一人でやらないことがエラーを防ぐ上で重要である。また日本からのレビューではEmbaseをいれていないことが多いが、データベースに偏りがないことも重要である。コクラン系統的レビューでは、検索から1年以内に出版することを義務づけているため、検索してから投稿までスピートが必要になる。

E. 健康危険情報

　該当なし

F. 研究発表

　1. 論文発表

　なし

　2. 学会発表

　なし

G. 知的財産権の出願・登録状況

　1. 特許取得

　　なし

　2. 実用新案登録

　　なし

　3. その他

　　なし

DALYs を活用した食品由来疾病対策の政策評価モデルの構築

研究分担者　　西浦　博　東京大学大学院医学系研究科国際保健政策学　助教

研究要旨

　本研究班（食品安全行政における政策立案、政策評価に資する食品由来疾患の疫学的推計手法に関する研究）では食品由来疾患の被害実態を人口の疾病負荷として把握し，障害調整生存年（disability-adjusted life years ; DALYs）を用いて被害実態を推定することを主眼に研究プロジェクトを遂行してきた．特に，カンピロバクター属菌，サルモネラ属菌および腸管出血性大腸菌（EHEC）に由来する食品由来疾患を調査対象に据えて，原因食品や感染自然史の詳細はもちろんのこと，個々の疾患の DALYs を時系列で推定してきた．本分担研究では，これら調査に基づく DALYs を活用することによって，食品由来疾患の疾病負荷を異なる疾病間で比較し，個々の予防策について，その費用対効果も含めて検討することを目的に今年度から構想を開始したものである．現在進行中の具体的事例として食肉への HACCP 導入による細菌性食中毒の予防効果の推定ならびに費用対効果の推定研究を開始した．コンパートメント型モデルを用いて感受性を有する者が一定の感染ハザードを経験することを仮定し，カンピロバクター族菌とサルモネラ菌の両方の感染が起こるモデルを構築し，HACCP によって食鳥の汚染リスクが下がることによる食中毒予防の費用対効果を検討した．予備的検討の結果，カンピロバクター属菌単独あるいはサルモネラ属菌単独の対策では十分な費用対効果を達成することが困難であるが，HACCP は病原体特異的に作用するものでなく 2 つ以上の食品由来疾病に同時に作用する可能性が期待され，その場合には十分に費用対効果に優れた結果が得られるものと期待された．今後，HACCP における 1 つひとつの過程の定量化あるいは 1 種類の消毒薬の効果などに焦点を絞って統計学的推定に着手することが必要と考えられた．

A．研究目的

　本研究班（食品安全行政における政策立案、政策評価に資する食品由来疾患の疫学的推計手法に関する研究）では食品由来疾患の被害実態を人口レベルの疾病負荷として定量的に把握し，障害調整生存年（disability-adjusted life years ; DALYs）を用いて被害実態を推定することを主眼に研究プロジェクトを遂行してきた．特に，カンピロバクター属菌，サルモネラ属菌および腸管出血性大腸菌（EHEC）に由来する食品由来疾患を調査対象に据えて検討を

進めた．公表された統計資料や系統的レビューに基づき，原因食品や感染自然史の詳細はもちろんのこと，個々の疾患のDALYsを時系列で推定してきた．本分担研究の目的は，これら調査に基づく DALYs を活用することによって，食品由来疾患の政策評価を考案することである．

そもそも，DALYs を活用する利点として以下の4点が挙げられる：

①単純な病気の発生頻度に留まらず，当該疾病の社会的損失として数値を解釈することが可能であること．

②異なる疾患を同じ尺度で測るため，罹患率や有病率などの指標では全く比較することができない疾病について明示的な比較が可能であること．

③食品由来疾患に関して何らかの予防的介入を実施したときの費用対効果を推定することが可能であり，特定の疾病対策が経済的に許容できる範囲にあるのか否かを明示的に評価することが可能であること．

④その他の医療経済評価，例えば費用便益分析などの基礎を形成することが可能であること．

関連する分析には数理モデルを用いることがあるが，数理的検討は必須と考えられた場合のみに実施すべきである．本報告書で記載する予備的研究では費用対効果分析を念頭に研究を実施しているが上記のDALYs の有用性を念頭に他の用途も含めて使用する術を考えつつ本研究を遂行した．

B．研究方法

B-1．食中毒対策のコンセプトモデル

図 1 に食中毒対策として実施するHACCP の費用対効果分析に関するコンセプトを示す．カンピロバクター属菌およびサルモネラ属菌の食品由来感染は食鳥を原因とするものが最も頻度が高いため，本研究では鳥肉の製造・加工過程に注目してHACCP の効果を分析することとした．HACCPが実施されていないときのDALYs損失が X_0 であったとする．もちろん，それには費用を要さない．一方，HACCP を導入して流行対策の費用が C を要するとき，その DALYs 損失が X_1 に減少する．費用対効果分析では増分費用効果比（ICER）を用いて同対策に要する費用が正当化されるものであるのかを検討する．ICER は以下で与えられる．

$$ICER = \frac{C}{X_0 - X_1} \qquad [1]$$

ICER は生存年 1 年を獲得するために要する対策費用を表す．閾値を利用する場合は，生存年 1 年につき英国では 3 万ポンド，米国では 5 万ドルが許容可能上限とされることが多い．これは日本円で換算すれば 1 生存年あたり 500 万円程度に相当する．

B-2．数理モデル

図 2 にコンパートメントモデルの概略を示す．消費者（感受性宿主）X は時間当たりの感染ハザード λ_c をカンピロバクターに，λ_s をサルモネラに関して経験しており，感染者 Y_1 あるいは Z_1 となる．同時感染（混合感染）は稀であるため無視できるものとする．2 つの疾患の間には交差免疫がないため，それぞれ感染後に他方に感染するリスクが残る．
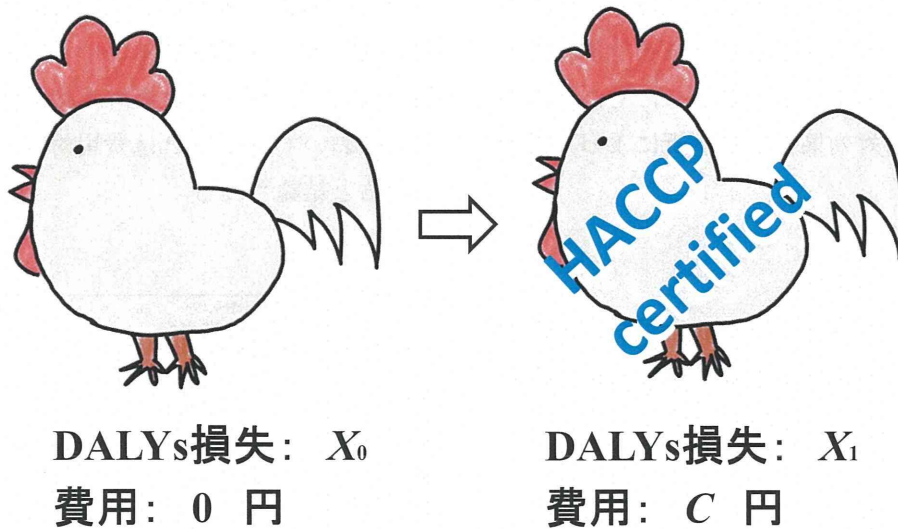
DALYs損失：X_0
費用： 0 円

DALYs損失：X_1
費用： C 円

図1．食中毒対策のコンセプトモデル

HACCP が実施されていないときの DALYs 損失が X_0 であったとする．もちろん，それには費用を要さない．一方，HACCP を導入して流行対策の費用が C を要するとき，その DALYs 損失が X_1 に減少する．

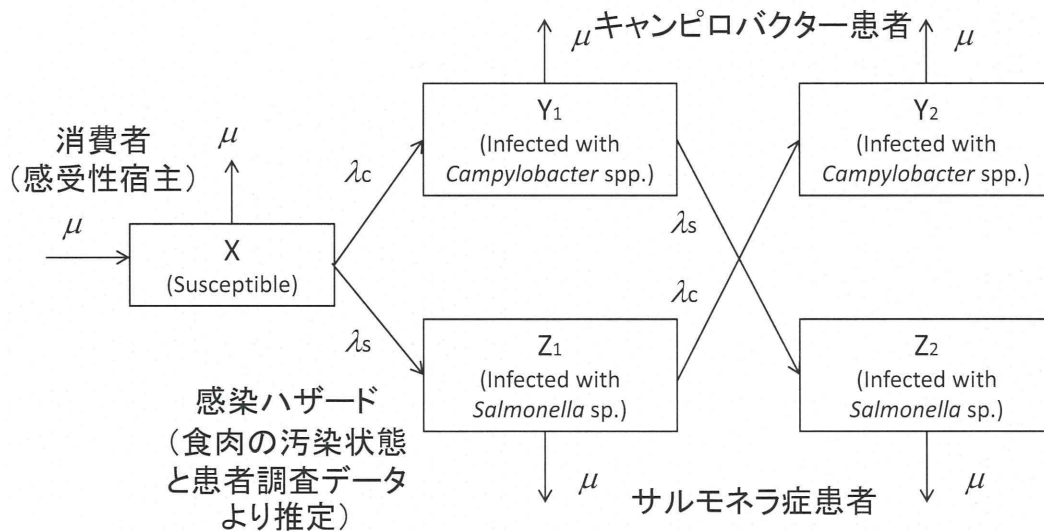図2．コンパートメントモデルの概略図

消費者（感受性宿主）X は時間当たりの感染ハザード λ_c をカンピロバクターに，λ_s をサルモネラに関して経験しており，感染者 Y_1 あるいは Z_1 となる．同時感染（混合感染）は稀であるため無視できるものとする．2 つの疾患の間には交差免疫がないため，それぞれ感染後に他方に感染するリスクが残る．μ は自然死亡率である．

μ は自然死亡率であり，$1/\mu$ は出生時平均余　　命を与える．

ここでハザードが HACCP によって相対的に減少するシナリオを考える．それがカンピロバクター属菌とサルモネラ属菌の両方に独立に効くことを想定し，そこから得られる費用対効果を数値解析によって検討した．

（倫理面への配慮）
本研究は 2 次データと数理モデルを利用した理論疫学研究であり，個人情報を扱う倫理面への配慮を必要としない．

C．研究結果

図 3 にカンピロバクター属菌単独で HACCP の費用対効果を検討した結果を示す．横軸に平行な点線が増分費用効果比の閾値として使用した 1 生存年あたり 500 万円である．HACCP による増分費用効果比を 1 つの疾患単独で検討したとき，HACCP による感染ハザードの相対的減少のごく一部の範囲においてのみ HACCP が費用対効果に優れているものと結論される．
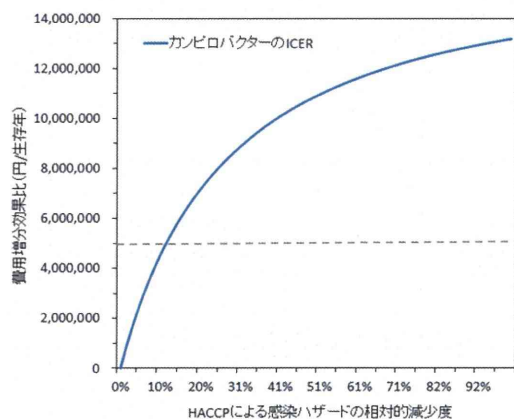

図 3．カンピロバクター属菌について単独で検討した増分費用効果比

しかし，HACCP は病原体に特異的でなく，複数の感染症に独立に波及するものと期待される．ここでカンピロバクター単独でなく，カンピロバクター属菌およびサルモネラ属菌の両方の増分費用効果比を検討した結果を以下の図 4 に示す．閾値を利用すると，ハザードの相対的減少度のほとんどにおいて HACCP は費用対効果に優れていると結論される．
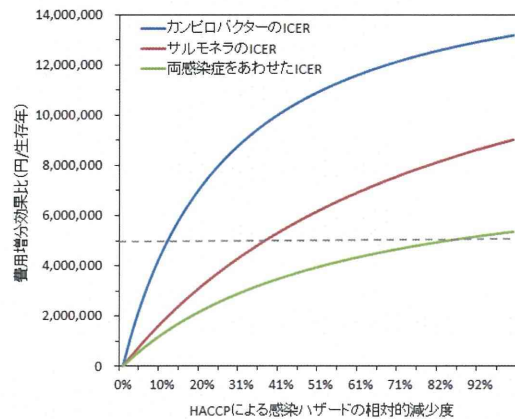

図 4．カンピロバクター属菌とサルモネラ属菌の両方に独立に HACCP が作用すると仮定した場合の増分費用効果比

D．考察

予備的検討の結果，カンピロバクター属菌単独あるいはサルモネラ属菌単独の対策では十分な費用対効果を達成することが困難であるが，HACCP は病原体特異的に作用するものでなく 2 つ以上の食品由来疾病に同時に作用する可能性が期待され，その場合には十分に費用対効果に優れた結果が得られるものと期待された．これは HACCP に限らず次亜塩素酸ソーダによる消毒など，病原体に非特異的である一方で一定以上の効果が期待できる感染症対策の全てに当てはまる．政策判断としての費用対効果を検討する場合にはその作用が独立である限りは対象疾病の全てを考慮すべきであるものと考えられた．

今後，HACCP における 1 つひとつの過

程の定量化あるいは 1 種類の消毒薬の効果などに焦点を絞って統計学的推定に着手することが必要と考えられた.

E．結論

　これまでの調査に基づく DALYs 推定値を活用することによって，食品由来疾患の疾病負荷を異なる疾病間で比較し，個々の予防策について，その費用対効果も含めて検討することを目的に今年度から政策評価モデリングの構想を開始した．具体的事例として食肉への HACCP 導入による細菌性食中毒の予防効果の推定ならびに費用対効果の推定研究を開始した．予備的検討の結果，カンピロバクター属菌単独あるいはサルモネラ属菌単独の対策では十分な費用対効果を達成することが困難であるが，HACCP は病原体特異的に作用するものでなく 2 つ以上の食品由来疾病に同時に作用する可能性が期待され，その場合には十分に費用対効果に優れた結果が得られるものと期待された.

F．健康危険情報

　なし

G．研究発表
1．論文発表

　なし（本分担研究は初年度である）

2．学会発表

　なし（本分担研究は初年度である）

H．知的財産権の出願・登録状況
　（予定を含む）
1．特許取得

　なし

2．実用新案登録
　なし

3．その他
　なし

日本の食品安全行政の現状分析

研究分担者　宮川昭二　　国立感染症研究所　国際協力室

研究要旨
　WHO/FERGの食品由来疾患による健康時間の損失に係るカントリー・スタディ研究枠組みで求められる政治状況に関する分析(Policy Situation Analysis)を実施した。昨年度の分担研究においては東京電力福島第一原子力発電所事故への食品安全行政の対応についてレビューを行ったが、今年度は過去3年間に実施された食品、特に海産魚類における放射線物質に関するモニタリングに着目した。

A. 研究目的

　WHO/FERG (Foodborne Disease Burden Epidemiology Reference Group)が進める食品由来疾患による健康時間の損出に係るカントリー・スタディの研究枠組みの一環として、昨年度に引き続き我が国における政治状況に関する分析(Policy Situation Analysis(PSA))を行った。

　昨年度の研究を踏まえ、本年度においても国際的関心の高い東日本大震災に伴う東京電力福島第一原子力発電所事故への我が国の対応、特に食品中で放射性物質汚染への対応に注目した。

B. 研究方法

　既存文献の調査、厚生労働省食品安全部等関係省庁ホームページを参照した。

C. 研究結果

1. 原子力災害対策特別措置法に基づく出荷制限を受ける海産魚類に対するモニタリング検査結果の分析等

　厚生労働省ホームページに公開されている平成23年度以降に都道府県等が実施したモニタリング成績から、海産魚類の一部について原子力災害対策特別措置法に基づく出荷制限を行う東北・関東の5県(岩手、福島、茨城及び千葉)の結果を抽出し、出荷制限を受ける魚種、放射線物質汚染状況、経年変化などについて調べた。

　モニタリング検査が実施された魚類のうち、コモンカスベ(*Okamejei kenojei*)の着目し、汚染状況について調べた。同種に着目したのは、1)経年的に一定数の検体について検査が実施されていること、2)放射線物質の濃度にばらつきが大きいことに加え、規制値を超える検体も多数あること、3)複数の県でのモニタリング結果が報告されていることなどからである。

　平成23年度から平成25年12月までに岩手、宮城、福島、茨城及び千葉の5県でコモンカスベのモニタリング結果が報告されており、このうち福島及び茨城で平成25年度のモニタリングにおいても食品衛生法に定める規制値(放射性セシウム)を超える検体が認められた。

福島県においては、年間150検体余りのコモンカスベが毎年検査されている。経年変化などを詳細な検討は今回行わなかったが、報告された結果を見る限りでは、平成25年度は検出値の最大や規制値を超える検体数も前年度より低下していた。

2. 海産魚類への放射性物質の移行等

海水などを汚染した放射性物質がどのように海産魚類に移行するのかなど、予備的に文献調査等を行った。

海産魚類への移行などについて、確たる文献は見当たらなかったものの、得られた資料によれば、生物的な濃縮など考えにくく、一般的な無機塩と同様な代謝によるものと推察された。

D、E. 考察と結論

食品における放射性物質対策において、平成24年度に食品衛生法に基づく残留基準の設定と都道府県ベースでの検査計画策定・実施が進められた。厚生労働省などが取りまとめ公表する検査結果及び出荷停止などの措置の状況から、食品に由来する放射性物質対策において重要となる食品の種類や産地を明らかにしてきている。また、厚生労働省が行った放射性物質の一日摂取量調査結果では、一般的な国民の食生活から取り込まれる放射性物質は限定的であることを示している。

今回、海産魚類のモニタリング検査に着目したが、コモンカスベなど規制値を超える放射性セシウムが検出された魚類は出荷制限が行われているものであり、国民の通常の食生活に伴うリスクに直接結び付くものではない。

一方、昨年度報告した WHO による健康リスク評価報告の中で食品汚染等については「継続的なモニタリングと評価が必要である」と指摘している。また、東京電力福島第一原子力発電所での汚染源対策は未だ継続されている

ことを踏まえると、食品、特に海産魚類の汚染についてモニタリングを継続し、定期的な評価を行うことが必要である。

また、海産魚類への放射性物質の汚染がどのようなメカニズムで起こるのか、海水など環境からどのように海産魚類を汚染するのか、海水などの環境のモニタリング成績と海産魚類のモニタリング成績がどうように相関するかなど今後検討するべき点も多い。

次年度以降も食品汚染等の実態調査などのモニタリング状況、政府等が行うリスク評価、また食品中の放射性物質への対策について、情報収集及び分析を行うことが重要であると考える。

F. 健康危険情報
　特記事項なし

G. 研究発表
　特記事項なし

H. 知的財産権の出願・登録状況
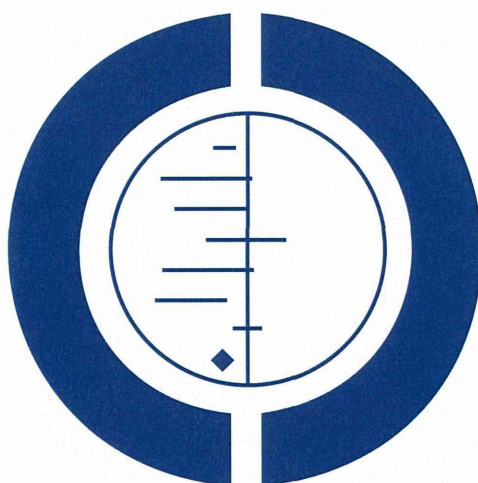　（予定を含む。）

特許取得
　特記事項なし

実用新案登録
　特記事項なし

その他
　特記事項なし

Ⅲ章

参考資料1
コクラン系統的レビュープロトコール（見本）

Behavioral interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries (Protocol)

Ota E, Wariki WMV, Hori N, Mori R, Shibuya K

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[Intervention Protocol]

Behavioral interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries

Erika Ota[1], Windy MV Wariki[1], Narumi Hori[2], Rintaro Mori[3], Kenji Shibuya[3]

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

1. To identify the studies done on behavioural interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries

2. To evaluate the effect of behavioural interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries.

BACKGROUND

Description of the condition

The HIV/AIDS epidemic continues to expand worldwide. Globally, there were an estimated 33 million people [range 30 million-36 million] living with HIV in 2008, and the annual number of new HIV infections declined from 3.0 million [range 2.6 million-3.5 million] in 2001 to 2.7 million [2.2 million-3.2 million] in 2007 (UNAIDS 2008). Overall, 2.0 million people [range 1.8 million-2.3 million] died due to AIDS in 2007, compared with an estimated 1.7 million [1.5 million-2.3 million] in 2001 (UNAIDS 2008).

Some of the most worrisome increases in new infections are now occurring in various high-income countries, such as in Western Europe (UNAIDS 2008; UNAIDS 2009). The rate of newly reported HIV infection in Europe nearly doubled between 2000 and 2007 (van de Laar 2008). In the United States, the Centers for Disease Control and Prevention estimated that annual HIV incidence has remained relatively stable since the early 1990s, although the annual number of new HIV infections in 2006 (56,300) was approximately 40% greater than previously estimated (Hall 2008). In Canada, official epidemiological estimates suggest that annual HIV incidence may have increased between 2002 and 2005 (Public Health Agency of Canada 2007).

Sex workers are defined as female, male and transgender adults and young people who receive money or goods in exchange for sexual services, either regularly or occasionally, and who may or may not consciously define those activities as income-generating (UNAIDS 2002). The World Health Organization (WHO) defines sex workers as one of four key populations globally for HIV/AIDS health initiatives, estimating that there are tens of millions of sex workers worldwide, with clients in the hundreds of millions (WHO 2006). Sex workers are at high risk for infection with HIV, and their clients may serve as a "bridging population" by spreading HIV to the general population (Ghys 2001). Talbott argued that the number of HIV-infected sex workers in an individual country is highly significant for explaining the HIV prevalence levels across countries (Talbott 2007). National estimates of median HIV prevalence among sex workers was 0.4% (range 0.1%-1.4%) in Western Europe in 2000, (Vandepitte 2006). It has been estimated that there are around 80,000 female sex workers (FSWs) in Britain (Scambler 2007) and that less than 2% of London's FSWs are HIV-positive (Day 2006a; Day 2006b), notwithstanding reports that almost half (43%) of new diagnoses of HIV in the United Kingdom in 2005 occurred in London (UNAIDS/WHO 2006).

In general, the living and working conditions of sex workers could result in a variety of interrelated risk factors for HIV infection: a large number of different sexual partners, and hence exposure to many other sexually transmitted infections (STIs) that could increase the probability of acquiring or transmitting HIV; unprotected sexual activity, often because clients or private partners refuse to use condoms; and drug injection by either the woman or her sexual partners (Estebanez 1993).

Migrant sex workers have become a bridge population in the global spread of HIV/AIDS in various high-income countries (Parrado 2004, O'Connor 1996), and their mobility causes problems for the establishment of support networks and ongoing medical care (Church S 2001, Wolffers 2002, Mardh 1999). An Australian study showed a higher risk of STIs and lower rates of condom use for international sex workers than for local sex workers (O'Connor 1996). Higher HIV rates are also found in foreign transsexual sex workers in Rome (Spizzichino 2001).

Description of the interventions

Several studies have indicated that many clients of sex workers refuse to use condoms during sexual relations (Estebanez 1993). The effect of behavioural intervention strategies could be increased by aiming for goals that are achieved by use of multilevel approaches, such as increases in condom use, with populations both uninfected and infected with HIV (Coates 2008). Female condom interventions may help empower women to protect themselves when they are unable to avoid sexual relations with HIV-infected partners or cannot persuade their partners to use a condom. In Amsterdam, a survey of men recruited from an STI clinic who had had relations with sex workers in the preceding four months found that less than half of these men always used condoms during vaginal intercourse with sex workers; only 7% used condoms with their private sexual partners (Hooykaas 1989).

Injecting drug use is the major risk factor associated with HIV infection among sex workers in Western countries (Estebanez 1993). In most cases, infection among injecting drug users probably results from sharing contaminated syringes or needles; however, some women may have acquired HIV through sexual contact with a drug-using partner. And non-injected recreational drugs may also cause people to fail to practice safer sex, contributing to HIV transmission. A number of investigators have reported that the disinhibiting effects of alcohol and other drugs decrease the likelihood of using condoms and may increase the tendency to engage in higher-risk forms of sexual activity (Robertson 1988, Plant 1990, Harcourt 1990). Among 118 sex workers studied in New York in 1985-1987, 31% of those who injected drugs versus only 7% of those who did not were HIV positive (Wallace 1987). A European survey of 866 sex workers from nine European centres (Amsterdam, Antwerp, Athens, Copenhagen, Lisbon, London, Paris, Vienna and eight cities in Spain) carried out in 1990-1991 found that HIV seroprevalence was 32% among women who were injecting drug users and <2% among women who did not inject drugs (European Working Group 1992). Similarly, a survey of 208 street-based sex workers in Glasgow found that 59% injected drugs (McKeganey 1990).

In regions where HIV infection is rare among FSWs, surveillance of risk behavior and STIs will indicate the potential for spread

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of HIV infection (UNAIDS/WHO 2006). Surveillance for behaviour, STI and HIV among sex workers is important because the results may indicate success or failure of the national response to the epidemic, including targeted programs to encourage safe sex between sex workers and clients (Ghys 2001). Interventions to change behavior among sex workers and their clients have been identified as a strategy to reduce HIV transmission. Fisher et al (Fisher 2006a, Fisher 2006b) concluded that critical components of interventions included not only information but also motivation and skills. Vaginal use of topical microbicides by women helps reduce the transmission of HIV (Poynten 2009) and other STIs (Behets 2008). Interventions for management of STIs were based on clinical diagnosis and serologic tests for herpes simplex virus type 2 (HSV-2) with a monoclonal blocking enzyme immunoassay (Kamali 2003).

How the interventions might work

Meta-analysis in developing countries have shown that behavior change interventions effectively resuce HIV transmission for sex workers (Merson 2000).Voluntary HIV counseling and testing has been associated with increased condom use, reduced number of partners, and decreased HIV and in sex workers and clients (Merson 2000).This effect results from behavior change subsequent to education, support, and the knowledge of one's HIV status. Care programmes and participation in research can have a similar effect(Michael 2005).

Male condoms reduce HIV and STI transmission in sex workers (Holmes 1994, Hanenberg 1994, Donovan 2004) and prevent STI complications such as pelvic inflammatory disease (Ness 2004). A reliable and accessible supply of good quality condoms is essential (UNAIDS 2002, Merson 2000, Michael 2005). Condom promotion distribution, and social marketing result in increased condom use and reduced STI and HIV infection rates, especially in female sex workers (Merson 2000). Local culture, language, and traditions should also be considered (Gerofi 1995). Female condoms have successfully prevented pregnancy and reduced STI transmission in analytical studies, (Fontanet 1998, Denlaud 1997, French 2003) and there is in-vitro evidence and biological plausibility for HIV prevention (Denlaud 1997). Female condoms empower women by enabling them to negotiate safe sex, by promoting healthy behavior, and by increasing self-effectiveness and sexual confidence (Gollub 2000). Female condoms are accepted by sex workers (Denlaud 1997, Michael 2005), but major difficulties include cost and poor availability.

Education for sex workers can improve healthy behavior by delivering the basic facts about disease, dispelling myths, and offering healthy lifestyle and work options (Michael 2005). Education can effectively reduce drug use, disease, violence, debt and exploitation (Vanwesenbeeck 2001, UNAIDS 2002; O'Connor 1996; Merson 2000). Peer education has resulted in substantial increases in STI and HIV knowledge, condom use, and safer sex practices, and reduced incidence of HIV and STIs (Vanwesenbeeck 2001, UNAIDS 2002, Michael 2005).

Community development has been successful in the promotion of safe sex, identification of injustice, support for HIV-infected workers, enhancement of self-esteem, cooperation with police and controllers, provision of legal and financial training, initiation of alternative income-generation schemes, and support for migrants and human rights (UNAIDS 2002, UNAIDS 1999, Michael 2005). Successful initiatives have resulted in enhanced self-esteem; improved negotiating skills; ability to refuse clients; access and use of condoms; training to recognize, avoid, and escape violence; STI and HIV preventive services; safe houses; drop-in centres; and STI treatment through pharmacies (Vanwesenbeeck 2001, UNAIDS 2002, UNAIDS 1999, Williamson 2001).

Why it is important to do this overview

The settings in which sex workers work, however, as well as the behavioural characteristics of these sex workers and their clients, may differ between the high-income developed world and low- and middle-income developing world. Hence, the intervention strategies may also be different.

Behavioural interventions are being undertaken in various parts of high-income countries (Dorfman 1992). However, there has been no systematic review that has examined and summarized their effects.

OBJECTIVES

1.   To identify the studies done on behavioural interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries

2.   To evaluate the effect of behavioural interventions to reduce the transmission of HIV infection among sex workers and their clients in high-income countries.

METHODS

Criteria for considering studies for this review

Types of studies

Studies which have evaluated the effect of behavioural interventions on any one of the outcome measures, specified below, and for methodological rigor based on study design (randomized controlled trials and certain quasi-experimental designs) in high-income countries, will be included. Randomised controlled trials in which the unit of randomisation is individuals and clusters (groups

or communities) will be included. From non-randomized studies, certain quasi-experimental prospective designs with a control group are considered eligible only if they include independent comparison groups where assignment to treatment status is not based on need or volition, and separate baseline measurements are also taken, as in the Untreated Control Group Design with Pretest and Posttest (Cook 1979).

Examples of studies that are not eligible are those that compared:
- People who chose to participate in an intervention with those who did not
- Baseline and follow-up measures with no separate comparison condition
- Only follow-up measures without baseline measures when either individuals or groups were assigned to treatment condition by a non-random process

High-income countries are those that are technologically advanced and enjoy a relatively high standard of living. For the purposes of this review, we will consider these to be the 66 countries identified by The World Bank as having "high-income economies" (World Bank).

Types of participants

1. Sex workers (female, male, and transgender)
2. Clients of sex workers (female and male)

Types of interventions

behavioural or social interventions designed to promote sexual risk reduction and thereby to reduce transmission of HIV or other STIs. These interventions may be delivered to individuals, groups, or communities.

Types of outcome measures

Primary outcomes:
-Change in biological variables for prevention among FSWs and their male clients, including HIV incidence, HIV prevalence, STI incidence, STI prevalence

Secondary outcomes:
-Change in self-reported behavior or change in observed behavior (e.g. knowledge, attitudes, intentions, self-reported sexual behavior, biological outcomes).

These outcome measures include:
1. Condom use (male/female)
2. Needle change
3. Increasing self-efficacy for protective behavior
4. Improving communication with partners (male clients and private partners) regarding safer sexual practices
5. Use of microbicides (post-exposure and pre-exposure)
6. Treatment of STIs and reproductive tract infections
7. Less risky types of sex

Search methods for identification of studies

Intervention strategies for behavioural changes may be heterogeneous and influenced by social, demographic, and cultural factors, according to local situations. Reporting strategies for the effect of these interventions might not be uniform and there may be coniderable grey literature and local publications dealing with this issue. Hence, relevant studies will be identified by the following procedures:

a) Electronic databases: To begin with, a comprehensive list of electronic databases will be made in consultation with the HIV/AIDS Review Group Coordinator, the Trial Search Coordinator and some of the experts in HIV/AIDS research and service projects working in high-income countries. Opinions from policy makers and healthcare administrators also will be sought regarding sources of databases. This list will serve as the key document for extraction of data from electronic databases.

The Cochrane Central Register for Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, MEDLINE, PsycInfo, ERIC, Web of Science, the National Research Register, CINAHL, Dissertation Abstract International (DAI), EMBASE, and Cochrane HIV/AIDS Group specialized register will be included in the database list. The publication sites of the World Health Organization, the US Centers for Disease Control and Prevention, and other international research sites also will appear in the database list.

An extensive search strategy string will be developed in consultation with the Trial Search Coordinator of the HIV/AIDS Review Group. All possible keywords will be included in the string to get an exhaustive electronic literature search. Journals in all languages will be included in the search. Articles from other languages will be translated into English with the help of experts, and data will be extracted.

b) Handsearching: Because some of the publications might not have appeared in electronic databases, a handsearching strategy will be developed and adapted for high-income countries.

c) Personal communication: Key personnel and organizations working in HIV/AIDS interventions in high-income countries, including members of the various networks of sex work researchers and activists in high-income countries including the United Kingdom and the United States, will be contacted for published and unpublished references and data.

d) Cross-references: The quoted references of studies identified by the above procedure will be further scrutinized to locate more studies.

e) Conference proceedings of national and international conferences related to HIV/AIDS will be searched.

The search strategy will be iterative in that references of the included studies will be searched for additional references.

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Data collection and analysis

The methodology for data collection and analysis is based on the Cochrane Handbook of Systematic Reviews of Interventions (Higgins 2009).

Selection of studies

All studies that have adressed behavioural interventions in high-income countries will be identified. High-income countries include all high-income countries in the World Bank. A high-income country is one with an annual gross national income (GNI) per capita equivalent to $11,906 or greater in 2009 (World Bank). The abstracts of all identified studies will undergo initial screening in an inclusive manner, based on the objectives of the study, and will be short-listed. The full articles of short-listed studies will be obtained and scrutinized independently by two sets of reviewers for possible inclusion. Scrutiny for inclusion will be based on the type of study, type of participants, type of interventions, and outcome measures. A standard proforma will be developed and used for documenting the decision process. Each set of reviewers will independently document in the proforma the determination of the study's inclusion or exclusion and the reasons. In case of disagreement, a fifth reviewer will serve as arbitrator. Thus, the agreed-upon studies will be included in the review. In the case of excluded studies, a summary statement will be made about the reasons for exclusion.

Data extraction and management

The data from selected studies will be extracted by two teams independently, using a pre-designed data extraction sheet. The data extraction sheet contains details of key entries, namely the trial's identification, its methods, types of participants, the intervention, and the outcomes.

We will use data collection forms to extract data on study design. For eligible studies, two review authors will extract the data using the agreed upon form. We will resolve discrepancies through discussion or, if required, we will consult an additional review author. We will enter data into Review Manager software (RevMan 2008) and check for accuracy. When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2009). We will resolve any disagreement by discussion or by involving an additional assessor.

1) Sequence generation (checking for possible selection bias)
2) Allocation concealment (checking for possible selection bias)
3) Blinding (checking for possible performance bias)
4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)
5) Selective reporting bias
6) Other sources of bias
7) Overall risk of bias

Measures of treatment effect

Dichotomous data: We will present results as a summary risk ratio with 95% confidence interval.

Continuous data: We will use the mean difference if outcomes are measured in the same way between trials. We will use the standardised mean difference to combine trials that measure the same outcom but use different methods.

Unit of analysis issues

individually randomized trials, cluster-randomized trials and cross-over trials will be included.

Dealing with missing data

For included trials, we will note levels of attrition. We will explore the impact of including trials with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes we will carry out analysis on an intention-to-treat basis. The denominator for each outcome in each trial will be the number randomized minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We will use the I^2 statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity ($I^2 > 50\%$), we will explore it by prespecified subgroup analysis.

Assessment of reporting biases

Where we suspect reporting bias, we will attempt to contact study authors, asking them to provide missing outcome data. Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such trials in the overall assessment of results by a sensitivity analysis.

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 2008). We will use fixed-effect inverse variance meta-analysis for combining data where trials are examining the same intervention and the trials' populations and methods are judged sufficiently similar. Where we cannot explain heterogeneity between trials' treatment effects, we will use random-effect meta-analysis.

Subgroup analysis and investigation of heterogeneity

If we can include a number of trials, we plan to carry out subgroup analysis for the primary outcome of the HIV incidence, HIV prevalence, STI incidence and STI prevalence. For fixed-effect meta-analysis, we will conduct planned subgroup analysis, classifying whole trials by interaction tests as described by Deeks (Deeks 2001). For random-effect meta-analysis, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis

We will perform sensitivity analysis based on trial quality, separating high-quality trials from trials of lower quality. For the purposes of this sensitivity analysis, we will define "high quality" as a trial having adequate allocation concealment, and classify as "unrea-

sonably expected loss to follow-up" as less than 20%, given the stated importance of attrition as a quality measure (Tierney 2005). If we include any cluster-randomized trials, other sensitivity analysis may also be desirable. If cluster trials have been incorporated with an estimate of the ICC borrowed from a different trial, we will perform a sensitivity analysis to see what the effect of different values of the ICC on the results of the analysis would be.

ACKNOWLEDGEMENTS

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* Indicates the major publication for the study

WHAT'S NEW

Last assessed as up-to-date: 21 April 2010.

Date	Event	Description
2 September 2010	New citation required and major changes	New protocol, new author team.

HISTORY

Protocol first published: Issue 2, 2006

Date	Event	Description
15 February 2010	New citation required and major changes	Made protocol a "clean slate" for new author team.
11 November 2008	Amended	Converted to RevMan 5, and re-published without new citation.