

# EVIDENCE-BASED MEDICINE AND WOMEN: DO THE PRINCIPLES AND PRACTICE OF EBM FURTHER WOMEN'S HEALTH?

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## ABSTRACT

*Clinicians and policy makers the world over are embracing evidence-based medicine (EBM). The promise of EBM is to use summaries of research evidence to determine which healthcare interventions are effective and which are not, so that patients may benefit from effective interventions and be protected from useless or harmful ones. EBM provides an ostensibly rational and objective means of deciding whether or not an intervention should be provided on the basis of its effectiveness, in theory leading to fair and effective healthcare for all.*

*In this paper I closely examine these claims from the perspective of healthcare for women, using relevant examples. I argue that the current processes of evidence-based medicine contain a number of biases against women. These biases occur in the production of the research that informs evidence-based medicine, in the methods used to analyse and synthesise the evidence, and in the application of EBM through the use of guidelines. Finally, the biomedical model of health that underpins most of the medical research used by EBM ignores the social and political context which contributes so much to the ill-health of women.*

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## INTRODUCTION

Thirty years ago, a British epidemiologist called Archie Cochrane argued that medical care could be improved by greater use of research evidence. He drew attention to our collective ignorance about the effects of healthcare, saying that: 'It is surely a great criticism of our profession that we have not organised a critical

summary, by specialty or subspecialty, adapted periodically, of all relevant randomized controlled trials.<sup>1</sup>

Cochrane was concerned that without some kind of critical summary, important effects of healthcare (good and bad) will not be identified promptly, with the result that patients may receive useless or even harmful treatments whilst not receiving treatments which work. In addition, without systematic, up-to-date reviews of previous research, plans for new research will be ill informed, so that promising leads are missed or existing research duplicated.

Today, Cochrane's beliefs have become enshrined in an international phenomenon known as evidence-based medicine or EBM. EBM is the term coined to represent both a critical summary of relevant research and the use of that evidence to make decisions about medical care. EBM has become widely adopted around the world, with evidence playing a critical role in informing health policy, commissioning resources and directing clinical practice through mechanisms such as evidence-based clinical guidelines.<sup>2</sup> Governments in Europe, America and Australasia have created and funded institutions based upon the principles of EBM to synthesise evidence and produce evidence-based guidelines which may be used by policy makers and clinicians alike.

EBM promises an objective and rational basis for healthcare, a promise that has proved irresistible. And yet there are concerns. In this paper I briefly describe the nature and methods of EBM, and then explore the relationship between EBM and women's health.<sup>3</sup> Does EBM point the way to better healthcare for women, or are there significant flaws in its methods and application? I argue that despite the potential benefits of EBM, there are several reasons why EBM may not deliver better healthcare for women.

## EVIDENCE-BASED MEDICINE

What is evidence-based medicine? EBM has been defined as 'the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.'<sup>4</sup> This

<sup>1</sup> Cited on the Cochrane Collaboration website [www.cochrane.org](http://www.cochrane.org) (accessed October, 2001).

<sup>2</sup> S. Woolf, R. Grol, A. Hutchinson, M. Eccles & J. Grimshaw. Potential Benefits, Limitations, and Harms of Clinical Guidelines. *BMJ* 1999; 318: 527-530.

<sup>3</sup> I use the term 'EBM' in its widest sense, including both methodological issues and practical applications such as evidence-based guidelines and evidence-based health policy.

<sup>4</sup> D. Sackett. Evidence Based Medicine: What it is and What it isn't. *BMJ* 1996; 312: 71-72.

involves tracking down the best available evidence from research in order to answer questions about healthcare. The research may be about diagnostic tests or prognosis, but to date the main focus of EBM has been on answering questions about the efficacy of therapeutic interventions.

Searching for evidence is time consuming and requires expertise. There are well-defined techniques, known as systematic reviews, which aim to collect all of the research evidence (published and unpublished) about specific interventions.<sup>5</sup> The results from randomised controlled trials (RCTs) can be pooled using meta-analyses so as to provide more conclusive evidence about the benefits and harms of interventions. Once results from multiple trials have been reviewed and combined, the final result is considered to be the best available evidence we have on the topic. This evidence can then be used to inform decisions about healthcare, either directly, as the basis for guideline recommendations, or at a policy level.

The process of searching the evidence can be done by individual practitioners, but a thorough systematic review may take several months and be costly. To make the process easier dedicated organisations, such as the Cochrane Collaboration<sup>6</sup>, perform systematic reviews and publish summaries of evidence, appraised according to 'uniform scientific principles.'<sup>7</sup>

A further synthesis of evidence occurs in the production of evidence-based clinical guidelines.<sup>8</sup> Guidelines are summaries of evidence on specific topics, produced with the aim of making the evidence accessible to busy practitioners. During the production of guidelines, decisions are made about what counts as effective treatment, and when the use of such treatment is appropriate, resulting in an often didactic list of instructions for the practitioner. Guidelines are the familiar face of EBM for many clini-

<sup>5</sup> D. Sackett, W. Richardson, W. Rosenberg & R. Haynes. 1997. *Evidence-Based Medicine: How to Practice and Teach EBM*. New York. Churchill Livingstone; I. Chalmers & D. Altmann. 1995. *Systematic Reviews*. London. BMJ Publishing Group.

<sup>6</sup> The Cochrane Collaboration is an international organisation with centres in 14 countries (Australia, Brazil, Canada, China, France, Germany, Iberoamerica, Italy, the Netherlands, New England, Scandinavia, San Francisco, South Africa, and the UK). Cochrane reviews are produced by a network of international review groups.

<sup>7</sup> Sackett et al., *op. cit.* note 5, p. 15.

<sup>8</sup> In the UK, the National Institute for Clinical Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN) produce and disseminate evidence-based guidelines on a variety of topics.

cians, as they provide a convenient way to access the products of systematic reviews.

Why do we need EBM? Many doctors do not use up to date research results to inform their clinical practice. Doctors use information that they learned at medical school, which may be twenty or thirty years out of date, or rely upon educated guesswork, tradition, or information from pharmaceutical representatives.<sup>9</sup> When new effective medical technology is developed or its efficacy recognised in research, it can take many years to be used in practice.<sup>10</sup> The use of antenatal steroids to prevent lung disease in premature babies and the use of thrombolytics after acute heart attacks are two examples of therapies that took many years to be adopted into practice after there was research evidence about their efficacy. Sometimes doctors use treatments that have never been proven to work, or which may actually be harmful. Also, there are wide variations in practice, for example in the rate of caesarean sections.<sup>11</sup> This means that some people are getting unnecessary surgery, or that others are not getting enough.

The rhetoric of EBM promises that doctors will use the best available evidence to provide medical care of proven effectiveness. People will receive treatments that benefit their problems, and will not receive futile or harmful treatments, thus meeting the ethical requirements of both beneficence and non-maleficence.<sup>12</sup> Explicit use of evidence can bring greater openness into clinical decision-making. EBM has the potential to enhance patient autonomy by providing evidence about the benefits and harms of different treatments to inform patients' choices.<sup>13</sup>

EBM has proved very attractive to policy makers.<sup>14</sup> The idea of using only proven, effective medical interventions is intrinsically appealing. EBM is also appealing as a basis for allocating health-care goods. Policy decisions based upon EBM encourage expenditure on effective treatments, with the understanding that money

<sup>9</sup> A. Oakley. 2000. *Experiments in Knowing: Gender and Method in the Social Sciences*. Oxford. Polity Press.

<sup>10</sup> Sackett et al., *op. cit.* note 5.

<sup>11</sup> A. Coulter. Theory into Practice: Applying the Evidence across the Health Service. *Bailliere's Clinical Obstetrics and Gynaecology* 1996; 10: 715–729.

<sup>12</sup> W.A. Rogers. Are Guidelines Ethical? Some Considerations for General Practice. *British Journal of General Practice* 2002; 52: 663–669.

<sup>13</sup> W.A. Rogers. Evidence-Based Medicine in Practice: Limiting or Facilitating Patient Choice? *Health Expectations* 2002; 5: 95–103.

<sup>14</sup> S. Macintyre, I. Chalmers, R. Horton & R. Smith. Using Evidence to Inform Health Policy: Case Study. *BMJ* 2001; 322: 222–225; L.W. Niessen, E. Grijseels & F. Rutten. The Evidence-Based Approach in Health Policy and Health Care Delivery. *Social Science and Medicine* 2000; 51: 859–869.

will not be wasted on treatments which have been shown not to work.<sup>15</sup> EBM provides an apparently clear and objective basis for decision making, based on evidence that may be less open to criticism than overtly political policies.<sup>16</sup>

In an ideal world, EBM would further the health of all people, including women. Effective treatments would be rapidly introduced into practice, whilst use of treatments with unknown or harmful effects would cease. Women would have better choices as there would be more high quality information about the efficacy of different treatments, and would not be subject to interventions with no benefits. There are some examples of this occurring. A Cochrane review shows that policies that advocate routine use of episiotomies are more harmful than policies that restrict the use of episiotomies.<sup>17</sup> This information allows women to challenge birthing units with routine episiotomy policies. Similarly, another Cochrane review shows that there are almost no benefits from continuous electronic heart rate monitoring for foetal assessment in labour.<sup>18</sup> Citing the evidence can be a powerful way for women to resist practices entrenched through tradition or physician preferences.

Despite these positive examples, EBM and its uses raise a number of issues for women's health. EBM is superimposed upon current medical practice, repeating and reinforcing existing biases against women, both in research and in treatment. The methods of EBM potentially disenfranchise women, both in defining 'the best evidence' and in developing guidelines. The model of health underpinning EBM neglects gendered differences in the causes of ill health. Despite these problems, EBM has become

<sup>15</sup> It is important to distinguish between evidence of lack of efficacy (i.e., demonstrated not to work) and lack of evidence of efficacy (i.e., unknown whether or not the intervention works) as a basis for decision-making. Only the first of these should count as EBM, however, it may be easy to gloss over the distinction when citing 'lack of evidence' as the reason for withholding an intervention or service. T. Hope. Evidence-Based Medicine and Ethics. *Journal of Medical Ethics* 1995; 21: 259–260.

<sup>16</sup> S. Harrison. The Politics of Evidence-Based Medicine in the United Kingdom. *Policy and Politics* 1998; 26: 15–31.

<sup>17</sup> Routine use of episiotomies compared to restricted use leads to more posterior perineal trauma, more suturing, and more complications. There are no benefits with regard to pain and severe vaginal or perineal trauma. G. Carroli & J. Belizan. Episiotomy for Vaginal Birth (Cochrane Review). *The Cochrane Library* 2001; 4. Oxford. Update Software.

<sup>18</sup> S. Thacker, D. Stroup & M. Chang. Continuous Electronic Heart Rate Monitoring for Fetal Assessment during Labour (Cochrane Review). *The Cochrane Library* 2001; 4. Oxford. Update Software.

enormously influential in health policy, research and clinical practice. The effect of embracing EBM may be to further strengthen an already highly interventionist and reductionist healthcare system, at the risk of ignoring many aspects of women's ill health. I discuss each of these areas in turn.

## DEVELOPING AND PERFORMING RESEARCH: INHERITED DISCRIMINATION

Evidence-based medicine is reliant upon existing research, which is the raw material for its processes of summarising and synthesising evidence. This means that EBM reflects any gaps or bias in existing research. Current medical research programmes discriminate against women in two ways: the first is in developing research agendas and the second is in performing research.

### *Developing research agendas*

Current research agendas reflect an uneasy combination of too much attention to gender in some areas, and too little in other areas; that is, there is both biological essentialism and gender blindness.

Biological essentialism refers to a focus on women as reproducers, so that research into women's health is primarily conceived in terms of reproductive capacity and function.<sup>19</sup> If we consider research into women's health, we can identify large numbers of studies into, for example, pharmaceutical treatments for the menopause and to control fertility, or interventions in pregnancy and childbirth. Breast cancer, gynaecological cancer and menstrual disorders all figure as major topics in 'women's health.' Undoubtedly, fertility related issues are a major cause of mortality and morbidity for women, with approximately 500 000 maternal deaths occurring each year world-wide.<sup>20</sup> However, defining women's health as a single risk category associated with reproductive biology ignores the ways in which the social, rather than the biological, effects of gender impact upon women's health.<sup>21</sup>

Biological essentialism marginalises women's health issues that are not related to biological aspects of reproduction. The focus

<sup>19</sup> M. Inhorn & K. Whittle. Feminism meets the 'new' Epidemiologies: Towards an Appraisal of Antifeminist Biases in Epidemiological Research on Women's Health. *Social Science and Medicine* 2001; 53: 553–567.

<sup>20</sup> L. Doyal. Gender Equity in Health: Debates and Dilemmas. *Social Science and Medicine* 2000; 51: 931–939.

<sup>21</sup> Inhorn & Whittle, *op. cit.* note 19.

on women as reproducers seems to exhaust interest in women's health, leading to gender blindness with regard to other health problems which have important gender dimensions, such as HIV/AIDS, coronary heart disease, depression, tropical infectious diseases and tuberculosis. There are recognised sex differences in the causes, incidence, response to treatment and prognosis of all these diseases, due to a combination of biological factors, social conditions or social processes, all of which may have important gender dimensions.<sup>22</sup> Research questions tend to be blind to the potential for gender related differences in aetiology, treatment, responses and experiences of any conditions not directly related to biological sex, with the result that the research base for EBM does not address many questions which are directly relevant to the health of women.

The burden of disease with HIV/AIDS is increasingly falling upon women, who now have a greater mortality from HIV/AIDS than men. There are also gender differences in the morbidity and mortality associated with cardiovascular disease (heart disease plus stroke), with nearly one million more women than men dying of cardiovascular diseases in 1999 (see Table 1).

Table 1. Death Rates by Cause and Gender, Estimates for 1999 (% of all causes of death)<sup>23</sup>

Disease	Males	Females
HIV/AIDS	1 302 000 (4.5%)	1 371 000 (5.1%)
Cardiovascular disease	8 059 000 (27.6%)	8 911 000 (33.2%)

<sup>22</sup> Doyal, *op. cit.* note 20; Inhorn & Whittle, *op. cit.* note 19; S. Kjeldsen, R. Kolloch, G. Leonetti, J. Mallion, A. Zanchetti, D. Elmfeldt, I. Warnold & L. Hansson. Influence of Gender and Age on Preventing Cardiovascular Disease by Antihypertensive Treatment and Acetylsalicylic Acid. The HOT study. Hypertension Optimal Treatment. *Journal of Hypertension* 2000; 18: 629–642; D. Lawlor, S. Ebrahim & G. Davey Smith. Sex Matters: Secular and Geographical Trends in Sex Differences in Coronary Heart Disease Mortality. *BMJ* 2001; 323:541–545; L. Mosca, C. McGillen & M. Rubenfire. Gender Differences in Barriers to Lifestyle Change for Cardiovascular Disease Prevention. *Journal of Women's Health* 1998; 7: 711–715; J. Ussher. 2000. Women and Mental Illness. In *Women, Health and the Mind*. L. Sherr & J. St Lawrence, eds. Chichester. John Wiley and Sons Ltd: 77–90.

<sup>23</sup> WHO. 2000. *Statistics World Health Report 2000: Deaths by Cause, Sex and Mortality Stratum in WHO Regions, Estimates for 1999 (Annex Table 3)*.

These sex differences relate to complex differences in both biological and social risk factors and susceptibility. However, the research base in these two fields related specifically to gender differences remains small.<sup>24</sup>

A further problem occurs when the results from various research projects are combined using the techniques of EBM. For example, of three recent reviews on heart disease in adults listed in the Cochrane library,<sup>25</sup> only one provides information about the gender of participants in the trials. Even where information about gender is provided, none of the reviews analyse by gender.<sup>26</sup> This means that we do not know how much being female matters with regard to aetiology, treatment, or response. The evidence as synthesised in these reviews is gender blind. A similar situation occurs in Cochrane reviews on depressive disorders, which omit mention of gender, with the exception of reviews of post-partum depression or use of anti-depressants in breast-feeding women.

The evidence currently produced by research about diseases that are major causes of morbidity and mortality in women may not be relevant to women. Instead, we have an over-abundance of evidence related to fertility and a lack of evidence about health problems in which gender plays an important role.

Obviously EBM cannot be held responsible for the contents of research agendas reaching back one or two decades. However,

<sup>24</sup> Inhorn & Whittle, *op. cit.* note 19.

<sup>25</sup> A search of the Cochrane library using the MeSH term HEART-DISEASES-ME, exploded term (accessed 6-9-01) gave 11 hits under Cochrane database of systematic reviews, three of which were about heart disease in adults: B. Mayosi, J. Volmink & P. Commerford. Interventions for Treating Tuberculous Pericarditis (Cochrane Review). *The Cochrane Library* 2001; 3. Oxford. Update Software; S. Ebrahim & G. Davey Smith. Multiple Risk Factor Interventions for Primary Prevention of Coronary Heart Disease (Cochrane Review). *The Cochrane Library* 2001; 3. Oxford. Update Software; M. Cucherat, E. Bonnefoy & G. Tremeau. Primary Angioplasty versus Intravenous Thrombolysis for Acute Myocardial Infarction (Cochrane Review). *The Cochrane Library* 2001; 3. Oxford. Update Software.

<sup>26</sup> In the review by Mayosi et al., 3 trials were reviewed with a total of 411 participants. There was no analysis by gender and no reporting of gender in tables of study characteristics. Ebrahim and Davey Smith reviewed 18 trials, with a total of 141 477 participants. 7 trials were men only, with 109 740 participants; 2 trials were women only, with 3428 participants, and for the remainder (28 309 participants) the gender was not stated. There was no analysis by gender. Cucherat et al. reviewed 10 trials with a total of 2573 participants. There was no reporting of gender in the table of study characteristics, and no analysis by gender. Sub-group analysis by gender may not always be methodologically possible, and may increase the risk of errors, but if there is a reasonable belief that gender is significant, trials should be designed to allow for this.

there is a responsibility for the authors and publishers of EBM reviews to highlight any deficiencies in the research base, and this is not apparent with regard to the lack of research into gender differences in diseases which are of major significance to women.

*Gender bias in performing research*

Once a research agenda has been set, the specific details have to be sorted out, as to the nature of the interventions, the outcomes to be measured as proof of effectiveness, and the participants in the trials. How do women fare in these areas?

Many factors influence which interventions are investigated by research, with the source of funding being of prime importance. Pharmaceutical companies are major funders of medical research; unsurprisingly there is much research into drug treatments.<sup>27</sup> However, non-pharmaceutical interventions may be more useful than drugs for many women as they are more likely to be safer for pregnant or breast feeding women. In addition, women have good historical reasons to be suspicious of pharmaceutical solutions to their perceived health problems.<sup>28</sup> Interventions that cannot be patented, such as exercise programmes, are less attractive to commercial research funders.

Research to establish the efficacy of new interventions compares new treatments with existing treatments. Therefore research tends to cluster around a narrow range of interventions, reinforcing current patterns. It is much easier to run a double blind randomised controlled trial (RCT) comparing a new drug with an existing one, than it is to test the efficacy of two different interventions, such as acupuncture versus an established drug. Publicly funded research may be directed towards national health priority areas, set by government and responsive to what may be short-term political agendas.

Traditionally and practically, women have little control over the choice of interventions that are researched.<sup>29</sup> Women are poorly represented in positions of authority and power, both at the policy level and as leaders of research projects.<sup>30</sup> The research questions

<sup>27</sup> T. Bodenheimer. Uneasy Alliance: Clinical Investigators and the Pharmaceutical Industry. *NEJM* 2000; 342: 1539–1540.

<sup>28</sup> For example, many women suffered from the widespread prescription of the benzodiazopene anxiolytics.

<sup>29</sup> S. Sherwin. 1992. *No Longer Patient: Feminist Ethics and Health Care*. Philadelphia. Temple University Press.

<sup>30</sup> L. Sherr. 2000. Women and Clinical Trials. In *Women, Health and the Mind*, *op. cit.* note 22, pp. 47–58.

that interest women may not be considered relevant or interesting by research teams or may not be financially attractive to funders.

Bastian notes, of the research reviewed by the Cochrane Pregnancy and Childbirth group, that 'issues of obvious significance to women are often conspicuous by their absence.'<sup>31</sup> Many obstetrical interventions cause pain and discomfort for women, yet the research focuses upon neonatal well-being and tells us nothing of the comfort or otherwise of the women involved. Bastian cites the example of pain relief after caesarean section as an area with very little research despite the frequency of the operation and the complexities of pain relief for women who are breast-feeding.

The choice of outcomes also depends upon a number of factors. Hard outcomes, which are easy to measure, figure more prominently than less 'objective' measures such as patient well-being or pain, even though at times the latter may be more appropriate. For example, a Cochrane review of the effectiveness of enemas in childbirth used outcomes relating to foetal and maternal morbidity and mortality.<sup>32</sup> The aim of the review was to discover whether enemas actually decrease maternal and neonatal infection due to decreased contamination with faecal matter during delivery, which was the original rationale for enema use. The reviewers recognised that enemas are costly and uncomfortable, but looked only at outcomes related to maternal and neonatal morbidity and mortality, and did not include outcomes relating to maternal satisfaction (which may not have been available in the original research). The review found that there was insufficient evidence to recommend the routine use of enemas during labour. However, rather than comment upon the lack of relevant outcome measures, the reviewers ended with the recommendation that: 'Better quality and ideally blind, randomized clinical trials are needed to provide data to this review in order to give an evidence-based recommendation.'<sup>33</sup> This would require an RCT of many thousands of women in order to show either the presence or absence of significant effects of enemas on morbidity and mortality. In contrast, research using maternal satisfaction as a major outcome might provide a conclusive answer very swiftly.

<sup>31</sup> H. Bastian. 1994. *The Power of Sharing Knowledge: Consumer Participation in the Cochrane Collaboration*. Cochrane Consumer Network website: <http://www.cochraneconsumer.com/index.asp?SHOW=HotTopics> (accessed October, 2001).

<sup>32</sup> L. Cuervo, M. Rodriguez & M. Delgado. *Enemas During Labor* (Cochrane Review). *The Cochrane Library* 2001; 3. Oxford. Update Software.

<sup>33</sup> *Ibid.*

The quest for evidence appears to have blinded the reviewers about the relevance of their chosen outcomes to the women subjected to the enemas.

A similar problem occurred with research into heavy menstrual bleeding, a condition which can lead to hysterectomy. The main outcomes that have been used in research trials are change in measured blood loss and haemoglobin.<sup>34</sup> These outcomes ignore the fact that women with heavy periods have a constellation of symptoms, including the pattern of loss, flooding, and pain and discomfort as well as total blood loss. The review concluded that a drug called norethisterone, which is very commonly prescribed, is not effective for reducing measured total blood loss. However, clinical experience indicates that many women find norethisterone to be helpful for the problem of heavy periods. The evidence seems to have targeted the wrong outcomes whilst ignoring outcomes of importance to women.

Choices about interventions and outcomes may relate as much to the relative power of consumers and researchers as to gender per se. However, given the way that divisions of power tend to mirror those of gender in our society, women are over-represented amongst those who have little power to influence research. Whilst men as consumers may be under-represented in positions of power, men in general undoubtedly benefit from the influence of the men who have commissioned and performed so much research into their own health needs, creating a solid evidence base about relevant interventions for coronary heart disease, lung cancer and peptic ulcer in men.<sup>35</sup>

The gender bias amongst participants in clinical trials is well known.<sup>36</sup> Women have been excluded from research for many years, for a variety of reasons including the alleged need for homogenous populations, the fear of harms to pregnant women, the cost of including women, and the purported difficulty of recruiting women.<sup>37</sup> Despite robust criticisms, the bias towards male participants in research trials remains. In the US, 85% of research participants are male; this rises to 95% in Canada.<sup>38</sup>

<sup>34</sup> The Management of Menorrhagia. 1995. *Effective Health Care Bulletin*. York. NHS Centre for Reviews and Dissemination, University of York.

<sup>35</sup> Inhorn & Whittle, *op. cit.* note 19.

<sup>36</sup> R. Dresser. Wanted: Single, White Male for Medical Research. *Hastings Center Report* 1992; 22: 24–29; Sherr, *op. cit.* note 30.

<sup>37</sup> *Ibid.*

<sup>38</sup> Sherr, *op. cit.* note 30.

Reviews of gender bias in, for example, cardiovascular research consistently find under-representation of women.<sup>39</sup> The very large studies from the 1980s used exclusively men. Later trials have included women, in some trials up to 48% of the total, but the mean is only 24%.<sup>40</sup> Even when women are included, there is little or no analysis by gender. These imbalances remain despite the adoption of gender-related policies requiring equal numbers of male and female participants in research funded by government agencies.<sup>41</sup> There are no large-scale trials that are for women only. Reviews published in 2001 continue to identify the lack of data on cardiovascular interventions in women.<sup>42</sup>

Research into HIV/AIDS shows a similar pattern. Women were 5.4% of participants in relevant HIV trials between 1995–1998.<sup>43</sup> The situation is slowly changing with the initiation of research into HIV in women, however much of this focuses exclusively on maternal-foetal transmission.<sup>44</sup>

The potential for women to ‘catch up’ in terms of research data is low. Research that repeats previous investigations, albeit with different participants, is of lower status than new research. This makes it less attractive to investigators and funders, and less likely to be published.

A further gender bias occurs with the exclusion of elderly people from many clinical trials. Elderly people are excluded from trials for a variety of reasons, such as co-morbidity, leading to a lack of evidence about the efficacy of recognised interven-

<sup>39</sup> S. Ebrahim & G. Davey Smith. Systematic Review of Randomised Controlled Trials of Multiple Risk Factor Interventions for Preventing Coronary Heart Disease. *BMJ* 1997; 314: 1666–1674; R. Raine, T. Crayford, K. Chan & J. Chambers. Gender Differences in the Treatment of Patients with Acute Myocardial Ischemia and Infarction in England. *International Journal of Technology Assessment in Health Care* 1999; 15: 136–146; P. Rochon, J. Clark, M. Binns, V. Patel & J. Gurwitz. Reporting of Gender-Related Information in Clinical Trials of Drug Therapy for Myocardial Infarction. *Canadian Medical Association Journal* 1998; 159: 321–327.

<sup>40</sup> Rochon et al., *ibid.*

<sup>41</sup> *Ibid.*

<sup>42</sup> L. Hooper, C. Summerbell, J. Higgins, R. Thompson, N. Capps, G. Davey Smith & S. Ebrahim. Dietary Fat Intake and Prevention of Cardiovascular Disease: A Systematic Review. *BMJ* 2001; 322: 757–763; D. Krummel, D. Koffman, Y. Bronner, J. Davis, K. Greenlund, I. Tessaro, D. Upson & J. Wilbur. Cardiovascular Health Interventions in Women: What Works? *Journal of Women's Health & Gender-Based Medicine* 2001; 10: 117–136.

<sup>43</sup> Sherr, *op. cit.* note 30.

<sup>44</sup> Most of the women with HIV/AIDS live in developing countries, and thus are doubly disadvantaged both by their gender and by the lack of research in these countries.

tions in this group.<sup>45</sup> Women form a greater proportion of the elderly population due to their relative longevity, with the result that a lack of evidence about effective interventions in the elderly has a greater impact upon the health of women.

So far, these sources of bias are pre-existing in medical research, rather than due to any flaws in the processes of EBM. Indeed, the identification of these gaps is facilitated by the existence of systematic reviews that collect information about research. If EBM is a tool to facilitate access to research, it may hardly be fair to blame EBM for what we find when we use that tool. However, if one of the roles of EBM is to identify gaps in the research base to inform new research, this must surely create a responsibility for those reviewing the evidence to be attentive to all omissions, including those related to gender. When evidence is presented as convincing, objective and authoritative, and yet pertains only to men, reviewers miss an opportunity to speak out about gender inequalities. In much of its reporting, the reviews of EBM continue the tradition that male bodies are the norm in our society, and that women only count in relation to their reproductive differences.

## BIAS IN THE METHODS OF EBM

The methods of EBM include collecting and reviewing evidence, and then the further synthesis of this evidence into guidelines suitable for use by practitioners. Both of these processes have gender implications.

### *What kind of evidence?*

EBM draws much of its authority from its methods, which follow strict protocols for finding research results and combining them in specified ways to ensure that the end results are valid.<sup>46</sup> Part of the process, especially in the production of evidence-based guidelines, uses an internationally accepted hierarchy of evidence that has evidence from RCTs at the top.<sup>47</sup> (See Box 1.)

<sup>45</sup> K. Hall & R. Luepker. Is Hypercholesterolemia a Risk Factor and should it be Treated in the Elderly? *American Journal of Health Promotion* 2000; 14: 347–356.

<sup>46</sup> Chalmers & Altmann, *op. cit.* note 5; Sackett et al., *op. cit.* note 5.

<sup>47</sup> P.G. Shekelle, S.H. Woolf, M. Eccles & J. Grimshaw. Developing Guidelines. *BMJ* 1999; 318: 593–596. Note that the original descriptions of EBM (by, for example Sackett et al, *op. cit.* note 5) do not include a hierarchy of evidence, but this has now become widely incorporated into much of the literature and is linked to the strength of recommendations in many evidence-based guidelines.

*Box 1: Hierarchy of Evidence*

- Ia Evidence obtained from meta-analysis of randomised controlled trials.
- Ib Evidence obtained from at least one randomised controlled trial.
- IIa Evidence obtained from at least one well designed controlled study without randomisation.
- IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.
- III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
- IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

The use of this hierarchy privileges the results of RCTs over results from other research methods, implying that RCT results are more reliable or valid than other results. Of course, for some research questions RCTs do give the most reliable results, but this hierarchy does not acknowledge that research methods must be tailored to the question at hand, and that for some questions, the best evidence comes from other research designs. This ranking of research methods is significant, as there is considerable debate about the connections between gender and methods in research.<sup>48</sup> In the so-called paradigm wars, quantitative methods such as RCTs have been characterised as masculine, objective, experimental and controlling, in contrast with qualitative methods which are seen to be feminine, subjective, observational, and context-dependant. Qualitative methods are favoured by some feminist researchers for allowing the voices of women to be heard, in describing problems and in finding solutions.<sup>49</sup> For example, a qualitative research project is ideally suited to yield useful information about domestic violence against women, or the use of condoms to prevent transmission of HIV.<sup>50</sup>

<sup>48</sup> See Oakley, *op. cit.* note 9, for a full review of these debates.

<sup>49</sup> E. Annandale & K. Hunt. 2000 Gender Inequalities in Health: Research at the Crossroads. In *Gender Inequalities in Health*. E. Annandale & K. Hunt, eds. Buckingham. Open University Press: 1–35; Inhorn & Whittle, *op. cit.* note 19.

<sup>50</sup> S. Craddock. 2001. Scales of Justice: Women, Equity and HIV in East Africa. In *Geographies of Women's Health*. I. Dyck, N.D. Lewis & S. McLafferty, eds.

Oakley argues that maintaining strict distinctions between masculine/quantitative and feminine/qualitative research can be difficult, as both kinds of research often contain elements of the other.<sup>51</sup> More importantly, both provide valuable and complementary sources of information. Yet the current evidence hierarchy makes it impossible for evidence from qualitative research to reach anything above level III, effectively making qualitative research a less powerful source of evidence than quantitative evidence. Given the current culture of research in which there are these gendered divisions along methodological lines, widespread use of an evidence hierarchy which discounts evidence from qualitative research has implications for women's health, both in terms of women as researchers influencing research agendas and women as participants in research.

### *Making guidelines*

As mentioned previously, an important part of EBM is the use of evidence to generate guidelines for clinical and policy use. These guidelines are the end products and visible face of EBM, developed by groups of dedicated individuals. The group defines the scope of the guideline, the interventions to be assessed and the outcomes of interest. Guideline development groups combine the evidence-finding techniques of EBM with the group's considered judgement to develop recommendations. The final recommendations are influenced by the composition of the group, reflecting the interests of those involved.<sup>52</sup> However, despite a commitment to multi-disciplinary membership, women are under-represented in guideline development groups. The chart below shows the composition of seventeen recent guideline development groups working in the Scottish national guideline programme.

Men form the majority in fourteen out of these seventeen groups; there are only three female chairs. Given the importance of group composition upon guideline recommendations, this lack of women in the groups suggests that women's interests may be under-represented in guideline recommendations, unless the group pays particular attention to gender issues. In addition,

London. Routledge: 41–60; S. Ruangjiratain & J. Kendall. Understanding Women's Risk of HIV Infection in Thailand through Critical Hermeneutics. *Advances in Nursing Science* 1998; 21: 42–51.

<sup>51</sup> Oakley, *op. cit.* note 9.

<sup>52</sup> Woolf et al., *op. cit.* note 2.

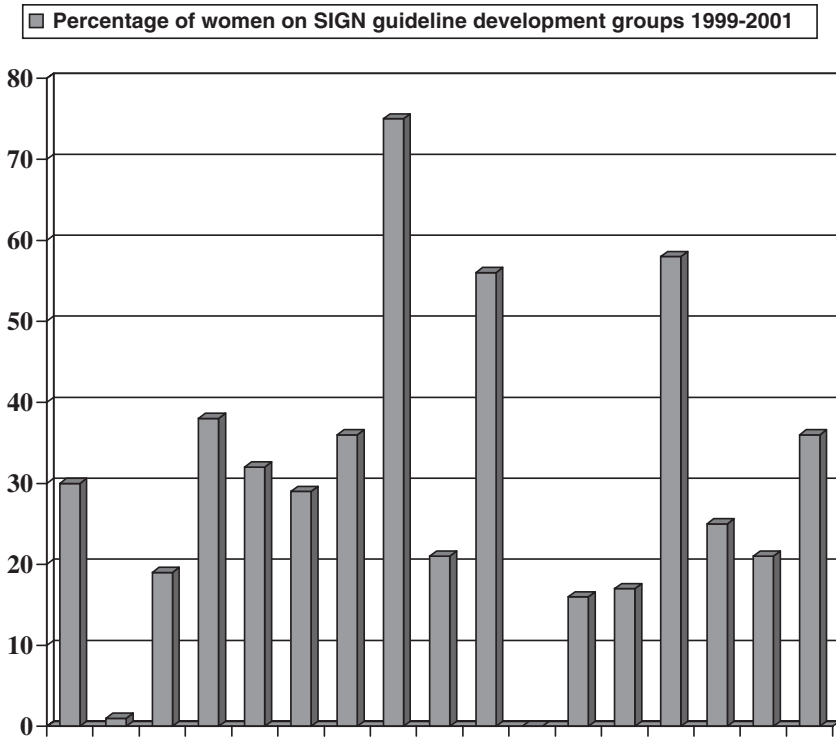


Chart 1: Graph Showing Gender Composition of Seventeen Guideline Groups Convened by the Scottish Intercollegiate Guidelines Network (SIGN)

guideline groups advise on areas requiring further research, indicating another way in which women's interests may be disenfranchised.

These biases in the methods of EBM are not insurmountable. There is a growing awareness of the need to fit the research method to the type of problem, and a recognition that RCTs cannot provide all of the answers. The Cochrane Collaboration has a 'Possible Cochrane Qualitative Research Methods Group.' The composition and functioning of guideline development groups are coming under increasing scrutiny.<sup>53</sup> Yet it is disappointing that a new and idealistic technique such as EBM has so faithfully repeated well-recognised patterns of discrimination against women.

<sup>53</sup> C. Pagliari, J. Grimshaw & M. Eccles. The Potential Influence of Small Group Processes on Guideline Development. *Journal of Evaluation in Clinical Practice* 2001; 7: 191-199.

## GENDER BIAS IN USING THE EVIDENCE

Once the research has been performed, reviewed into evidence and packaged into guidelines, it can be used for clinical practice and for policy. The lack of evidence about the effectiveness of interventions in women has two major implications: withholding treatment and inappropriate treatment.

A relative lack of evidence which is applicable to women may lead to the withholding of treatment because there is no proof that it will work in women.<sup>54</sup> Gender differences in the treatment of cardiovascular diseases are well recognised.<sup>55</sup> The reasons for the under treatment of women are not clear, but a belief that the evidence does not apply to women has been proposed as a possible reason for this.<sup>56</sup>

Sometimes lack of evidence may serve as an excuse not to introduce an intervention, diverting attention away from the underlying reason. Low dose oral contraceptives were not available to Japanese women for many years. One of the reasons cited for this was lack of evidence that these drugs were safe in Japanese women, despite the established safety record in women of other nationalities. This reasoning invoked an overtly objective basis to decision-making (i.e., lack of evidence), coupled with an apparent reluctance to expose Japanese women to possible harms from an 'untested' drug. However, it seems that other interests were at stake, as the pill was not approved for several years after the completion of Japanese trials.<sup>57</sup> This suspicion seems to be confirmed by the observation that when Viagra came on to the market, it was introduced immediately into Japan despite the lack of trials on Japanese men.

<sup>54</sup> See also footnote 15 on blurring the distinction between lack of evidence of efficacy and evidence of lack of efficacy.

<sup>55</sup> J. Brophy, J. Diodati, P. Bogaty & P. Theroux. The Delay to Thrombolysis: An Analysis of Hospital and Patient Characteristics. Quebec Acute Coronary Care Working Group. *Canadian Medical Association Journal* 1998; 158: 475–480; L. Davis, J. Evans, J. Strickland, L. Shaw & G. Wagner. Delays in Thrombolytic Therapy for Acute Myocardial Infarction: Association with Mode of Transportation to the Hospital, Age, Sex, and Race. *American Journal of Critical Care* 2001; 10: 35–42; R. Raine, T. Crayford, K. Chan & J. Chambers. Gender Differences in the Treatment of Patients with Acute Myocardial Ischemia and Infarction in England. *International Journal of Technology Assessment in Health Care* 1999; 15: 136–146.

<sup>56</sup> Rochon et al., *op. cit.* note 39; I. Sharp. 1998. Gender Issues in the Prevention and Treatment of Coronary Heart Disease. In *Women and Health Services*. L. Doyal, ed. Buckingham. Open University Press: 100–112.

<sup>57</sup> A. Goto, M. Reich & I. Aitken. Oral Contraceptives and Women's Health in Japan. *JAMA* 1999; 282: 2173–2177.

Lack of applicable evidence may lead to inappropriate treatment for women if they are given interventions that have been shown to be effective only in men. Despite the enormous amount of research into cardiovascular disease, we still have very little information about which interventions are effective in modifying risk factors for cardiovascular disease in women.<sup>58</sup> The latest as yet unpublished research claims to provide the first clear evidence of the benefits of lowering cholesterol in women through the use of statins, but we are no further forward with non-pharmaceutical interventions.<sup>59</sup>

#### BIAS IN THE NATURE OF EBM: MODELS OF HEALTH AND DISEASE

There is a large body of research demonstrating the intimate connection between gender inequalities and health.<sup>60</sup> Gender inequality and discrimination harm girls' and women's health directly and indirectly, throughout the life cycle.<sup>61</sup> Female infanticide, inadequate food and medical care, physical abuse, genital mutilation, forced sex and early childbirth are directly responsible for the deaths of many women.<sup>62</sup> These factors are also implicated in the genesis of specific diseases such as heart disease, mental illness and infectious diseases. (See Box 2.)

Poverty is also a major risk factor for ill health. Whilst poverty affects both men and women, poverty itself and the effects of poverty are gendered.<sup>63</sup> Women are more likely than men to be poor, and thus to suffer the ill health consequences of poverty. In addition, within poor households, limited access to healthcare has a greater relative impact on women than men.

The health gap between poor and non-poor exists for both males and females, but the risks are greater for women. Poverty

<sup>58</sup> Hooper et al., *op. cit.* note 42; Kjeldsen et al., *op. cit.* note 22; Krummel et al., *op. cit.* note 42.

<sup>59</sup> I am referring to the Heart Protection Study (lead investigator R. Collins, reported in the News section of the *BMJ* 2001: 323; 1145).

<sup>60</sup> Reviewed by Doyal, *op. cit.* note 20.

<sup>61</sup> L. Doyal. 1995. *What Makes Women Sick: Gender and the Political Economy of Health*. Basingstoke, Hampshire. Macmillan Press Ltd.

<sup>62</sup> United Nations Population Fund. 2001. *The State of World Population 2000*. Chapter 2 (accessed electronically:

<http://www.unfpa.org/swp/2000/english/index.html>).

<sup>63</sup> M. Bartley, A. Sacker, D. Firth & R. Fitzpatrick. 2000. Dimensions of Inequality and the Health of Women. In *Understanding Health Inequalities*. H. Graham, ed. Buckingham. Open University Press: 58–78; Doyal, *op. cit.* note 20; Inhorn & Whittle, *op. cit.* note 19.

*Box 2: Health Effects of being Female*

<b>Primary effects</b>	<b>Secondary effects</b>	<b>Tertiary effects</b>
selective abortion	physical injury	early death
infanticide	malnutrition	disability
genital mutilation	sexually transmitted	acute infections
social neglect	diseases	chronic infections
medical neglect	forced pregnancy	anaemia
sexual abuse		heart disease
poverty		mental illness
discrimination		

*Table 2. Risk of Dying in Poor Households Compared to Non-Poor Households<sup>64</sup>*

Age group	Females in poverty	Males in poverty
Children aged under 15	4.8	4.3
Adults aged 15–59	4.3	2.2

quadruples the risk of dying for women in poor households compared to women in non-poor households; for poor men the risk is doubled compared with non-poor men (see Table 2).

The adverse health effects of both female gender and poverty are mediated through society rather than biology, so that we must seek social rather than biological solutions. However, the efforts of EBM are by and large located within a biomedical model in which identifiable causes lead to disease outcomes, such as raised cholesterol increasing the risk of heart disease, or inoculation with the tuberculosis bacterium leading to TB. This way of defining problems lends itself to a research agenda in which the immediate and identifiable causes are investigated and treated. The focus is upon physical interventions acting on the diseased person, such as taking medicines to kill infectious agents or surgery to removed diseased parts. The problem with this model of disease is that it ignores the wider determinants of health such as poverty, discrimination and oppression, which are major causes of ill health in women.<sup>65</sup>

Measuring oppression and discrimination poses considerable methodological challenges. There are no scales or biological

<sup>64</sup> United Nations Population Fund *op. cit.* note 62, chapter 5.

<sup>65</sup> D. Acheson. 1998. *Independent Inquiry into Inequalities in Health*. London. Stationery Office.

markers to indicate degree of oppression or level of discrimination. This does not mean that we cannot or should not investigate these topics, but points to the difficulty of devising interventions which can be investigated by research methods meeting the methodological requirements of EBM.<sup>66</sup> Evidence of efficacy is best proved by changes in well defined outcomes such as weight of babies, number of deaths or level of blood pressure; where it is not possible to define these kind of outcomes, it is more difficult for research to demonstrate effectiveness. A narrowly biomedical research programme receiving much of its funding from the pharmaceutical industry is unlikely to embrace research into effective social interventions, such as income support, or programmes to decrease violence against women.

A further problem with biomedical research is the focus on the individual. This allows researchers to ignore the social and political context leading to increased risks of ill health. If the aim is to provide interventions at the individual level, the wider context conveniently drops out of the picture.<sup>67</sup> Thus a campaign aiming to curb the transmission of HIV/AIDS may ignore the social and cultural situation of women in order to concentrate on the perceived risky behaviour of individual women, such as unprotected intercourse. This might lead to an intervention aimed at increasing condom use, ignoring sexual power relations that leave women little control over condom use or the promiscuity of their partners.<sup>68</sup>

EBM cannot be considered responsible for the biomedical model, which has long been criticised. Perhaps it is unreasonable to expect biomedical researchers to repudiate their traditional ways. However, EBM is a powerful influence upon the way we think about health and illness. Framing health problems in terms of the search for evidence of effective interventions tends to maintain discussions of health within the narrow biomedical model, diverting attention and resources away from alternative views.

The overall effect of EBM occurring within a biomedical framework is to provide evidence about the effectiveness of medical interventions for a narrowly defined range of disease states. This narrow focus is especially worrying when governments adopt

<sup>66</sup> M. Whitehead, F. Diderichsen & B. Burstrom. 2000. Researching the Impact of Public Policy on Inequalities in Health. In *Understanding Health Inequalities*. H. Graham, ed. Buckingham. Open University Press: 203–218.

<sup>67</sup> Inhorn & Whittle, *op. cit.* note 19.

<sup>68</sup> Ruangjiratain & Kendall, *op. cit.* note 50.

policies based upon evidence.<sup>69</sup> A commitment to funding only health interventions which are supported by evidence legitimises governments' continued reluctance to tackle the wider causes of ill health. Treating the effects of poverty and discrimination rather than the causes allows perpetuation of the social structures that cause ill health.

## CONCLUSION

Before the introduction of EBM, healthcare practices were often biased and unreliable. *Prima facie*, basing health interventions on evidence rather than limited experiences, hope or advice from an equally out of date colleague will benefit those receiving healthcare. Research evidence can be a powerful tool for challenging and changing practice, for women as patients as well as amongst professionals. On balance, finding and using relevant evidence is surely better than not doing so. However, for EBM to make its full contribution towards improving the health of women, some changes are needed.

Attention to gender across all the processes of EBM is a necessary step. Ways to redress the gender imbalance in research might include withholding funding and ethical approval and refusal to publish the results for trials that do not include equal numbers of men and women. The evidence hierarchy should be revised to remove the implicit assumption that RCT evidence is always better than evidence from other research methods. Improving career structures for research staff is crucial, to avoid the pressure and insecurity of short-term contracts which are the fate of many women in research. Better employment conditions will facilitate the participation of women in all aspects of research. Encouraging, supporting and funding women (professional and lay) to participate in guideline development groups may overcome some of the barriers imposed by the largely voluntary nature of many of these groups.

All of these measures may lead to the production of evidence that is more relevant to women's health, which is to be welcomed. The larger question remains about the place of biomedical research within our healthcare systems. The quest for better evidence may blind both healthcare providers and policy makers as to the overall desirability and potential contribution to the health of women of narrowly biomedical interventions. No matter how

<sup>69</sup> G. Davey Smith, S. Ebrahim & S. Frankel. How Policy Informs the Evidence. *BMJ* 2001; 322: 184–185.

good the evidence for specific interventions, if they are used in a world in which gender is a risk factor for women's health, their impact will remain limited.

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