Effectiveness of condoms to prevent STDs J. Gerofi

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Introduction

The measurement of condom effectiveness is a very complex issue, due to difficulties in definition and measurement. The range of issues to be addressed is broad, and has been categorised in a report to WHO[i], called the Condom Effectiveness Matrix, produced in 1994. It posed a graded series of nine questions, starting with questions about the condom as a device, and working through to the effectiveness of condoms to prevent the transmission of diseases as a public health measure at the population level. For each of the nine levels, it considered the contributing factors, research necessary to resolve outstanding issues, and the criteria by which outcomes would be assessed.

In this present article, discussion will largely be confined to a subset of issues - the actual protection against disease offered by condoms in human use.

The protectiveness of condoms against diseases in general can be assessed in three different ways:

1 How well do they protect the individual user, if the user follows the instructions carefully?

2 How well do they protect the typical user?

3 What is the long-term effect on the population as a whole, of widespread condom use?

The answers to these questions could be quite different, yet equally important from different perspectives. For the purposes of this analysis the primary focus will be the effectiveness for individuals using condoms 100% of the time, as this gives information to assist the individual in making choices. The long-term protective effect on the population is also relevant, as it has important economic and public health implications.

Effect of the type of condom

It is known that some condom manufacturers produce higher quality condoms than others. Usually, quality is measured in terms of adherence to national or international standards, and there is an implicit assumption that the condoms that perform best on tests in the standards are the best in use.

In clinical trials assessing condom effectiveness against pregnancy or disease, the characteristics of the condoms used are rarely assessed. It is therefore usually only possible to report on condoms generically. In some cases there are trials done in

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[i] Spencer B. E. The Condom Effectiveness Matrix, Les Editions INSERM, 1994

countries with laxer condom quality requirements than one would find in developed countries, but there is rarely adequate information available to separate the effects of condom quality from other confounding variables, even if a parallel study is done in another country. Studies done in the USA, Europe and Australia in the last few years almost certainly used condoms which met the then (1996) ISO standard for condoms - the accepted yardstick for good quality.

Condoms are also made in a variety of designs and a range of sizes. It is likely that using a condom of the wrong size could cause in increase in the risk of failure, and the effect of other aspects of condom design (ie thickness, shape and texture) on condom slippage and breakage is virtually unexplored.

What are we comparing with?

Another important issue is to ascertain the basis for comparison. Using condoms is generally less safe than sexual abstinence, or than limiting sexual contact to uninfected partners (especially in a monogamous situation). One of the driving forces that brought about the workshop discussed below was pressure from a group of people who were making a case that abstinence and fidelity were the strategies to be advocated, especially to the US public. Unfortunately, although abstinence has 100% method effectiveness, it also has significant user failure. People who intend to abstain do not always do so, and if they are unprepared for their lapses, then it is likely that they will not have a condom ready to provide protection. Comparing the actual effectiveness of condoms with the theoretical effectiveness of abstinence is thus pointless. Some aspects of this issue are discussed in [ii]

Difficulties in measuring condom effectiveness

All medical research project designs are limited by ethical considerations, requiring protection for the participants. As some of sexually transmitted infections are incurable, it is not possible to expose people to such infections for experimental purposes. People in studies found to have diseases need to be treated. Participants cannot be encouraged to take risks they would otherwise not take.

Thus human studies can in general only be observational and it is not possible to conduct experiments on the use of condoms on animals.

[ii] Pinkerton S. A relative risk-based disease-specific definition of sexual abstinence failure rates. Health Education and Behavior, 28(1), 2001, pp 10-20.

Many of the sexually transmitted infections are asymptomatic some of all of the time in some individuals. Thus true incidence or prevalence should be measured by pathology testing rather than by clinical signs and symptoms.

Vaginal or anal penetration are recognised as sexual contact and accepted as means of disease transmission. Other activities, particularly oral sex, can also transmit some diseases. While oral HIV transmission is unlikely, oral transmission of gonorrhoea and herpes is becoming more common.

As most sexually active people have some awareness that condoms protect against disease, there may be a tendency among study subjects to tell researchers that they do use condoms, even if they do not.

Finally, it is very difficult to ascertain exactly how and when the condom was used, apart from relying on reports from the user, since most people want to have their sexual activity in private. Indeed, many people find it very difficult and embarrassing to describe in fine detail exactly how they used the condom, and exactly what they did during intercourse.

Under these circumstances, it is difficult to ascertain the level of exposure any individual study participant has had to a particular infection, and any meaningful comparison between using condoms and not using them should be based on equal exposure.

Given all these constraints, it is to be expected that researchers will be faced with considerable difficulties in designing and carrying out condom effectiveness studies.

Inference from results of sample studies

Inevitably, studies will involve a sample of a population. From what happens to the sample, one must infer what is happening in the population. With such studies, whatever the precision of knowledge about the results in the sample, the question of whether the sample was representative or not will remain. Results from the studies are usually reported with 95% confidence intervals, indicating the confidence with which the sample results represent the overall situation. Accordingly, even in the best-designed of studies, the results found for the sample have a finite probability of being contrary to those for the population.

It is also possible that a study sample is unrepresentative of the population due to a design flaw. As in all studies relying on reporting by the participants, the data collected depends on the questions asked, and these must be designed with great care. Poorly worded questions can result in unclear outcomes.

Definition of condom use

In each act of intercourse, a condom may be used or not used. If used, it may be

used correctly, or at various levels of incorrectness, giving varying exposure to pathogens. Similarly, one particular person may use a condom every time, never, or any intermediate percentage of the time. Thus, unless very searching questions are asked in a study, the record of how often and how well condoms were used will be a very coarse one, even if the respondents answer with complete recall and candour. Many studies do not report the level of detail needed to indicate the level of condom usage by individuals, and many choose to treat condom use by an individual over the period of the study as a dichotomous variable. The line between "used" and "did not use" varies from study to study. Some studies classify into "ever used" and "never used" while others classify into "always use" and "do not always use". Still others may say "use more often than 50% of the time" and "use less than 50% of the time". Infinite variations are possible.

A reliable assessment of the effect of condom use on infection or disease outcomes requires at least a 3-way classification of condom use - always, never and sometimes. The clearest definitive information comes from comparing "always" and "never" users. But as many people are inconsistent in their condom use, such an analysis may result in abandoning a lot of the data that have been collected with great difficulty.

A more effective approach may be to create a continuous variable to describe the proportion of the time condoms are used by each participant, and to use a logistic regression analysis. This approach has not been used in any of the studies referred to in this document.

Data could also be collected on the types of condom used, on how they are used and on any notable problems with their use. But many of the studies on STI transmission are not specifically designed to assess condom efficacy, and certainly not to differentiate between different types of condom.

The situations of different users may also be different. Apart from the way in which they use the condoms, and the exact nature of their sexual activity, the infected partners may be more or less infective, and the other partner may be more or less susceptible, depending on a number of factors.

Sample studies are generally not large and sophisticated enough to deal with all these variables.

Information sources for this review

The literature abounds with articles which relate directly or indirectly to the effect of condoms on the spread of STIs. Since it is beyond the scope of this review to analyse all of these ab initio, this document will distill two significant reviews of these articles published since 2000. The first is a chapter in a book, Condoms[iii], published

[iii] Mindel A (ed) Condoms, BMJ Books, 2000

in 2000, and the second is the report of a workshop-meeting of experts convened by the NIH[iv] in the USA, also held in 2000. Both these documents were compiled by world-renowned experts in sexually transmitted infections.

This document will review the two documents above, and will also review some articles published on the topic since the beginning of 2000.

The Book

Condoms was published by BMJ Books in 2000, and edited by Professor Adrian Mindel, Professor of Sexual Medicine Medicine, University of Sydney, Australia and Director of the Sexually Transmitted Infections Research Centre, Westmead Hospital. It contains 14 chapters, covering the history, manufacture, quality, use and effectiveness of condoms.

Chapter 5 deals specifically with condoms for the prevention of sexually transmitted infections. It has 85 references, and covers the following conditions:

Gonorrhoea
Chlamydia and related conditions
Syphilis
Tropical STIs (including chancroid)
HIV
HSV
HPV and associated conditions
Hepatitis A, B and C
Human T-cell lymphotropic virus type 1 (HLTV 1)

The authors were Professor Mindel and Claudia Estcourt, who is a consultant physician in genitourinary medicine, Bart's Sexual Health Centre, St Bartholemew's Hospital, London.

The approach taken in the book is to analyse the case-based and epidemiolgical data, as well models of transmission dynamics to make an assessment of the effectiveness of condoms for each infection, using a balance of probabilities based on evaluation of the data cited.

The Workshop

Four US Government agencies (USAID, FDA, CDC and NIH) co-sponsored the workshop held in June 2000, to evaluate the published evidence establishing the

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[iv] Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease Prevention, National Institute of Allergy and Infectious Diseases, NIH, Dept of Health and Human Services, 2001

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effectiveness of latex male condoms in preventing STDs. Consideration was limited to penile-vaginal intercourse.

Eight diseases were considered:

HIV
Gonorrhoea
Chlamydia trachomatis
Trichomonas vaginalis
HSV
Chancroid
Syphilis
HPV

The workshop examined only peer-reviewed literature. 138 relevant papers published in or before June, 2000 were compiled and reviewed. These included several papers on condom breakage, slippage and leakage, and some on prevalence of condom use, as well as those related to transmission of particular diseases. An individual expert presented an analysis for each disease. The individual expert determined which of the papers to consider, based on their assessment of the quality of the evidence contained in the papers.

The review panel, which then wrote the final report, and re-evaluated the material from the individual presenters, concentrating mainly on the papers they chose to include.

As a result of the process used, studies that presented outcomes for multiple infections in aggregate were generally excluded.

The scope of the workshop was limited to three areas:

1. The device
2. The route of infection for the diseases covered
3. Condom effectiveness as determined in clinical studies on the eight diseases.

The final report was almost exclusively dependent on the last of the above areas.

The workshop was constrained by:

1. Not being able to consider data from homosexual use
2. Not considering aggregate data for multiple infections
3. Restricting data to that which had been published in peer-reviewed journals.

The general approach of the workshop report was to give an affirmative opinion on condoms only if evidence of adequate quality was found to substantiate the hypothesis that condoms reduced the transmission of a particular infection or

disease. While the condom's integrity as a device was considered, as were slippage and breakage trials, these issues did not play a direct part in the assessments. Heaviest weight was given to cohort studies in which a risk ratio could be determined directly.

It is interesting that of the 180 articles referred to by one or other of the book and the workshop, only 45 were referred to by both.

Other Information

While there is little point in reviewing the papers in the above analyses again, there have been some relevant articles published since they were done. These are referred to in the text below, categorised by disease.

Types of Study and Measure

Generally, the types of user study that may shed light on the effectiveness of condoms include:

1. Prospective cohort (longitudinal) studies, in which individuals at risk are identified and followed over a set period, to see when and whether they contract a particular disease. In the case of condom effectiveness, data would be collected on the extent of use of condoms (and ideally on the level of exposure to disease), to make a quantitative assessment. This is usually reported as a risk ratio, but alternatively the odds ratio may be calculated. These two parameters are described in the annex.

2. Case control studies. In these studies, people presenting for treatment for a particular disease are compared retrospectively with a control group who do not have the disease, but who are selected to match the characteristics of the people with the disease as far as possible. For condom effectiveness, the extent of condom use among those with the disease is compared with those in the control group.

   In these studies, the Odds ratio can always be calculated, but the risk ratio can only be calculated in special cases. As long as the disease prevalence is low, the Odds ratio can be used to approximate the risk ratio. In any case, if the condoms have no effect, both the Odds ratio and the risk ratio are 1.0. This is also discussed in the annex.

3. Intervention studies. In such studies, the incidence of a disease may be measured before and after a certain public health intervention, for example the 100% condom use campaign in Thailand. The reduction of HIV incidence after such a study is persuasive that the condoms were effective, but it is almost impossible to quantify the effect because of confounders, for example simultaneous messages urging sexual fidelity.

4. Cross-sectional studies. could test a sample of the population for a disease and ask about their condom usage. Again, such studies may give persuasive indications, but probable causality is much harder to establish because of confounding factors.

5. Ecological studies. In these studies, the occurrence of particular diseases in different communities is measured, and related to different exposure factors peculiar to the community. Disease prevalence may be measured in a community of condom users, and compared that in a community of non-users. The unit of observation is the community.

The first two types of study potentially yield direct quantitative information on condom effectiveness, and, of them, the prospective studies are regarded as the more reliable. They can also generate information in terms of risk ratio and Odds ratio, while the case control studies usually only give the Odds ratio. This is explained in the Annex.

Other terms used in evaluating condoms are efficacy and risk reduction. They are essentially identical. Efficacy is defined as (1 - relative risk) where the relative risk is the failure rate using condoms divided by the failure rate for non-users. It may be expressed as a fraction or a percentage.

The condom as a device

The purpose of the condom is to put a barrier between the partners. In the workshop, the effectiveness of the barrier was evaluated. On the basis of hydraulic and mechanical considerations, it was concluded that a condom with a hole in it still provided a significant reduction in exposure compared with not using a condom. It was also calculated that even a broken condom would, on average, provide some reduction in exposure.

On the basis of a review of literature, it was concluded that intact condoms were impervious to both HIV and HBV. It was then inferred that other viruses, being bigger, were also unable to penetrate condoms.

As far as pregnancy is concerned, it is widely believed that if the condom is properly put on, is hole-free and does not break or slip off, it will be effective. Thus there are a number of slippage and breakage studies in the literature, and these are generally used to evaluate new condom designs.

However, the workshop's conclusions about the efficacy of condoms were based almost exclusively on disease-specific human studies.

The conclusions from the book and the workshop are discussed below disease by disease.

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HIV

The book categorises the relevant studies into four types:

1. Prospective studies of seroconversion rates in serodiscordant couples
2. Meta analyses of the above studies
3. Models of transmission dynamics
4. Indirect evidence from comparison of prevalence and incidence of HIV among condom users and non-users.

A 1997 overview of 10 studies, including a meta-analysis of many of them, by Pinkerton and Abramson[v] was heavily relied on. The analysis selected studies where "never use" and "always use" were used as categories, and combined the risk ratios from those studies. The relative risks from the different studies were pooled using the Mantel-Haenszel formula. It concluded that the efficacy per contact of condoms was 95%, and that overall in the studies, the effectiveness had been 90 to 95%. Seven additional studies were reviewed, and gave efficacies in the range 50% to 95%.

The book also refers to two studies of intervention programmes which included condom promotion. The success of the interventions at reducing HIV incidence is an indicator of the effectiveness of condoms.

The workshop heard a presentation from Susan Weller, co-author of a meta-analysis of studies on discordant heterosexual couples published in 1999[vi]. Her estimate was that condoms were almost 87% effective, with a confidence interval of 60% to 96%. The earlier meta-analysis by Pinkerton and Abramson was not evaluated. Weller's analysis covered 17 studies, including all that were in Pinkerton and Abramson's analysis, but not all were used in the quantitative assessment . Because several of the studies did not have both a "never use" category and an "always use" category, the "never use" and "always use" data were taken from different studies. In her earlier analysis, Weller used a "continuity correction" for those cases where there were no sero-conversions. Basically, zero was treated as 0.5. While it is plausible that a non-zero incidence is more likely than 0, it must be accepted that 0.5 is arbitrary, and 0 is the estimate resulting from the data. Using the continuity correction reduced the risk reduction figure that was calculated. It is not known whether the continuity correction was used in the 1999 meta-analysis. The approach used by Davis and Weller, of taking "always" users from one study and "never" users

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v Pinkerton SD and Abramson PR, Effectiveness of condoms in preventing HIV transmission, Soc Sci Med, 44(9) 1997, pp 1303-1312

vi Davis K R and Weller S C The effectiveness of condoms in reducing heterosexual transmission of HIV, Family Planning Perspectives, 31 (6), 1999, pp 272-9

from another is an unusual one, and it may give rise to the risk of different exposure and other behaviour in the two groups.
The report of the workshop interestingly reduced the Davis and Weller estimate of effectiveness to 85%.

Early in 2002, Weller and Davis produced another meta-analysis of condom effectiveness[vii], available only through the Cochrane Library. This document appears to rely on the same studies as their previous meta-analysis, and appears to be largely a correction to the published paper. The conclusion from the revised analysis indicated a slightly lower level of protection. Three different figures were given, using different assumptions for the non-user group. The authors chose 80.2%, while including all "never" users gave 82.9% and transfusion/haemophiliac "never" users yielded 77.6%.

In terms of the accuracy available from the analyses, both the book and the workshop came to similar conclusions - the difference between the 87% and 95% figures is small compared with the confidence intervals of both values. Even the 2002 analysis results fall well within the 95% confidence intervals of the earlier studies.

Davis and Weller found Pinkerton and Abramson's analysis wanting because it did not have a "never" user category. Rather the authors (through necessity) grouped together the "sometimes" and "never" groups. The effect of this would be to increase the apparent effectiveness of condoms, in line with the slight differences between the two groups' results.

A newer study by Aklilu et al[viii] among sex workers in Ethiopia showed only a moderate reduction in HIV prevalence among condom users. It showed that sex workers who used condoms for contraception as well as disease prevention had lower HIV prevalence than those who used condoms for disease prevention only. Many sex-workers[ix, x] use condoms with their clients, but not with their life partners, who may themselves have other partners. The questions asked in many studies did

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vii Weller S & Davis K. Condom effectiveness in reducing heterosexual HIV transmission. The Cochrane Library, January 2002

viii Aklilu M, Messele T, Tsegaye A, Biru T, Mariam D, van Benthem B, Coutinho R, Rinke de Wit T and Fontanet A. Factors associated with HIV-1 infection among sex workers of Addis Ababa, Ethiopia, AIDS 15(1) 2001, pp 87-96

ix Day S. Ward H. & Perrotta L. Prostitution and risk of HIV: male partners of female prostitutes. BMJ. 307(6900), 1993 Aug 7 pp 359-61

x Roddy RE Cordero M..Ryan KA & Figueroa J. A randomized controlled trial comparing nonoxynol-9 lubricated condoms with silicone lubricated condoms for prophylaxis. Sexually Transmitted Infections. 74(2), 1998 Apr pp 116-9

not draw out this distinction, and the sex workers frequently do not think of mentioning their sexual behaviour with their partners.

There is much less literature on homosexual transmission of HIV. One study found an Odds ratio of 16.2 comparing seroconversion in men who never used condoms with those who always did[xi].

Gonorrhoea

The book begins by referring to a modelling study by Kretzschmar et al[xii], which concluded that even a relatively low level of condom use has a significant epidemiological effect in reducing the spread of Gonorrhoea, and other STIs.

For men, it relies significantly on the Barlow[xiii] study, which suggests a relative risk of around 30% for condom users compared with non-users. It refers also to a US Navy study, by Hooper[xiv], which when published showed a reduction that was not statistically significant, but on re-analysis by Cates and Holmes[xv], did show a statistically significant reduction in transmission. None out of 29 condom users developed the disease, compared with 51 of 499 (10.2%) non-users. The reliability of the result is limited by the small number of consistent condom users. Another cross-sectional study of 3 STD clinics in the USA gave a less impressive result, but statistically significant, result, with an Odds ratio of 0.72[xvi]. A case control study by

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xi Williams DI. Stephenson JM. Hart GJ. Copas A. Johnson AM. Williams IG. A case control study of HIV seroconversion in gay men, 1988-1993: what are the current risk factors? Genitourinary Medicine. 72(3), 1996 Jun. pp193-6

xii Kretschmar M, van Duynhoven T and Severijnen A. Modelling prevention strategies for gonorrhoea and chlamydia using stochastic network simulations. American Journal of Epidemiology, 144, 1996, pp 306-317.

xiii Barlow D. The condom and gonorrhoea, Lancet, October 15, 1977, pp 811-813.

xiv Hooper, R, Reynolds G, Jones O et al. Cohort study of venereal disease I: The risk of gonorrhoea transmission from infected women to men. American Journal of Epidemiology, 108, 1978, pp 136-144.

xv Cates W and Holmes K. Condom efficacy against gonorrhoea and non-gonococcal urethritis. American Journal of Epdiemiology, 143, 1996. 843-844.

xvi Ellen J, Langer L, Zimmerman R, Cabral R and Fichtner R. The link between the use of crack cocaine and sexually transmitted diseases of a clinic population: a comparison of adolescents and adults. Sexually Transmitted Diseases 23, 1996, 511-516.

Schwartz et al[xvii] showed significant protection with an Odds ratio of 0.31.

For women, the book quotes a study from Denver[xviii], in which condom users had a 30% reduction in incidence, but there was no attempt to categorise use by correctness or consistency. Examination of the article shows a higher reduction. A larger study by Sanchez et al in Peru[xix] gave an Odds ratio of 0.04 (mis-referenced in the book), but the result was not statistically significant (p=0.07), apparently because the number of consistent users was too low. Other studies cited gave Odds ratios from about 0.2 to 0.4. In a study conducted in London[xx], none of 106 women who always used condoms developed the disease compared with 13 out of 376 who never used condoms, suggesting a relative risk of 0.3 or less.

Other studies among Australian, Burmese, Dutch, Greek, Indonesian and Thai sex workers showed a significant degree of protection for users. Often the design of these studies did not allow the direct comparisons sought by the workshop panel. For example, an Australian study compared condom usage among local and (usually illegal) foreign immigrant sex workers. The immigrant sex workers had higher prevalence rates for all diseases assessed, and also had a much lower condom usage rate. About 14% of immigrant workers had gonorrhoea and chlamydia, compared with none of the local workers. 92% of the local workers used condoms with all their clients, compared with 21% of the immigrant workers[xxi].

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xvii Schwartz M, Lafferty W, Hughes J and Handsfield H. Risk factors for urethritis in heterosexual men. Sexually Transmitted Diseases, 24, 1997, 449-455.

xviii Rosenberg M, Davidson A, Chen J-H, Judson F and Douglas J. Barrier contraceptives and sexually transmitted diseases in women: a comparison of female-dependent methods and condoms. American Journal of Public Health, 82, 1992, 511-516.

xix Sanchez J. Gotuzzo E. Escamilla J. Carrillo C. Moreyra L. Stamm W. Ashley R. Swenson P. & Holmes KK. Sexually transmitted infections in female sex workers: reduced by condom use but not by a limited periodic examination program. Sexually Transmitted Diseases. 25(2), 1998 .pp 82-9

xx Evans B, Kell P, Bond R and MacRae K. Heterosexual relationships and condom use in the spread of sexually transmitted diseases to women. Genitourinary Medicine, 71, 1995, 291-294.

xxi O'Connor, C. Berry, G. Rohrsheim, R. & Donovan, B.Sexual health and use of condoms among local and international sex workers in Sydney. Genitourinary Medicine 72(1) Feb 1996 pp 47-51

The book also refers to three US studies on transmission in women, in which transmission of gonorrhoea in women using barrier contraceptives (not disaggregated) and other contraceptives was compared. These gave very similar results to the more specific studies quoted above.

The book also points out that there is one study that failed to demonstrate a large or statistically significant protection from condoms, and refers to some (showing a lower level of protection) in which the categorisation of users and non-users is not as rigorous as is in the ones quoted above. No specific conclusions are offered regarding the efficacy of condoms, but the overwhelming impression from the studies cited is that they provide a large degree of protection.

The workshop panel reviewed 13 studies, but found only 6 (4 for men, 2 for women) adequate to use for assessment. It referred to the US Navy study[14], and the Barlow study[13], and to the Schwartz study[17], but not to the two others in the book.. It considered the Barlow study the most reliable and reported a 71% risk reduction (as did the book).

The workshop's interpretation of the US Navy study did not take account of the Cates and Holmes analysis[15], and thus concluded that the difference in transmission rates (quoted as 0% vs 10.2%) was not statistically significant, while Cates and Holmes found that the result was statistically significant. The quantitative information (which applies only to men) adopted by the workshop is that condoms provide a risk reduction of over 70%. In the US Navy study, even if one of the condom users had developed the disease, the relative risk would have been about 0.05, and the risk reduction would be 95%.

For women, the workshop considered no study that compared infection rates between those who used condoms consistently and those who did not use condoms. The workshop refers to the study by Rosenberg et al[18] in which the only relevant categories are women who used condoms for contraception and those who used no barrier methods. There was no measure of consistency of use. Studies like the latter study can only underestimate the benefit of condoms. Nonetheless, a protective effect was seen, with 30% risk reduction quoted in the book, and a 39% " relative risk reduction" in the workshop report. The article itself gives adjusted Odds ratios of 0.61 and 0.66 on multvariate analysis, depending on the approach used in calculation.

The workshop report also looks at PID and tubal infertility as an outcome, but the studies do not distinguish whether the cause was due to gonorrhoea or chlamydia. Nonetheless, both studies showed a reduction among condom users, although in one case it was statistically insignificant, and in the other the distinction was between women that had ever used condoms, and those who had never.

The panel concluded that the literature demonstrated correct and consistent condom use caused a reduction of risk for men, but was insufficient to allow valid quantitative assessment of protection for women. .The studies cited do collectively

suggest that there is a significant level of protection, even though it is difficult to quantify precisely.

If condoms protect men, it follows that at the population level, women will be less exposed to infection as a result. Thus even if the barrier only worked in one direction, which is improbable, it can be seen that for the population as a whole, the risk to women would be decreased.

On the basis of studies quoted in the book, it is likely that the risk reduction for women is similar to that for men, even though women are more likely to get infected in a single contact than men.

Chlamydia

The book did not find any prospective cohort or intervention studies to assess prevention of chlamydia. Nonetheless there were several case control and cross-sectional studies showing a degree of protection for consistent condom users.

Odds ratios and relative risks varied, but were not as impressive as for HIV.

In the section on syphilis, the book reported on a study in Peru[xxii], in which clients of female sex workers who used condoms more than half the time over the last 12 months had a 70% lower prevalence of antibodies to syphilis, chlamydia and HSV2.

A Swedish study[xxiii]

[xxii] Sanchez J, Gotuzzo E, Escamilla J et al. Gender differences in sexual practices and sexually transmitted infections among adults in Lima, Peru. American Journal of Public Health, 86, 1996, p 1098.

[xxiii] Ramstedt K, Forssman L, Gieseke J and Granath F. Risk factors for Chlamydia Trachomatis infection in 6810 young women attending family planning clinics. International Journal of STD & AIDS, 3, 1992, 117-122.

used cultures to compare prevalence in women who used condoms and women using no contraception. The adjusted Odds ratio was 0.55. As the women were using the condoms for contraception, they may have chosen to use them only during their fertile periods. A large study of female military recruits in the USA compared chlamydia prevalence in women whose partners always used condoms with those whose partners did not, and found an Odds ratio of about 0.71[xxiv]. Other studies showing mild reductions in incidence were also quoted in the book, but none compared "always users" with "never users".

The Australian sex worker study referred to in the section on Gonorrhoea suggested a significant level of protection offered by condoms[21]. Again, the prevalence of Chlamydia in local sex-workers who used condoms over 90% of the time was 0, while about 14% of the foreign sex workers were infected with Chlamydia.

The workshop report found six studies adequate for inclusion. Three referred to transmission to women, and three to transmission to men.

One was a prospective study on transmission to men, incorrectly attributed to Zenilman et al[xxv].
It found none of 72 men who always used condoms developed the infection, while 6.3% of the 251 who sometimes or never used them developed Chlamydia. A case control study was also considered[xxvi]. It found a 33% risk reduction among consistent condom users, while the cross-sectional study found no reduction.

For women, the report discusses three studies. One, in Indonesia[xxvii], asked women sex workers whether they had used condoms in the previous week. Of those that had, 10% had Chlamydia, compared with 14% of those that had not. In the second study[15], 1.5% of women who used condoms had the disease, compared with 12% of those who had not. The third study, in US military recruits, referred to above, found a statistically higher rate of infection among non-users than among users.

Neither source reported on the results for Gonorrhoea in the Thai study[37], in which incidence at public clinics fell by 82% over the period that condom use by sex

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xxiv Gaydos C, Howell M, Pare B et al. Chylamidia trachomatis infections in female military recruits. New England Journal of Medicine, 339, 1998, 739-744.

xxv Zenilman J et al. Condom use to prevent incident STDs: the validity of self-reported condom use. Sexually Transmitted Diseases, 22(1), 1995, 15-21

xxvi Schwartz M et al. Risk factors for urethritis in heterosexual men. The role of fellatio and other practices. Sexually Transmitted Diseases, Sept 1997, pp 449-455.

xxvii Joesoef M Linnan M, Barrakbah Y, Idajadi A, Kambodji A & Schulz K. Patterns of sexually transmitted disease in female sex workers in Surabaya, Indonesia, International Journal of STD & AIDS, 8, 1997, pp 576-580.

workers increased from 14% to 94%.

In April 2001, a Japanese study[xxviii] indirectly confirmed the effectiveness of condoms by examining the incidence of chlamydia among sex workers. The proportion of sex workers with a chlamydial infection history was significantly lower in those using condoms "regularly and correctly" than in those who did not use condoms, or who use them inconsistently (Odds ratio 0.08, CI 0.01 to 0.68). A US study by Noell et al[xxix], published in January 2001, covering Chlamydia, HSV, HBV, HCV and HIV showed that inconsistent condom use was the primary factor associated with a significantly greater risk of Chlamydia and HSV2.

It is relatively recently that it has been possible to distinguish between different types of NGU, but it now appears that condoms offer some protection against non-gonococcal, non-chlamydial NGU (OR 0.59)[17]

Condom use by men is also associated with a lower risk of Mycoplasma colonisation. Their relationship to NGU is unclear (RR=0.33)[xxx].

Syphilis

The book identified a case-control study in the US, in which condom usage and the acquisition of early syphilis was studied[xxxi]. Any condom usage in the last 3 months was associated with an Odds ratio of 0.24 for men and 0.89 for women. The overall Odds ratio was 0.41. A similar result was obtained in a study of Peruvian study[19], in which female sex workers who used condoms consistently over the last 12 months had a 70% reduction of risk of current syphilis.

Studies of the relationship between positive syphilis serology and condom use yielded mixed results, with some studies showing and association and others not.

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xxviii Kimoto K. Relations between taking contraceptive pills, condom use and sexually transmitted disease history among female sex workers. Japanese Journal of Public Health. 48(4) April, 2001, pp 268-275.

xxix Noell J. Rohde P. Ochs L. Yovanoff P. Alter MJ. Schmid S. Bullard J. Black C. Incidence and prevalence of chlamydia, herpes, and viral hepatitis in a homeless adolescent population. Sexually Transmitted Diseases. 28(1):4-10, 2001 Jan

xxx McCormack W, Lee Y-H & Zinner S. Sexual experience and urethral colonisation with genital mycoplasmas. Annals of Internal Medicine, 78, 1973, pp 696-698.

xxxi Finelli L, Budd J & Spitalny K. Early syphilis: relationship to sex, drugs and changes in high-risk behaviour from 1987-90. Sexually Transmitted Diseases, 20, 1993, pp 90-95

There are also intervention studies that suggest a decline in syphilis with condom use. The book reports on two studies - one in Greece[xxxii] that showed a reduction in prevalence from 17.1% to 3.2% in 350 female sex workers over a three year period. The second was in a group of 824 female sex workers in Japan, in which syphilis prevalence fell from 7.5% to 0.3% in a three year period in which consistent condom use increased from 6.3% to 25.3%[xxxiii].

The workshop report refers to two cross-sectional studies[11, xxxiv], both of which showed a 60% to 70% reduction in prevalence of syphilis, but the results were both reported as being statistically insignificant. These were not the studies in the book. Another cross-sectional study showed no significant association between consistent condom use and positive syphilis serology among transvestite prostitutes in Rome[xxxv]. Always users had 72.2% seropositivity compared with 81.6% of those who reported inconsistent or never use. Seropositivity is a less meaningful indicator than early syphilis infection.

An Indonesian cross-sectional study[27] among female sex workers found that women reporting any condom use at all in the past week had a statistically significant lower prevalence of syphilis than those reporting no use (8% (30/380) vs 14% (141/1006)).

A case control study[31] (also referred to in the book) of 144 STD clinic attenders found a statistically significant reduction (59%) in primary syphilis infection for persons reporting any vs no condom use in the last 3 months.

Interestingly, the workshop report's analysis of the Peruvian study[22] was that there was no significant association between people who had ever used condoms and infection with syphilis, chlamydia and HSV-2. While this was true of the population as a whole, the important association noted in the book, regarding clients of sex workers whose risk fell by a factor of more than 3 if they used condoms, was not

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xxxii Roumeliotou A, Papautautsakis G, Kallinikos G & Papaevangelou G. Effectiveness of condom use in preventing HIV infection in prostitutes. Lancet, 2 (8622) 1998, p 1249.

xxxiii Tanaka M, Nakayama H, Sakumoto M, Matsumoto T, Akazawa K & Kumazawa J. Trends in sexually transmitted diseases and condom use patterns among commercial sex workers in Fukuoka City, Japan 1990-3. Genitourinary Medicine, 72, 1996, pp 358-361.

xxxiv Pemberton, J et al. Sociomedical charateristics of patients attending a VD clinic and the circumstances of infection. British Journal of Venereal Disease, 48, 1972, pp 391-396.

xxxv Gattari P et al. Syphilis serology among transvestite prostitutes attending an HIV unit in Rome. European Journal of Epidemiology, 10, 1994, pp 683-686.

noted.

It also reported on the Japanese study referred to above, although it pointed out that the study did not directly assess the relationship between condom use and syphilis infection. (Such assessments are extremely difficult in multi-faceted interventions.)

Overall, the report acknowledged that the studies suggest a protective effect, with the caveat that they were all hampered by design limitations. Therefore, no rigorous assessment of the degree of reduction offered by consistent condom use was made by the panel. Examination of the studies indicates that in most cases the comparison made was between those who did not use condoms and those who had used at least one. One must therefore conclude that the figures for reduction presented represent lower bounds for condom effectiveness.

Neither source reported on the results for Syphilis in the Thai study[37], in which incidence at public clinics fell by 68% over the period that condom use by sex workers increased from 14% to 94%.

Tropical STIs

The book quotes a study of female sex workers in Nairobi in which 16% of patients presenting with GUD (excluding Gonorrhoea and HSV) were consistent condom users, compared with 45% who never used them[xxxvi].

The workshop report identified two studies, one the Kenyan study above, although the incidence of disease among always-users was mis-reported as 18%. The other study was from Thailand, covering the Government's "100% Condom" campaign between 1989 and 1993[xxxvii]. In this period the incidence of Chancroid and Lymphogranuloma Venereum diagonsed at public STD clinics fell by about 93%, coincident with a rise in condom use by sex workers from about 14% to about 94%, despite improved access to the STD clinics.

The workshop panel felt that the above results were not reliable since the diseases were not diagnosed by culture, but rather by clinical judgement.

It is likely that Chancroid, Donovanosis and Lymphogranuloma Venereum are transmitted in the same way, and one can thus conclude that condoms offer a degree of protection against all three diseases.

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xxxvi Cameron D, Ngugi E, Ronald A et al. Condom use prevents genital ulcers in women working as prostitutes. Sexually Transmitted Diseases, 18, 1991, pp 188-191.

xxxvii Hanenberg R, Rojanapithayakorn W, Kunasol P & Sokal D. Impact of Thailand's HIV-vontrol programme as indicated by the decline of sexually transmitted diseases. Lancet 344, July 23, 1994, pp 243-245.

Effectiveness of condoms to prevent STDs J. Gerofi

The workshop report uses the term Genital Ulcer Disease in a broader way, and includes HSV, syphilis and chancroid.

Herpes Simplex Virus

The book identifies a single study designed to determine the efficacy of condoms against HSV. It was conducted in Costa Rica[xxxviii], among 766 women aged 25 to 59, randomly selected. Of the women whose partners had ever used condoms for 2 years or more, 28.9% were HSV positive, compared with 44.3% of those whose partners never used condoms. There was no information about whether the condom users used them all the time, or not. Two other studies failed to confirm a protective effect.
The workshop found five cross-sectional studies that allowed assessment of condom effectiveness against HSV transmission. None of these was judged to be designed specifically to measure condom effectiveness. Apart from the Costa Rica study, the workshop report refers to some studies that reveal a slight protective effect, and others that are inconclusive.

In the section on syphilis, the book reported on a study in Peru[22], in which clients of female sex workers who used condoms less than half the time over the last 12 months had a 70% lower prevalence of antibodies to syphilis, chlamydia and HSV2.

A study by Wald et al[xxxix], published in June, 2001, examined the effect of condom use on HSV transmission from men to women. The subjects in the study were 528 monogamous couples discordant for HSV-2 infection. Condom use was dichotomised, and two break-points were used for different determinations. These were at lifetime condom use 50% of the time and at 25% condom use during the study. The basis for these divisions, particularly the second one, is difficult to understand, especially as tabulated data in the article disaggregates condom use into 5 steps, never, 1 to 25%, 26 to 50%, 51 to 99% and always. The authors attempt to explain the 25% usage level by saying that it was close to the median usage, and that few subjects reported condom use between 25% and 100%of the time. In fact, according to the tabulated data, 31% of the subjects reported condom use between 25% and 100% of the time.

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xxxviii Oberle M, Rosero-Bixby L, Lee F, Sanchez-Braverman M, Nahmias A & Guinan M. Herpes Simplex Virus Type 2 antibodies: high prevalence in monogamous women in Costa Rica. American Journal of Tropical Medicine & Hygiene, 41, 1989, pp 296-299

xxxix Wald A, Langenberg A, Link K, Izu A, Ashley R, Warren T, Tyring S, Douglas J & Corey L. Effect of condoms on reducing the transmission of Herpes Simplex Virus Type 2 from Men to Women. Journal of the American Medical Association, 285 (24) 2001, pp 3100-3106.

There was a strong risk reduction associated with lifetime condom use (>50% of the time). This was 0.08 (CI 0.01 to 0.60) apparently for both sexes combined. There was also a table from which a simple Odds ratio for always use against never use (during the study) could be calculated. This came to 0.053 for both sexes combined.

Further multivariate analysis was carried out based on condom use during the study, with the break point at 25% usage. The adjusted risk ratio for acquisition was 0.25 (CI 0.07 to.88). This was further disaggregated by sex, and it was concluded that women were protected but men were not. The authors state an adjusted risk ratio of 0.085 for women, and 2.02 for men. This last figure is surprising to say the least, especially in view of material in the text that states that only 5 men acquired the disease, and that only two of these reported condom use more than 50% of the time. One must conclude that the risk ratio of 2.02 is an artefact of the low numbers involved, the break-point chosen to dichotomise condom use, and the modelling.

This is a longitudinal cohort study in discordant couples, very similar in design to those used to establish the effectiveness of condoms in preventing HIV infection. It is complicated by the use of Acyclovir to suppress symptoms, and presumably reduce the risk of transmission. It was also originally designed to test a vaccine (which turned out to be ineffective), but the data were then re-analysed to examine the effect of condoms. It is the most definitive study on HSV and condoms so far.

Trichomonas Vaginalis

The book refers to five studies that showed a degree of protection against trichomonas. A Taiwanese study[xl] with almost16,000 women showed condom usage was associated with a 60% reduction in risk of trichomonas. It was diagnosed on pap smear samples, but the test is relatively unreliable one..

A study by Rosenberg et al[18] gave a 70% Odds ratio for women who used condoms as their main method of contraception, compared with women who had no method or had had a tubal ligation. Thus there was no measure of whether the women used condoms all the time.

Another study[xli] reported approximately 45% risk reduction among condom users,

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xl Wang P & Lin R. Epidemiologic differences between candidal and trichomonal infections as detected in cytological smears in Taiwan. Public Health, 109, 1995, pp 443-450.

xli Fennema J, van Ameijden E, Coutinho R & van den Hoek A. Clinical sexually transmitted diseases among HIV-infected and noninfected drug-using prostitutes. Sexually Transmitted Diseases, 24, 1997, pp 363-371.

compared to non-users or seldom-users (the division between user and non-user was not the same in the two studies), and the last two gave an unquantified risk reduction.

The workshop found only one study was of adequate standard to review. This was the Rosenberg study mentioned above.

HPV

HPV is a difficult virus to study. There are over 40 different sub-types, of which some are known to cause malignant cervical tumours, and others are believed to cause only genital warts and similar cervical lesions, as well as low-grade pap smear abnormalities. The more serious disease outcomes appear only years after initial infection, and it is believed persistent infection is necessary for these outcomes. The incubation period of warts is unclear. Most infections appear to clear up spontaneously, but infections are very common and it has been estimated that prevalent (usually asymptomatic) HPV infection is present in about 30% of sexually active adolescent girls and young women in the USA.

Design of a good study to detect HPV infection and correlate it with prior condom use is therefore extremely difficult, and would need to start with HPV-free volunteers, who would have to come into sexual contact with infected persons. Diagnosis of infection (and checking of status of volunteers) would need to be done by DNA PCR or some similar technique. The trial would presumably have to last many years. The validity of HPV serology in relation to epidemiological studies is, however, still being determined.

The book identifies eight studies on HPV and condoms, of which three showed no protection. The other five showed a degree of protection. A case-control study, by Wen et al[xlii] reported a reduction (of over 50%) in genital warts among both men and women who used condoms. The degree of protection was higher for men than for women (Odds ratios about 0.25 and 0.4 respectively). The other studies quoted covered clearance rate of warts in men[xliii], prevalence of flat cervical warts[xliv],

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xlii Wen L, Estcourt C, Simpson J & Mindel A. Risk factors for the acquisition of genital warts: are condoms protective? Sexually Transmitted Infections, 75, 1999 pp 312-316

xliii Hippilainen MI, Hippilainen M, Saarikoski S & Syrjanen K. Clinical course and prognostic factors of HPV infections on men. Sexually Transmitted Diseases, 21, 1994, pp 272-279.

xliv Syrjanen K, Vayrynen M, Castren O et al. Sexual behaviour of women with HPV lesions of the uterine cervix. British Journal of Venereal Diseases, 60, 1984, pp 243-248.

squamous carcinoma of the cervix[xlv] and carcinoma in situ or invasive cervical cancer[xlvi]. This last study had a relative risk of 0.2, suggesting a high degree of protection.

The workshop report was critical of the fact that published studies had used disease (rather than infection) as their outcomes. However the PCR tests have only recently become available, and thus older studies could not possibly have measured infection. Having to use such a test means that clinical data from people presenting with symptoms of HPV infection would not be adequate, resulting in a massive increase in the cost of collecting data.

The report nonetheless found 16 studies adequate to review. Of these, 11 were case-control studies, four were cross-sectional studies and one was a cohort study. Fourteen of the studies investigated only women, one investigated only men, and one looked at both men and women. The outcomes used varied, including HPV infection, genital warts, cervical intra-epithelial neoplasia (CIN) and invasive cervical cancer. Only four of the 16 studies were considered in the book.

Four studies looked at condoms as a factor in the risk of acquiring the infection. None of these reported a risk reduction for HPV infection associated with condom use.

Genital warts were investigated in two studies[xlvii, 42]. Both reported risk reduction in men. Only one provided data on women, but the report stated that the risk reduction for women (of about 30%) was not statistically significant. The tables in the original reference suggest that the reduction was indeed statistically significant, and that the reduction itself was over 50%. For the same reference, the report states a risk reduction of 52%, but a better estimate appears to be about 60%.

In 10 of the studies, the outcome was cervical dysplasia, carcinoma in situ or invasive cancers. They were either case-control studies or cross-sectional studies. Of these, six showed a statistically significant reduction in risk, ranging from 39% to 80%. Two others showed risk reductions that were not statistically significant, and the remaining two found no evidence of protection.

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xlv Thomas D, Ray R, Pardthaisong T et al. Prostitution, condom use and invasive squamous cell cervical cancer in Thailand. Americam Journal of Epidemology, 1, 1990, pp 266-272.

xlvi Kjaer S, de Villiers E-M, Dahl C et al. Case control study of risk factors for cervical neoplasia in Denmark. 1: role of the male factor in women with one lifetime sexual partner. International Journal of Cancer, 48, 1991, pp 39-44.

xlvii Hippelainen M et al. Prevalence and risk factors of genital HPV infections in healthy males: A study on Finnish conscripts. Sexually Transmitted Diseases, 20(6), 1993, pp 321-328.

The panel concluded that there was no evidence of risk reduction for HIV infection, but that was a suggestion that condom use might afford some reduction of HPV-associated diseases. Considering that eight out of 12 studies showed a reasonable level of protection from HPV-related disease, this seems to be a very pessimistic interpretation.

While there are possible explanations for how condom use could prevent the manifestation of an HPV-related disease in an infected person, the more likely explanation is that the condoms prevent infection in the first place. The workshop did not propose any mechanism along the former lines, and a basic principle of scientific inference is to accept the simplest of a range of explanations unless there is a reason not to do so.

Two recent studies both demonstrate a degree of protection. Slavinsky et al[xlviii] studied seroprevalences of HPV 6/11 and 16 among STD clinic attendees (predominantly male). Condoms were found to be partially protective against HPV 16, but not HPV 6/11. The simple Odd ratios were 2.14 (95% CI, 0.96 to 4.76) for HPV 16 and 1.25 (95% CI 0.6 to 2.63) for HPV 6/11. Adjusted Odds ratios were not presented for condom use. A Mexican study among female sex workers by Juarez-Figueroa et a[xlix]l used DNA amplification to test for 27 HPV types. It showed an Odds ratio of 2.3 for non-users of condoms over users.

Hepatitis B and C

Hepatitis B is often transmitted sexually. Hepatitis C is occasionally transmitted sexually. It is known that in vitro, intact, hole-free condoms are impervious to these

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xlviii Slavinsky J, Kissinger P, Burger L, Boley A, DiCarlo R and Hagensee M. Seroepidemiology of low and high oncogenic risk types of HPV in a predominantly male cohort of STD clinic patients. International Journal of STD and AIDS, 12(8), 2001, pp 516-523.

xlix Juarez-Figueroa L, Wheeler C, Uribe-Salas, F Conde-Glez C, Zampilpa-Meija L, Garcia-Cisneros S & Hernandez-Avila M. HPV: A highly prevalent sexually transmitted disease among female sex workers from Mexico City. Sexually Transmitted Diseases 28(3) 2001, pp 125-130.

viruses. There are no clinical studies that relate Hepatitis B transmission and condom use. There is one study on risk factors for Hepatitis C acquisition, but that did not identify condoms as protective. As the most common transmission routes for Hepatitis C are not sexual, it would require a very large study to establish the effect of condoms in this respect.

Longer Term Issues

Risk ratios and Odds ratios are derived from clinical studies which deal with the probability of a single individual becoming infected over a limited time. The risk of becoming infected during any one sexual encounter is proportional to the product of a number of terms, including the probability of the partner being infected. In populations where sexually transmitted diseases are spreading, the fact that one infection has been prevented means that in a subsequent encounter, the probability of the infection being spread is reduced. This effect is not measured in clinical trials, and increases the long-term benefit to the population of any preventative measure.

Epidemiological modelling is necessary to determine the magnitude of this effect.

Non-Latex Male Condoms

As far as this reviewer can ascertain, there is no published clinical information on the efficacy of non-latex condoms in disease prevention. These products are relatively new, they are relatively expensive and their market penetration is small.

One must expect that unless the usage of non-latex condoms increases considerably, it will be many years before sufficient clinical data are assembled to enable any reliable conclusions to be drawn about their ability to prevent sexually transmitted infections.

On the other hand, there are five recent published studies comparing slippage and breakage of non-latex condoms with latex condoms[l, li, lii, liii, liv]. While slippage rates are

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[l] Cook L, Nanda K & Taylor D. Randomised crossover trial comparing the eZ.on plastic condom and a latex condom. Contraception, 63(1), 2001, pp 25-31.

[li] Callahan M, Mauck C, Taylor D, Frezieres R, Walsh T, & Martens M. Comparative evaluation of three Tactylon and a latex condom during vaginal intercourse: slippage and breakage. Contraception 61(3), 2000, pp 205-215.

[lii] Frezieres R, Walsh T, Nelson A, Clark V & Coulson A. Evaluation of the efficacy of a polyurethane condom: results from a randomised controlled clinical trial. Family Planning Perspectives, 31(2) 1999, pp 81-87.

[liii] Frezieres G, Walsh T, Nelson A, Clark V & Coulson A. Breakage and acceptability of

comparable, the studies suggest a higher breakage rate for the non-latex products. The actual breakage rates reported vary. The studies were performed by independent groups, and they found breakage rates between 4 and 6.5 times the latex breakage rates, except in one of the studies. The earliest studies on these products, including those done for the manufacturers, reported breakage rates comparable to those of latex condoms.

One small study was performed by the developers of a particular condom design[lv]. It concluded that the slippage and breakage rates for the new device were similar to that of the latex condom. A similar conclusion was reached in a clinical trial done to support the approval for marketing in the USA of the Avanti condom, although subsequent studies concluded the contrary (as above).

One of the independent studies[52] above also measured the 6-month pregnancy rate for polyurethane and latex condoms. Among consistent users, it was 2.4% for the polyurethane condoms and 1.1% for the latex ones. The difference was not statistically significant, but given the difference in breakage rate, would probably be confirmed in a larger study.

On the basis of the limited information available, it must be concluded that the present generation of non-latex condoms (polyurethane and SBS) are probably less effective at preventing STIs than latex condoms. Given the high price and lack of market penetration of these devices, it will be difficult and expensive to quantify their efficacy in this respect.

Female Condoms

The female condom is a special case of a polyurethane (non-latex) condom. Data from clinical studies suggest that the pregnancy in women using the female condom is almost twice that for male condoms. Only one study is known to this reviewer that examines disease prevention using female condoms[lvi]. This study offered one group of users both make and female condoms, and the control group male condoms only. There was virtually no difference in disease outcomes between the two groups.

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a polyurethane condom: a randomised, controlled study. Family Planning Perspectives, 30(2), 1998, pp 73-78.

[liv] Frezieres R, & Walsh T. Evaluation of a natural rubber latex, a polyurethane, and a new non-latex condom. Contraception 61(6) 2000, pp 369-377.

[lv] Farr G, Katz V, Spivey S, Amatya R, Warren M & Oliver R. Safety, functionality and accetpability of a prototype polyurethane condom. Advances in Contraception, 13(4), 1997, pp 439-451.

[lvi] Feldblum PJ. Kuyoh MA. Bwayo JJ. Omari M. Wong EL. Tweedy KG & Welsh MJ Female condom introduction and sexually transmitted infection prevalence: results of a community intervention trial in Kenya. AIDS. 15(8):1037-44, 2001 May 25.

Given the good film properties of the device, one must conclude from the pregnancy data that there is either a design problem (the penis can pass beside the device rather than into it, or the outer ring gets pushed into the vagina) or there is a user failure (probably not inserting the device).

Although the female condom may potentially provide a barrier covering more of the genitals than the male condom, it does appear from the pregnancy data that the latter is more effective in practice, and one would therefore expect a lower level of protection from the female condom than from the male condom. However, there are no direct clinical data to verify that.

Discussion

The approach of the workshop was to say that condoms offered protection only when there was convincing evidence that they did so. It appears that the report had the aim of quantifying the relative risk of infection with and without condom use. It decided studies that used clinically diagnosed disease as the outcome were not as useful as those which actually determined infection by pathology tests. In addition, the workshop was constrained by 95% confidence limits. Any study in which the Odds ratio's or relative risk's 95% confidence interval included 1.0 was deemed to a have a statistically insignificant outcome, and was in many cases not integrated into the overall conclusion.
This is the standard epidemiological approach for situations where a null hypothesis (in this case that condoms have no protective effect) is put forward and tested. The null hypothesis is only rejected when there is only a very small probability (conventionally 5% or less) that it is true.

Yet the 95% confidence interval is an arbitrary but commonly used indicator of the degree of certainty that a particular conclusion did not occur by chance. If the 95% confidence interval for an Odds ratio or relative risk just covers 1.0, that simply means that the probability of the effect not being protective is in excess of 2.5%. If a 90% confidence interval had been chosen as the standard yardstick then more of the studies would have been taken as giving a significant result.

The workshop also tended not to take into account studies that reported on changes in STD incidence overall, rather than specifically by disease, and studies that reported on decreases in STD incidence which coincided with increases in condom use (but were not specifically linked in a controlled trial).

While such studies usually cannot provide quantitative measures of protection, they nonetheless provide considerable corroboration for those controlled studies that are available.

To the scientifically trained, the conclusions of the workshop are in line with the approach outlined above, although in several cases, the figures presented appear

pessimistic about condom effectiveness. Key cases are:

* Use of Davis and Weller's results for HIV, while not referring to Pinkerton and Abramson's study. The prevalence of GUD in condom users in one study was also over-stated at 18% instead of 16%.

* The use of the original US Navy study analysis to determine condom effectiveness against gonorrhoea, rather than the corrected analysis by Cates and Holmes

* Not considering several studies on gonorrhoea transmission to women, which, although individually not statistically significant, nonetheless point to a protective effect of similar magnitude to that found for men.

* Treating as statistically insignificant the result for male to female transmission in the Wen study on HPV transmission and condoms.

* Conceding that condoms may prevent some diseases related to HPV, but not that they may actually reduce HPV transmission

* Failure to consider long term beneficial population effects of partial protection, as can be demonstrated by mathematical modelling of prevalence rates.

* Not taking into account studies that suggest a protective effect without giving a quantified reduction.

The workshop thus drew conclusions based on an epidemiological paradigm, although some of the ways in which it treated some data are debatable. The paradigm required a very high level of confidence that condoms are effective before the workshop report said they were. It appeared to be seeking to quantify protection.

There are formidable difficulties in determining a numerical value for the protective effect of condoms. The cost of doing studies that determine the figure to the level of certainty desired by the workshop is most likely prohibitive and the money may be better spent elsewhere. The transmission of a disease from one individual to another depends on a wide range of factors (involving the individuals, what they are doing, and the condoms), and in the field of sexually transmitted diseases, studies that can explore all of these systematically have not yet been done. Thus overall effectiveness measures as determined from clinical studies will of necessity differ, and care must be taken in translating such measures back to probable outcomes for specific individuals.

For most diseases, there were some studies which demonstrated a protective effect from condoms, and some which did not. On the other hand, studies that indicated that condoms actually caused harm, by increasing transmission were rare (one - and this anomalous finding is questionable on theoretical grounds). It thus appears that overall, the protective effect is not a statistical artefact, but there is still a difficulty in quantifying the effect. This does not mean that most of the studies referred to were flawed, rather that many of them had a different primary focus.

It is also necessary to consider what is the appropriate public health message for the lay public. Given the inherent imprecision of all the determinations of effectiveness available, and the need to offer the best possible advice to people seeking to avoid infection, it seems more appropriate to base that advice on the actual values of risk ratio or Odds ratio determined in the various trials.

In many cases, the results from case-control or prospective studies are not as definitive as one would desire, especially if the confidence interval is very wide. It is nonetheless necessary to give people guidance on whether condoms are useful in preventing various STIs. Under such circumstances, it is appropriate to reinforce the conclusions from longitudinal and case-control studies using logical reasoning, biological plausibility and less rigorous studies like cross-sectional, intervention and ecological studies to form an interim judgement, and deliver the most responsible public health message.

Conservative elements in the USA are arguing that as condoms do not provide perfect protection against STIs it is irresponsible to promote their use, instead of promoting abstinence and fidelity. While condoms are not fully effective, it must be recognised that abstinence is not 100% effective in practice either, and advocacy of abstinence is even less effective. People who intend to abstain do not always do so, and if they are unprepared for their lapses, then it is likely that they will not have a condom ready to provide protection. In fact, the workshop's approach was to require rigorous proof that condom use is effective to prevent diseases among sexually active people, but the alternative offered was abstinence and fidelity.
There is no comparative study as showing the relative effectiveness in disease prevention of advocating condom use and advocating abstinence.

There is thus no benefit in underestimating condom efficacy, unless it underpins some ideological commitment to discouraging condom use.

Given the wide range of results in different studies, any consensus estimate of condom effectiveness must be approximate. Some indicative estimates follow.

HIV has been most thoroughly studied. The general consensus appears to be that 100% condom use reduces the risk of infection by a factor of about 6 to 10 or more. The effect on other diseases has not been as thoroughly studied, and it appears from the incomplete data available that the protective effect for most of them is not as great as for HIV.

Overall, a high level of protection, reducing infection by a factor of 3 to 4 or more is likely with gonorrhoea, and syphilis and other genital ulcer diseases. While condoms cannot be expected to provide protection against ulcers which they do not cover, it appears from the clinical data that the most vulnerable route of transmission involves the organs inside the labia majora in women, and the penis in men.

With chlamydia, there appears to be moderate protection, reducing infection by about

a factor of 2. The level of protection against HSV2 previously appeared to be only moderate, but a new study now suggests a high level of protection (10-fold or more), at least for women. This result presumably depends on the main routes of infection being covered by the condom. The data on HPV also suggest a risk reduction of around 50%, but it depends on the virus sub-type.

If one had to give a judgement based on logic and biological plausibilty, one would probably conclude that the transmission of diseases spread by genital secretions, such as gonorrhoea and HBV, is likely to be governed by similar mechanisms to HIV, and that more extensive and carefully controlled clinical trials could show higher levels of protection for these diseases than the present clinical evidence does. People with damaged skin around the genital area would probably be more vulnerable. The potential for condoms to reduce the spread of ulcerative diseases is probably less than for the discharge diseases.

There may be differences in effectiveness depending on the direction of transmission, although the clinical data are insufficient to draw this conclusion. Women are more vulnerable to most STIs than men, and because the transmission efficiency depends on the direction, the measured protective effectiveness may depend on the time over which the study is conducted, and differ between men and women.

The effectiveness of non-latex condoms, including female condoms, has had very little study, but it seems likely that the present products will be slightly less effective than latex condoms.

Apart from the level of protection an individual may receive from condoms, they also have an epidemiological impact. Mathematical modelling suggests that a relatively modest reduction in transmission due to condom use can change an increasing rate of incidence to a decreasing one and hence end an epidemic.

Clearly, the conclusions about effectiveness remain imprecise, although less so in the case of HIV, where most of the recent condom-effectiveness studies have been concentrated. More precision could possibly be gained from larger, more carefully designed studies, but the cost of these is likely to be very high. It may be difficult to do similar studies in the future, as there would be a need to treat the participants, resulting in transmission under different circumstances, and much higher costs. More elaborate case control studies on the curable diseases may be possible.

Another approach would be to employ an STI specialist, a bio-statistician and an epidemiologist to re-analyse selected existing studies by approaching the authors to obtain access to their raw data. This could give rise to more meta-analyses that could improve our estimates of the level of protection. Whether the original data has been kept, whether the authors would grant access to it and whether it could be re-structured to produce more meaningful conclusions are all open to question.

In any case, one needs to consider the purpose and potential gain from devoting resources to trying to make more precise quantities that depend on so many variables

including human behaviour. It is also necessary to consider the potential public health outcomes, and hence the message to the lay public.

If condoms were used always in high risk situations, the rate of HIV infection would drop by around 80 to 90%. This alone would be an enormous benefit to many countries, especially those in Africa and Asia. Even if the incidence of HIV and other sexually transmitted infections fell by a factor of 2, it would still be an enormous benefit.

Conclusions

While it would be irresponsible to claim 100% protection from condoms, it would be equally irresponsible to underestimate their effect, and to not make people aware of their potential.

The information on HIV, the most dangerous virus is the most extensive, and it indicates unequivocally that condoms give a very high level of protection. It also appears that condoms give very good protection against HSV, although the evidence is not as extensive.

For some other diseases, including gonorrhoea, and syphilis and other genital ulcer diseases, there appears to be a reasonable level of protection.

For HPV and Chlamydia, there appears to be some protection, also.

In addition to the effects on the individual user, condom use has population effects, which could turn an epidemic into a disease whose incidence rate decreases over time.

Taking into account all the available evidence, one must conclude that sexually active people at risk of contracting STIs are best advised to use condoms.

There is no clinical evidence on the effectiveness of non-latex male condoms or female condoms against STIs, but deduction from their behaviour in pregnancy trials and slippage and breakage trials suggests they may be less effective than latex condoms.

ANNEX - PARAMETERS FOR MEASURING EFFECTIVENESS

Generally, only prospective cohort studies and case control studies yield quantitative measures of condom effectiveness.

Essentially, most such studies compare the probability of getting a disease when using condoms with the probability when not using them. The most common measures are the Odds ratio and the relative risk (or risk ratio).

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The definition and connection between the two is illustrated below for a prospective study, with numbers as an example, and letters, for more general reference:

	Person gets disease	Person does not get disease	Total
Used condom	1 a	29 b	30 a+b
Did not use condom	9 c	21 d	30 c+d
Total	10 a+c	50 b+d	60 a+b+c+d

Odds in simple probability refers to the probability of event occurring, divided by the probability that it does not occur. In the above example, the Odds of getting a disease if the person used a condom is 1/29. Simply, this is a/b, but it can be written exactly in terms of the definition as [a/(a+b)]/[b/(a+b)] . In other words people using condoms are 29 times more likely not to get the disease as to get it.

The Odds ratio is the ratio of the Odds when the condom is used, to the Odds when the condom is not used. This works out at (a/b)/(c/d) = ad/bc, or 0.08 in this example. (Simple Odds are defined as the probability of getting the disease divided by the probability of not getting it.)

The relative risk is defined as the probability of getting the disease when using a condom, divided by the probability of getting the disease when not using one. This works out at [a/(a+b)]/[c/(c+d)] = a(c+d)/c(a+b), or 0.11 in the example..

For both the Odds ratio and the relative risk, a value of 1 indicates there is no effect from using the condom, a value close to 0 or very high indicates there is a big difference between using and not using the condom.

Effectively, either measure can be used for such two by two classifications. The risk ratio is easier to understand, but the Odds ratio is easy to calculate and has interesting mathematical properties. It can be calculated in exactly the same way in case control studies. Odds ratios are also used in multivariate analysis by logistic regression.

If condoms are effective to any degree at all (thus making the Odds ratio and risk ratio less than 1), the Odds ratio, as defined above, will always be less than the risk ratio. If the disease concerned is rare, then a<<b and c<<d. In such cases, the Odds ratio approximately equals the relative risk.

Clearly Odds ratio and relative risk can be defined inversely, that is with the unprotected case as the numerator. In that case, a high number indicates good protection.

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Other terms used in evaluating condoms are efficacy and risk reduction. They are essentially identical. Efficacy is defined as (1 - relative risk) where the relative risk is the failure rate using condoms divided by the failure rate for non-users. It may be expressed as a fraction or a percentage.

For cohort or prospective studies, it is normal to have protected (condom users) and unprotected (non-users) groups, and to measure the numbers infected and not infected in each group. In that way all the terms in the table are known, and it is possible to calculate the risks for users and non-users, the risk ratio and the Odds ratio directly.

In case-control studies, people presenting for treatment of particular diseases are matched with uninfected people with similar histories, and their prior exposure to infection is assessed (mainly by interview). Thus people with an STD would be asked about their previous condom use, and also matched with people who did not have the STD, who would also give information about their condom use. In this case, the Odds ratio can be calculated directly in exactly the same way as for the prospective study. On the other hand, the risk of developing the disease, either with or without condoms, while calculable from the table, is not directly available from a single group of subjects who were exposed. Once the table is filled in from data in the case control study, the risks can be estimated, nonetheless.

For the case control study, the table of possible outcomes is shown below:

	Person presents with disease	Persons without disease selected as controls	Total
Used condom	1 a	29 b	30 a+b
Did not use condom	9 c	21 d	30 c+d
Total	10 a+c	50 b+d	60 a+b+c+d

Normally, the number of controls is made equal to the number of cases, but in some cases it is chosen to be different. In mathematical terms, the bottom total (b+d) is the number under the researcher's control. The sums (a+b) and (c+d) are thus meaningless quantities, and any attempt to calculate a relative risk on that basis will give a result that is clearly dependent on the number of controls selected, since one would expect that the proportion using condoms in the control group should be independent of the sample size.

It is thus not normally possible to calculate relative risk directly from such a table in a case control study, while it is possible to calculate the Odds ratio, since multiplying the numbers in a column by a constant will not alter the Odds ratio.

Let us assume that there is a certain prevalence (P) of the disease in the population being studied.. Then we could notionally scale the total number of controls chosen, so that the ratio (a+c)/(a+b+c+d) = P. If the control sample has been well selected, then the ratio b/(b+d) (the proportion of disease-free people satisfying the criteria to be controls) is independent of the sample size (b+d). So the entire control column can be multiplied by any constant without affecting the validity of the table, except for the right hand column.

If the number of controls were chosen as above so that (a+c)/(a+b+c+d) = P, then the table could be used to calculate both the relative risk and Odds ratio. On the other hand, the formula for the Odds ratio involves only the ratio b/d - which is invariant no matter how the column is scaled. Therefore, the Odds ratio can always be calculated from the results of a case control study, no matter whether the disease prevalence is known or not, but to calculate the risk ratio directly, the size of the control sample must be related to the disease prevalence (which must be known) as above.

Odds ratios and relative risks are determined from a sample, and the results from the sample are used as an estimator for the values for the population. There is always some uncertainty associated with applying sample results to the whole population. The measure conventionally used to indicate this dispersion is the 95% confidence interval. There is a 95% probability that the population Odds ratio or risk ratio lies within this interval. It can be calculated from the sample data.

The conventional interpretation of an Odds ratio or risk ratio is that if the confidence interval does not include the value 1.0, then the result is clear, and is described as statistically significant. For example, if the relative risk of getting a disease when using condoms compared to not using condoms is being determined, a relative risk of 0.6, with a confidence interval of 0.3 to 0.9 means that the condoms are protective. If the confidence interval were 0.2 to 1.1 then although the result suggests that condoms are protective, there is more than 2.5% probability that the true mean is more than 1.0. Under those circumstances, the result is deemed to be not statistically significant, and essentially the study has not proved anything, although the result is highly suggestive that condoms are protective. Such findings may justify a repeat study, with a larger sample.

Odds ratios may also be derived from multivariate analyses. These are termed adjusted Odds ratios, since the multivariate analysis accounts for confounding variables before calculating the ratios. Essentially, the adjusted odds ratio is the odds ratio for the variable being considered, with all the other variables held constant. The most common form of multivariate analysis is logistic regression. This uses a particular mathematical formula to model the effect of each variable.

In some studies there is insufficient detail on the behaviour of individuals to enable calculation of Odds ratios or risk ratios. Such studies may still provide indirect evidence of a protective effect for condoms. Examples are indicated later in this paper.

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Cohort and case-control studies generally concentrate on the incidence of diseases, that is new infections found during the study. Cross-sectional studies are normally able to measure only prevalence of diseases - with incurable diseases this can only increase, unless the disease is fatal. Nonetheless, prevalence studies comparing condom users and non-users can provide useful indicative information about condom effectiveness..