2. What are the main findings of the review?

1. Deworming was beneficial when administered to children who were screened and found to have worm infestation as compared to no treatment.
2. Studies carried out in high endemic areas are expected to be more likely to show benefit following deworming than other regions; however, this was not observed in sub-group analyses in the review of trials conducted in high, moderate or low endemic areas.
3. More recent studies tended to show less benefits compared to earlier studies carried out in the same region.

3. What are the likely explanations for these findings?

It is well known that bulk of the health-related effects due to worm infestations depend on the worm loads. Indeed, when one screens children for worm infestation in an endemic area, one is separating those with higher worm loads from the rest. Similarly, there are likely to be more children with higher worm loads in high endemic areas. It seems very likely that if there has been a secular trend towards declining worm load in countries from where the data for this review emerged, then more recent studies will tend to show little or no benefit following mass deworming as compared to earlier studies.

4. Conclusions

This systematic review must compel health-planners in endemic areas to review their future course of action based on

Using evidence in other countries in South Asia

- Nepal Health Sector Reforms
- Sri-Lanka Medical Association Gudelines

HTA Assessment

NAAT TESTING FOR BLOOD DONORS

The Problem

- In spite of using the best standards and 4th generation serological tests, by 2010 there were documented instances of people having acquired Human Immunodeficiency Virus (HIV), Hepatitis B virus (HBV), and Hepatitis C virus (HCV) infections, through blood transfusions at Christian Medical College (CMC)
- Nucleic Acid Amplification tests (NAAT) detect and amplify viral nucleic acids of HIV-1, HBV and HCV present even in small amounts in infected blood donors in the infective "window period" that current serological tests cannot detect.
- The high costs of NAAT and doubts about their incremental cost-effectiveness have led to uncertainties about their inclusion as an additional screening method of blood donors in low- and middle-income countries (LMICs).

The Mandate

Request from CMC's Administration and Governing Council to:

- Review evidence for the incremental benefits, cost-effectiveness and affordability of NAT testing in CMC; particularly regarding the use of pooled tests versus individual testing of samples; and the implications for smaller mission hospitals if CMC were to institute NAT testing

The Process

1. **Convening a Health Technology Assessment group** consisting of content experts, epidemiologists, and experts in evidence synthesis.
2. **Framing questions for** which evidence is needed to evaluate the need for, the incremental benefit and the resource implications of introducing NAAT in screening blood donors
3. **Seeking the views and concerns** of administrators **and data** from the blood bank and the Department of Transfusion Medicine and Immunohaematology.
4. **Searching for evidence** regarding the incremental benefits of NAAT over serology in the context of the burden of transmission transmissible infections (TTI) in HICs and LMICs, and particularly India.
5. **Assessing alternatives** to NAAT.
6. **Evaluating the costs** of adding NAAT to serology to screen blood donors based on income and expenditure' for CMC's blood bank for 2010

7. **Contextualizing the evidence** within CMC's ethos and values.
8. **Sharing the contextualized evidence** with stakeholders (clinicians and other staff in CMC) and inviting their perspectives.
9. **Preparing a draft HTA report.**
10. **Finalizing the HTA report** and getting all HTTA members to sign off.
11. **Presenting the HTA report** to CMC's administration
12. **Circulating the HTA report** to CMC's governing council and presenting the report for approval.
13. **Collecting data** on the incremental yield with NAAT of TTI's in donors from 2011 to March 2013 to validate predications of TTI's averted.

The HTA group recommendation

- The HTA group recommended implementing NAT screening of blood donors at CMC because of legal, moral and ethical implications, since NAT, when added to serology, has the potential to minimize further the risk of iatrogenic infections due to blood transfusions.
- The costs of introducing NAT, though considerable, can be met from existing charges that CMC makes for blood and blood products.
- Revising tariffs for blood components for those who can afford it needs to be considered, though this also needs to balance regulatory, ethical, and equity issues.

Outcomes

- NAAT yields since testing commenced (May 2011 to March 2014): Total numbers tested : 82379; **Seronegative, NAAT +ve : 66**
- **HIV : 1; HCV: 3; HBV+HCV : 3; HBV : 59**
- **TTIs averted: ~150 to 170**

- For full report: email: prathap@cmcvellore.ac.in

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