



Parachute approach to evidence based medicine

Malcolm Potts, Ndola Prata, Julia Walsh and Amy Grossman

BMJ 2006;333:701-703
doi:10.1136/bmj.333.7570.701

Updated information and services can be found at:
<http://bmj.com/cgi/content/full/333/7570/701>

These include:

References

This article cites 22 articles, 6 of which can be accessed free at:
<http://bmj.com/cgi/content/full/333/7570/701#BIBL>

Rapid responses

2 rapid responses have been posted to this article, which you can access for free at:
<http://bmj.com/cgi/content/full/333/7570/701#responses>

You can respond to this article at:
<http://bmj.com/cgi/eletter-submit/333/7570/701>

Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Notes

To order reprints of this article go to:
<http://www.bmjournals.com/cgi/reprintform>

To subscribe to *BMJ* go to:
<http://bmj.bmjournals.com/subscriptions/subscribe.shtml>

Analysis and comment

Controversy

Parachute approach to evidence based medicine

Malcolm Potts, Ndola Prata, Julia Walsh, Amy Grossman

Waiting for the results of randomised trials of public health interventions can cost hundreds of lives, especially in poor countries with great need and potential to benefit. If the science is good, we should act before the trials are done

In 2003 Smith and Pell published an entertaining but profound article titled: "Parachute use to prevent death and major trauma due to gravitational challenge."¹ They used the lack of randomised controlled trials in testing parachutes to show that situations still exist where such trials are unnecessary. We argue that the parachute approach, where policies are set based on good science but without randomised trials, is often more suitable in resource poor settings. We use the examples of oral rehydration therapy, male circumcision to prevent HIV infection, and misoprostol for postpartum haemorrhage to show how an overemphasis on randomised controlled trials in poor settings poses important ethical and logistic problems and may incur avoidable deaths.

Childhood diarrhoea and oral rehydration therapy

In 1980 childhood diarrhoea was killing an estimated 4.6 million children annually.² Treatment with an intravenous drip is life saving but requires health facilities. Studies from 1977 onwards showed that infant diarrhoea could be treated with oral rehydration.³ The World Health Organization initiated a highly successful programme of oral replacement therapy in 1981 after it became obvious that the treatment saved lives and no alternative home based treatment was possible.⁴ Randomised controlled trials were later conducted in health facilities, confirming that oral replacement therapy was as effective as intravenous therapy.⁵⁻⁶ The initiation of large scale programmes for oral replacement therapy before the randomised trials meant that by 2000 there were three million fewer deaths from diarrhoea annually.²

HIV and male circumcision

Since the 1990s robust data have shown that male circumcision reduces the risk of men acquiring HIV through heterosexual intercourse.⁷ Circumcision seems to protect against HIV because the inside of the foreskin is poorly keratinised and rich in Langerhan's cells.⁸ Ethnographic observations, studies on serodiscordant couples, and prospective epidemiological studies all found that circumcision protected against HIV infection.⁹⁻¹⁰ In 2002, a consensus statement

concluded circumcision slowed heterosexual HIV transmission.¹¹

In 2003 in a Johannesburg township began a randomised controlled trial in which over 3000 informed volunteers aged 18 to 24 years were randomly allotted to immediate circumcision or circumcision 21 months later. All the men were counselled to use condoms. The relative risk of HIV infection among the circumcised men was 0.40 (95% confidence interval 0.24 to 0.68, $P \leq 0.001$).¹² The degree of protection was "so high it would have been unethical to continue."

A parachute strategy would have provided male circumcision on a large scale, ideally beginning in the 1990s or even now instead of waiting for more evidence. The demand for circumcision in Africa vastly exceeds the supply.¹³ If supplies of low cost, easy to use equipment were readily available, access could further improve.¹⁴

Postpartum haemorrhage and misoprostol

Worldwide, postpartum haemorrhage is the leading cause of maternal death, and most of those who die are women in developing countries delivering at home without a skilled birth attendant.¹⁵ Misoprostol is a low cost drug, with an excellent safety profile and long shelf life. It was originally approved to treat stomach ulcers, but its gynaecological uses have been reported in over 200 scientific papers in peer reviewed journals. Its use by minimally trained birth attendants in home births has also been documented.¹⁶⁻¹⁷

Several randomised controlled trials have been conducted in health facilities comparing misoprostol with current uterotonics or placebo. One of these was conducted in villages in Africa using trained traditional birth assistants.¹⁶ All trials found misoprostol equivalent to other uterotonics in stopping postpartum haemorrhage, and only one trial found misoprostol to be inferior to oxytocin.¹⁸

Because of concern of low effectiveness, agencies have delayed misoprostol's widespread use outside health facilities. Its ease of use and chemical stability make it ideal for use in remote locations. The question of whether conventional uterotonics are more effective is largely redundant, as these drugs can be given only

School of Public Health, University of California, 314 Warren Hall, Berkeley, CA 94720, USA

Malcolm Potts
Bixby professor, population and family planning

Ndola Prata
lecturer

Julia Walsh
adjunct professor
Amy Grossman
research assistant

Correspondence to:
N Prata
ndola@berkeley.edu

BMJ 2006;333:701-3



Sometimes it's best just to jump in

by skilled providers and are less stable in field conditions. A simple comparison of traditional birth attendants' use of misoprostol to treat postpartum haemorrhage provided the additional compelling evidence of the effectiveness of the intervention for home births.¹⁷

Price of delay

Evidence based medicine and randomised controlled trials are not synonymous. The parachute approach can be the most appropriate, especially in situations of high mortality and low resources, when a simple intervention can have a large impact. Randomised controlled trials are essential in many other settings and they have defined many life saving strategies and corrected some important mistakes.¹⁹⁻²¹ They are often needed when mortality has reached a low level because new treatments require large investment for relatively small improvements in therapy that may be difficult to distinguish.

The use of misoprostol to control postpartum haemorrhage and male circumcision to slow HIV acquisition are contemporary examples of where observational studies and clinical experience provide an appropriate and robust evidence base for policy. The parachute approach of providing misoprostol for home births has the potential to save tens of thousands of maternal deaths annually. However, WHO has not added misoprostol to the essential drugs list, possibly because of the lack of evidence from randomised trials in home settings. Failure to reduce maternal deaths as rapidly as knowledge permits would be reprehensible.

During the exponential growth of a new HIV epidemic (as may be the case in India) a modestly effective preventive intervention introduced early will save more lives than a highly effective method introduced 10 to 15 years later.²² This is because saving one infection pre-empts numerous downstream infections. In Africa, where transmission has finally declined slightly, circumcision could prevent most new infections. Circumcision also protects against penile cancer²³ and reduces the risk of cervical cancer in partners.²⁴

Circumcision can have complications, especially if older techniques are used. Nevertheless, given the scale of the HIV pandemic, the lack of a vaccine, and the difficulty of changing sexual behaviour, the health benefits of male circumcision to men and women heavily outweigh possible risks. The effect of circumcision will be much greater than that of increasing condom use or introducing microbicides as it happens once and protects for life. Microbicides may save 2.5 million lives over three years,²⁵ but circumcision would have a much greater effect because compliance is not an issue.

In 2002, a conference on circumcision concluded that male circumcision should not be actively promoted for HIV prevention until evidence from randomised controlled trials confirms its effectiveness.¹¹ We believe the South African trial meets that criterion. Efficacy of male circumcision overlaps with the projected performance of future vaccines and microbicides. Despite the high efficacy, WHO and UNAIDS are not endorsing circumcision and still have not committed to rapidly expand access. They rationalise delays until late 2006, when the results of two other trials may become available. While hundreds of millions of dollars continue to be invested in preventive measures of uncertain effectiveness, virtually nothing is being done to promote a method that provides important protection.

How much evidence is needed?

Good science, we suggest, is taking the research to the problem rather than conducting the research in the tallest ivory tower the investigator can find. Randomised controlled trials are needed and, when appropriate, should be part of the empirical evidence necessary for decision making. The question is how much evidence is needed to move from research to practice, when the matter is life saving interventions in poor settings. The yardstick for decision making should take into account the risks and benefits in the local conditions, not those of an ideal situation.

Summary points

Randomised controlled trials are usually required before new interventions are implemented

If other evidence of effectiveness is good, and potential benefits large, the resultant delays may be unethical

Examples from poor countries show the price of delaying interventions

Contributors and sources: The authors work for the Bixby programme in population, family planning, and maternal health at the University of California, Berkeley. All authors contributed equally to this article. MP and NP are guarantors.

Competing interests: None declared.

- Smith G, Pell JP. Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. *BMJ* 2003;327:1459-61.
- Victoria C, Bryce J, Fontaine O, Monash R. Reducing deaths from diarrhoea through oral rehydration therapy. *Bull World Health Organ* 2000;78:1246-55.
- Rahaman M, Aziz KM, Patwari Y, Munshi MH. Diarrhoeal mortality in two Bangladeshi villages with and without community-based oral rehydration therapy. *Lancet* 1979;ii:809-12.
- Avery M, Snyder JD. Oral therapy for acute diarrhoea. The underused simple solution. *N Engl J Med* 1990;323:89-94.
- Mackenzie A, Barnes G. Randomised controlled trial comparing oral and intravenous rehydration therapy in children with diarrhoea. *BMJ* 1991;303:393-6.
- Vesikari T, Isolauri E, Baer M. A comparative trial of rapid oral and intravenous rehydration in acute diarrhoea. *Acta Paediatr Scand* 1987;76:300-5.
- Halperin D, Bailey RC. Male circumcision and HIV infection: 10 years and counting. *Lancet* 1999;354:1813-5.
- Szabo R, Short RV. How does male circumcision protect against HIV infection? *BMJ* 2000;320:1592-4.
- Reynolds S, Shepherd ME, Risbid AR, Gangakhedkar RR, Brookmeyer RS, Divekar RS, et al. Male circumcision and risk of HIV and other sexually transmitted infections in India. *Lancet* 2004;363:1039-40.

- Weiss H, Quigley MA, Hayes RJ. Male circumcision and the risk of HIV infection in sub-Saharan Africa: a systematic review and a meta-analysis. *AIDS* 2000;14:2361-70.
- United States Agency for International Development, AIDSMARK. *Male circumcision: current epidemiological and field evidence*. Washington, DC: USAID, 2003. http://pdf.usaid.gov/pdf_docs/PNAC5892.pdf (accessed 9 Jul 2006).
- Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Purven A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. *PLoS Med* 2005;2:1-11.
- Bailey R, Muga R, Poulussen R, Abridt H. The acceptability of male circumcision to reduce HIV infections in Nyanza Province, Kenya. *AIDS Care* 2002;14:27-40.
- Al-Samarrari A, Mofu AB, Crankson SJ, Jawad A, Haque K, Al-Meshari A. A review of a Plastibell device in neonatal circumcision in 2000 instances. *Surg Gynecol Obstet* 1988;167:341-3.
- World Health Organization. *Making every mother and child count. World Health Report 2005*. Geneva: WHO, 2005.
- Walraven G, Blum J, Dampaha Y, Sowe M, Morison L, Winikoff B, et al. Misoprostol in the management of the third stage of labour in the home delivery setting in rural Gambia: a randomised controlled trial. *Br J Obstet Gynaecol* 2005;112:1277-83.
- Prata N, Mbaruku G, Campbell M, Potts M, Vahidnia F. Controlling post-partum hemorrhage after home births in Tanzania. *Int J Obstet Gynecol* 2005;89:51-5.
- Gulmezoglu A, Villar J, Ngoc NT, Piaggio G, Carroli G, Adetoro L, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. *Lancet* 2001;366:726-32.
- Fisher B, Anderson S, Redmond CK, Wolmark N, Wickerham DL, Cronin WM. Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. *N Engl J Med* 1995;333:1456-61.
- Wiles M, Navickis RJ. Patient survival after albumin administration. *Ann Intern Med* 2001;135:149-64.
- Briegleb J, Forst H, Haller M, Schelling G, Kilger E, Kuprat G, et al. Stress doses of hydrocortisone reverse hyperdynamic septic shock: a prospective, randomized, double-blind, single-center study. *Crit Care Med* 1999;27:723-32.
- Potts M, Anderson R, Boily MC. Slowing the spread of human immunodeficiency virus in developing countries. *Lancet* 1991;338:608-12.
- Tsen H, Morgenstern H, Mack T, Peters RK. Risk factors for penile cancer: results of a population-based case-control study in Los Angeles County. *Cancer Causes Control* 2001;12:267-77.
- Castellsague X, Bosch FX, Munoz N, Meijer CJ, Shah KV, de Sanjose S, et al. Male circumcision, penile human papillomavirus infection, and cervical cancer in female patients. *N Engl J Med* 2002;346:1105-12.
- Coplan P, Mitchnick M, Rosenberg ZF. Regulatory challenges in microbicide development. *Science* 2004;304:1911-2.

(Accepted 19 June 2006)

When actions speak just as loudly as words

Even if we dislike or have never watched *ER* or *Holby City*, few of us could convincingly deny a secret (or not so secret) desire to make a difference in a cardiac arrest or peri-arrest situation. Indeed, medicine would have been an unlikely career choice if this were not so. For those lucky, or unlucky, enough to have been involved in such situations the first time is always the most impressionable.

I remember the first occasion in which I took an important role, and can account for almost every second. The patient needed urgent cardioversion, and, to my surprise, my senior house officer agreed I could do the honours. As we arrived in the anaesthetic room and the doors closed behind us, I frantically attempted to remember the protocol for defibrillation. I finally heard the anaesthetist declare that the patient was ready, and with sweaty hands I reached for the paddles and took one last look at the electrocardiogram. My senior house officer nodded his approval for me to continue. I placed the paddles on the patient's chest and in a shaky voice said, "Charge." It seemed to take forever for the electronic sound of the charging defibrillator to peak, but then, to my horror, I found myself unable to recall the next word. As milliseconds turned to seconds, I looked round to make sure nobody was touching the bed and said, "Fire."

Thankfully the cardioversion was successful, but my inability to remember the simple word "Shock" has stayed with me. Now, whenever I attempt a cardioversion I find myself subconsciously repeating "Shock, shock, shock" to myself for at least five minutes beforehand. St David declared that getting the small things right was more essential to a peaceful mind than any big thing, and I can't help thinking that he must have predicted my experience.

Gwyn Samuel Williams *senior house officer, New Cross Hospital, Wolverhampton*
(gwynsamuelwilliams@hotmail.com)

We welcome articles up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. Please submit the article on <http://submit.bmj.com>. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.