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School-based interventions for preventing HIV, sexually transmitted infections, and pregnancy in adolescents (Review)

Mason-Jones AJ, Sinclair D, Mathews C, Kagee A, Hillman A, Lombard C

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[Intervention Review]

School-based interventions for preventing HIV, sexually transmitted infections, and pregnancy in adolescents

Amanda J Mason-Jones[1,2,3], David Sinclair[4], Catherine Mathews[5,6], Ashraf Kagee[7], Alex Hillman[1], Carl Lombard[8]

[1]Department of Health Sciences, University of York, York, UK. [2]Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa. [3]Interdisciplinary Health Sciences, University of Stellenbosch, Cape Town, South Africa. [4]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK. [5]Health Systems Research Unit, South African Medical Research Council, Tygerberg, South Africa. [6]School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa. [7]Department of Psychology, Stellenbosch University, Matieland, South Africa. [8]Biostatistics Unit, South African Medical Research Council, Cape Town, South Africa

Contact address: Amanda J Mason-Jones, Department of Health Sciences, University of York, Seebohm Rowntree Building, Heslington, York, YO10 5DD, UK. amanda.mason-jones@york.ac.uk, amandajmasonjones@gmail.com.

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ABSTRACT

Background

School-based sexual and reproductive health programmes are widely accepted as an approach to reducing high-risk sexual behaviour among adolescents. Many studies and systematic reviews have concentrated on measuring effects on knowledge or self-reported behaviour rather than biological outcomes, such as pregnancy or prevalence of sexually transmitted infections (STIs).

Objectives

To evaluate the effects of school-based sexual and reproductive health programmes on sexually transmitted infections (such as HIV, herpes simplex virus, and syphilis), and pregnancy among adolescents.

Search methods

We searched MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) for published peer-reviewed journal articles; and ClinicalTrials.gov and the World Health Organization's (WHO) International Clinical Trials Registry Platform for prospective trials; AIDS Educaton and Global Information System (AEGIS) and National Library of Medicine (NLM) gateway for conference presentations; and the Centers for Disease Control and Prevention (CDC), UNAIDS, the WHO and the National Health Service (NHS) centre for Reviews and Dissemination (CRD) websites from 1990 to 7 April 2016. We handsearched the reference lists of all relevant papers.

Selection criteria

We included randomized controlled trials (RCTs), both individually randomized and cluster-randomized, that evaluated school-based programmes aimed at improving the sexual and reproductive health of adolescents.

Data collection and analysis

Two review authors independently assessed trials for inclusion, evaluated risk of bias, and extracted data. When appropriate, we obtained summary measures of treatment effect through a random-effects meta-analysis and we reported them using risk ratios (RR) with 95% confidence intervals (CIs). We assessed the certainty of the evidence using the GRADE approach.

Main results

We included eight cluster-RCTs that enrolled 55,157 participants. Five trials were conducted in sub-Saharan Africa (Malawi, South Africa, Tanzania, Zimbabwe, and Kenya), one in Latin America (Chile), and two in Europe (England and Scotland).

Sexual and reproductive health educational programmes

Six trials evaluated school-based educational interventions.

In these trials, the educational programmes evaluated had no demonstrable effect on the prevalence of HIV (RR 1.03, 95% CI 0.80 to 1.32, three trials; 14,163 participants; *low certainty evidence*), or other STIs (herpes simplex virus prevalence: RR 1.04, 95% CI 0.94 to 1.15; three trials, 17,445 participants; *moderate certainty evidence*; syphilis prevalence: RR 0.81, 95% CI 0.47 to 1.39; one trial, 6977 participants; *low certainty evidence*). There was also no apparent effect on the number of young women who were pregnant at the end of the trial (RR 0.99, 95% CI 0.84 to 1.16; three trials, 8280 participants; *moderate certainty evidence*).

Material or monetary incentive-based programmes to promote school attendance

Two trials evaluated incentive-based programmes to promote school attendance.

In these two trials, the incentives used had no demonstrable effect on HIV prevalence (RR 1.23, 95% CI 0.51 to 2.96; two trials, 3805 participants; *low certainty evidence*). Compared to controls, the prevalence of herpes simplex virus infection was lower in young women receiving a monthly cash incentive to stay in school (RR 0.30, 95% CI 0.11 to 0.85), but not in young people given free school uniforms (Data not pooled, two trials, 7229 participants; *very low certainty evidence*). One trial evaluated the effects on syphilis and the prevalence was too low to detect or exclude effects confidently (RR 0.41, 95% CI 0.05 to 3.27; one trial, 1291 participants; *very low certainty evidence*). However, the number of young women who were pregnant at the end of the trial was lower among those who received incentives (RR 0.76, 95% CI 0.58 to 0.99; two trials, 4200 participants; *low certainty evidence*).

Combined educational and incentive-based programmes

The single trial that evaluated free school uniforms also included a trial arm in which participants received both uniforms and a programme of sexual and reproductive education. In this trial arm herpes simplex virus infection was reduced (RR 0.82, 95% CI 0.68 to 0.99; one trial, 5899 participants; *low certainty evidence*), predominantly in young women, but no effect was detected for HIV or pregnancy (*low certainty evidence*).

Authors' conclusions

There is a continued need to provide health services to adolescents that include contraceptive choices and condoms and that involve them in the design of services. Schools may be a good place in which to provide these services. There is little evidence that educational curriculum-based programmes alone are effective in improving sexual and reproductive health outcomes for adolescents. Incentive-based interventions that focus on keeping young people in secondary school may reduce adolescent pregnancy but further trials are needed to confirm this.

15 April 2019

Update pending

Studies awaiting assessment

The CIDG is currently examining a new search conducted in April 2019 for potentially relevant studies. These studies have not yet been incorporated into this Cochrane Review. All eligible published studies found in the last search (7 Apr, 2016) were included and five ongoing studies were identified (see 'Characteristics of ongoing studies' section).

PLAIN LANGUAGE SUMMARY

School-based interventions for preventing HIV, sexually transmitted infections, and pregnancy in adolescents

Cochrane researchers conducted a review of the effects of school-based interventions for reducing HIV, sexually transmitted infections (STIs), and pregnancy in adolescents. After searching for relevant trials up to 7 April 2016, they included eight trials that had enrolled 55,157 adolescents.

Why is this important and how might school-based programmes work?

Sexually active adolescents, particularly young women, are at high risk in many countries of contracting HIV and other STIs. Early unintended pregnancy can also have a detrimental impact on young people's lives.

The school environment plays an important role in the development of children and young people, and curriculum-based sexuality education programmes have become popular in many regions of the world. While there is some evidence that these programmes improve knowledge and reduce self-reported risk taking, this review evaluated whether they have any impact on the number of young people that contracted STIs or on the number of adolescent pregnancies.

What the research says

Sexual and reproductive health education programmes

As they are currently configured, educational programmes alone probably have no effect on the number of young people infected with HIV during adolescence (*low certainty evidence*). They also probably have no effect on the number of young people infected with other STIs (herpes simplex virus: *moderate certainty evidence*; syphilis: *low certainty evidence*), or the number of adolescent pregnancies (*moderate certainty evidence*).

Material or monetary incentive-based programmes to promote school attendance

Giving monthly cash, or free school uniforms, to encourage students to stay in school may have no effect on the number of young people infected with HIV during adolescence (*low certainty evidence*). We do not currently know whether monthly cash or free school uniforms will reduce the number of young people infected with other STIs (*very low certainty evidence*). However, incentives to promote school attendance may reduce the number of adolescent pregnancies (*low certainty evidence*).

Combined educational and incentive-based programmes

Based on a single included trial, giving an incentive such as a free school uniform combined with a programme of sexual and reproductive health education may reduce STIs (herpes simplex virus; *low certainty evidence*) in young women, but no effect was detected for HIV or pregnancy (*low certainty evidence*).

Authors' conclusions

There is currently little evidence that educational programmes alone are effective at reducing STIs or adolescent pregnancy. Incentive-based interventions that focus on keeping young people, especially girls, in secondary school may reduce adolescent pregnancy but further high quality trials are needed to confirm this.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Educational interventions versus no intervention

Educational programmes to reduce HIV, STIs, and pregnancy in adolescents

Patient or population: adolescents
Settings: schools and communities
Intervention: sexual and reproductive health educational interventions delivered through schools
Control: no intervention
Outcomes: confirmed biologically by blood or urine test

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (trials)	Certainty of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Sexual and reproductive health education			
HIV prevalence Follow-up: 18 months to 3 years	**10 per 1000**	**10 per 1000** (8 to 13)	**RR 1.03** (0.80 to 1.32)	14,163 (3 trials)	⊕⊕⊖⊖ **low** [1,2,3,4]
HSV2 prevalence Follow-up: 18 months to 3 years	**110 per 1000**	**114 per 1000** (103 to 127)	**RR 1.04** (0.94 to 1.15)	17,445 (3 trials)	⊕⊕⊕⊖ **moderate** [1,2,3,5]
Syphillis prevalence Follow-up: 18 months to 3 years	**30 per 1000**	**24 per 1000** (14 to 42)	**RR 0.81** (0.47 to 1.39)	6977 (1 trial)	⊕⊕⊖⊖ **low** [1,6,7]
Pregnant at end of trial Follow-up: mean 3 years	**90 per 1000**	**89 per 1000** (77 to 104)	**RR 0.99** (0.85 to 1.16)	8280 (3 trials)	⊕⊕⊕⊖ **moderate** [1,2,3,5]

The assumed risk is taken from the median control group risk across studies. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
Abbreviations: CI: confidence interval; HIV: human immunodeficiency virus; HSV2: herpes simplex virus-2; RR: risk ratio; STI: sexually transmitted infection.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[1]No serious risk of bias: none of the trials described blinding of outcome assessors but this deficiency was not considered serious enough to downgrade.
[2]No serious inconsistency: none of these trials found a statistically significant effect. Statistical heterogeneity was low.
[3]Downgraded by 1 level for serious indirectness: these trials were conducted in schools in low-income countries, and had extensive programmes of sexuality education including peers, teachers, and communities. However, the findings are not easily generalized to other programmes or settings.
[4]Downgraded by 1 level for imprecision: due to the low prevalence of HIV in these trials, both the trials and the meta-analysis remain underpowered to allow confident exclusion of small but clinically important effects.
[5]No serious imprecision: the meta-analysis is adequately powered to look for a 25% relative reduction, and the 95% CI is narrow and probably excludes clinically important effects.
[6]Downgraded by 1 level for serious indirectness: only a single trial from Tanzania evaluated this outcome. This does not exclude effects with different programmes in different settings.
[7]Downgraded by 1 level for serious imprecision: the 95% CI is wide and includes both clinically important effects and no effect.

Summary of findings 2. Incentive-based programmes versus no intervention

School-based incentive programmes to reduce HIV, STIs, and pregnancy in adolescents

Patient or population: adolescents
Settings: school and communities
Intervention: incentive-based programmes delivered through schools which aim to reduce HIV and STI among adolescents
Control: no intervention

Outcomes: confirmed biologically by blood or urine test

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (trials)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Incentive programmes			
HIV prevalence Follow-up: 18 months to 3 years	**10 per 1000**	**12 per 1000** (5 to 30)	**RR 1.23** (0.51 to 2.96)	3805 (2 trials)	⊕⊕⊖⊖ **low** [1,2,3,4]
HSV2 prevalence Follow-up: 18 months to 3 years	Not calculated	Not calculated	Not calculated	7229 (2 trials)	⊕⊖⊖⊖ **very low** [1,3,5]
Syphillis prevalence Follow-up: 18 months to 3 years	**30 per 1000**	**12 per 1000** (2 to 98)	**RR 0.41** (0.05 to 3.27)	1291 (1 trial)	⊕⊖⊖⊖ **very low** [1,6,7]
Pregnant at end of trial Follow-up: mean 3 years	**90 per 1000**	**68 per 1000** (52 to 89)	**RR 0.76** (0.58 to 0.99)	4200 (2 trials)	⊕⊕⊖⊖ **low** [1,2,3,8]

The assumed risk is taken from the median control group risk across studies. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
Abbreviations: CI: confidence interval; HIV: human immunodeficiency virus; HSV2: herpes simplex virus-2; RR: risk ratio; STI: sexually transmitted infection.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[1]No serious risk of bias: neither of these trials described blinding of outcome assessors. However, this deficiency was not serious enough to downgrade.
[2]No serious inconsistency: statistical heterogeneity was low.
[3]Downgraded by 1 level for serious indirectness: these two trials were conducted in Malawi and Kenya, and used very different interventions. Baird 2012 MWI gave a monthly cash transfer while Duflo 2015 KEN provided free school uniforms. It is difficult to extrapolate these result to different settings.
[4]Downgraded by 1 level for imprecision: due to the low prevalence of HIV in these trials, both the trials and the meta-analysis remain underpowered to allow confident exclusion of small but clinically important effects.
[5]Downgraded by 2 levels for serious inconsistency: Baird 2012 MWI reported a statistically significant reduction in HSV2 in young women, whereas Duflo 2015 KEN found no effect in either males or females alone or combined into one mixed gender group.
[6]Downgraded by 1 level for serious indirectness: only a single trial assessed this outcome. The lack of effect does not exclude the possibility of effects in other settings.
[7]Downgraded by 2 levels for serious imprecision: the prevalence of syphilis was very low and consequently the trial is underpowered to confidently exclude small but clinically important effects.
[8]Downgraded by 1 level for serious imprecision: the 95% CI is wide and includes both important effects and negligible effects.

Summary of findings 3. Combined incentive-based and educational interventions versus no intervention

School-based combined incentive and educational programmes to reduce HIV, STIs, and pregnancy in adolescents

Patient or population: adolescents
Settings: school and communities
Intervention: incentives to promote school attendance plus sexual and reproductive health education
Control: no intervention

Outcomes: confirmed biologically by blood or urine test

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (trials)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Incentive programmes			
HIV prevalence	**10 per 1000**	**15 per 1000**	**RR 1.53**	2506 (1 trial)	⊕⊕⊖⊖ **low** [1,2,3]

Follow-up: 18 months to 3 years		(5 to 51)	(0.45 to 5.13)		
HSV2 prevalence Follow-up: 18 months to 3 years	**110 per 1000**	**90 per 1000** (75 to 109)	**RR 0.82** (0.68 to 0.99)	5899 (1 trial)	⊕⊕⊖⊖ **low** [1,2,3]
Syphillis prevalence Follow-up: 18 months to 3 years	—	—	—	— (0 trials)	—
Pregnant at end of trial Follow-up: mean 3 years	**90 per 1000**	**81 per 1000** (60 to 107)	**RR 0.90** (0.67 to 1.19)	2782 (1 trial)	⊕⊕⊖⊖ **low** [1,2,3]

The assumed risk is taken from the median control group risk across studies. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
Abbreviations: CI: confidence interval; HIV: Human Immunodeficiency Virus; HSV2: herpes simplex virus-2; RR: risk ratio; STI: sexually transmitted infection.

GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[1]No serious risk of bias: this trial did not describe blinding of outcome assessors. However, this deficiency was not serious enough to downgrade.
[2]Downgraded by 1 level for serious indirectness: only a single trial assessed this outcome and consequently the results are difficult to extrapolate to different settings or alternative incentives or educational programmes.
[3]Downgraded by 1 level for serious imprecision: the 95% CI is wide and includes both important effects and negligible or no effect.

BACKGROUND

Description of the condition

Adolescents have been recognized as having an important place in the post-2015 development agenda (United Nations 2015); indeed three of the United Nation's sustainable development goals (SDGs) specifically target adolescent sexual and reproductive health, and access to appropriate health services as a human right. However, adolescents, particularly those under 16 years of age, constitute a high-risk group who are less likely to use or have access to condoms or contraceptives (Harrison 2005; Mathews 2009; Pettifor 2005; UNAIDS 2012).

Incident HIV infections amongst young people aged 15 to 24 years account for almost half of new infections (UNAIDS 2012). These have increased since 2000, with adolescents within the African region having 90% of the world's HIV-related adolescent deaths (World Health Organization 2014). Despite a downward trend in adolescent pregnancy worldwide (World Bank 2016), most pregnancies in girls under the age of 18 are unwanted and many are terminated. Restrictive abortion laws and lack of services can result in high levels of maternal mortality (Grimes 2006). If the pregnancy is continued and unwanted, it is associated with adverse outcomes for both the mother's and infant's health (Pallitto 2005). A meta-analysis that examined risk factors for pregnancy for girls aged between 13 and 19 years, found that sociodemographic indicators, family disruption, and leaving school early were the most consistently associated factors (Imamura 2007).

The effect of intimate partner violence on young women's ability to control their sexual and reproductive health has also been highlighted as an important issue (Garcia-Moreno 2013). Poor health-related outcomes can result from lack of autonomy and difficulty in accessing services. Pregnancy coercion and birth control sabotage has been linked to unintended pregnancy (Miller 2010; Thiel de Bocanegra 2010), and limitations on condom use (Katz 2015), which increases the risk and incidence of sexually transmitted infections (STIs), including HIV (Dhairyawan 2013). It is also associated with poor perinatal and maternal health with increased risk of low birth weight and preterm birth (Shah 2010).

Programmes that promote sexual abstinence and delay of sexual initiation in adolescence have been unsuccessful in reducing self-reported pregnancy and STIs (Underhill 2008; Oringanje 2016).

Description of the intervention

The school environment plays a pivotal role in the socialization and development of children and young people and has been considered to be an appropriate setting for interventions to promote adolescent sexual and reproductive health (Dick 2006; Mason-Jones 2012; UNAIDS 1997).

Schools bring together large numbers of young people within an established infrastructure, and can provide systems into which interventions can be incorporated. As many young people spend a substantial amount of time in school, it is also an arena for peer connections and the development of relationships that influence individual and group behaviour within the school, and beyond into local communities; although it is important to recognize that schools are not always supportive or safe social environments for young people (Abrahams 2006; Kaplan 2007; Plummer 2007). It is known that dropping out of school can result in adverse health outcomes for young people (Freudenberg 2007).

Schools have been the setting for many sexual and reproductive health programmes that have been regarded as being successful (Kirby 2006), and curriculum-based sexuality education programmes have become popular in many regions of the world. Most of these programmes have been based on the theory of social learning (Bandura 1977), the health belief model (Rosenstock 1988), the theory of reasoned action (Fishbein 2010) - or adaptations of these theories - and aim to change attitudes, intentions, behaviours, and social norms through improved knowledge and understanding of the risks of early sexual initiation, and the importance of contraceptive and/or condom use. Many studies have also incorporated the 17 characteristics of programmes that are considered previously to have been successful (Kirby 2009).

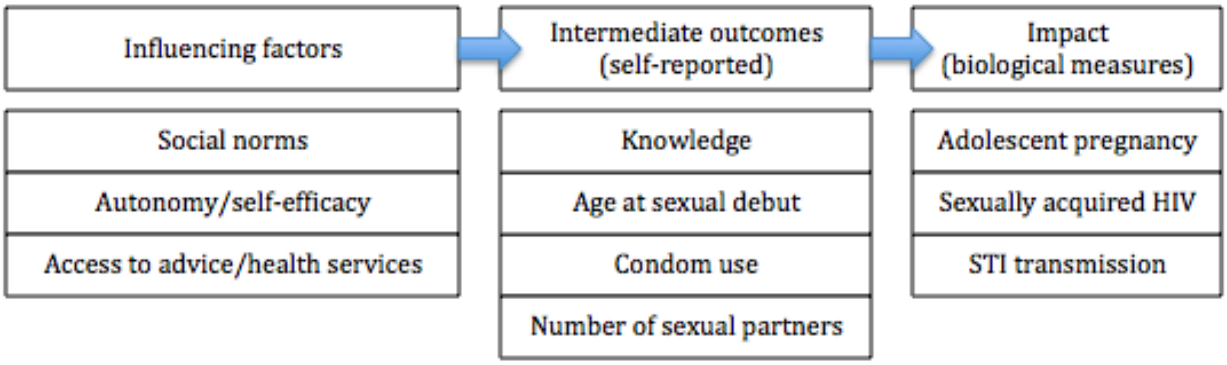
Thus, a range of educational interventions has been developed to promote sexual and reproductive health among adolescents, which aims to reduce the incidence of HIV, STIs, and early unwanted pregnancies. Many of these programmes encourage abstinence from sexual activity, the postponement of sexual debut until later years, or encourage secondary delay (that is, those who have their sexual debut delaying further sexual activity). They also encourage increase in condom use among those adolescents who are sexually active. Interventions include programmes delivered by teachers or peer educators that may be supplemented by condom distribution programmes, and others that include targeted health service provision and include drama, role play, and other engagement activities.

Other evidence suggests that simply staying on at school can have positive effects on sexual and reproductive health outcomes, and that encouraging school attendance helps girls in particular to avoid early sexual activity and pregnancy (Black 2008; Monstad 2008).

How the intervention might work

Many sexual and reproductive health education programmes are based on behavioural science theories (Glanz 2010), and aim to improve knowledge, change attitudes, intentions, behaviours, and social norms around sexual and reproductive health. There have been a large number of systematic reviews that evaluated the effectiveness of these programmes (Chin 2012; Dick 2006; DiClemente 2008; Flisher 2008; Gallant 2004; Harrison 2010; Johnson 2003; Johnson, 2011; Kim 2008; Kirby 2007; Lazarus 2010; Magnussen 2004; Medley 2009; Michielsen 2010; Paul 2008; Shepherd 2010; Yankah 2008), including reviews that have focused solely on school-based interventions (Bennet 2005; Fonner 2014; Kirby 2006; Lopez 2016; Paul 2008), and a review of reviews (Mavedzenge 2013). Many of these reviews have suggested that school- and community-based prevention programmes for adolescents have been effective in delaying self-reported sexual activity, HIV-related preventative behaviours, adolescent pregnancy, and STIs (Chin 2012; Fonner 2014; Johnson 2003; Johnson, 2011; Kirby 2009; Laud 2016), although others have reported less, or mixed, success (Bennet 2005; DiCenso 2002; Lopez 2016 Oringanje 2016). The logic model for how these programmes might be thought to influence sexual and reproductive health outcomes can be seen in Figure 1.

Figure 1. Logic model showing potential causal chain from influencing factors to impact.



As school dropout has negative effects on health outcomes for young people (Freudenberg 2007), researchers have become interested in using cash or other types of transfers (such as free school uniforms or vouchers) as incentives for adolescents to remain at school (Baird 2009; Baird 2010). Conditional and unconditional cash or other transfer programmes have been introduced to take into account the substantial financial barriers to remaining at school or to accessing health services (Pettifor 2012), especially where these are not freely provided on a universal basis. These programmes view staying at school - especially for girls - as a 'social vaccine', based on evidence that the longer adolescents stay in education the less likely they are to engage in high risk sexual behaviour, such as transactional sex, or because pregnancy or STI/HIV risks would interrupt their longer-term aspirations and career plans.

Why it is important to do this review

Most evaluations of school- and community-based programmes, or indeed of any interventions to improve the sexual and reproductive health of young people, have used self-reported sexual behaviours as their main outcomes. However, self-report measures have been found to be prone to bias (Langhaug 2011; Plummer 2004), and, as such, may well be an unreliable surrogate measure for effects such as sexually acquired infections and pregnancy (Brown 2015). Therefore, this review focuses on the effect of such interventions on biological outcome measures. Incidence of HIV or other STIs, or pregnancy are the most convincing indicators of the effectiveness of preventative interventions. This systematic review provides a unique contribution to the field because it only included studies if biological outcomes, such as HIV, STIs, or pregnancy, had been measured objectively. There are also varying interpretations of the strength of the evidence regarding school-based HIV, STIs, and pregnancy prevention programmes for adolescents. This systematic review also provides more detail about the current strength of the evidence by using the GRADE assessment tool.

OBJECTIVES

To evaluate the effects of school-based sexual and reproductive health programmes on sexually transmitted infections (such as HIV, herpes simplex virus, and syphilis), and pregnancy among adolescents.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) (both individually randomized and cluster-randomized).

Types of participants

Adolescents (defined as 10 to 19 year olds) attending primary, middle, or high (secondary) school at the time of the intervention.

In countries where children start school at a later age, or where school populations sometimes include young people over the age of 20 years, we included these studies if most of the participants (over 50%) were adolescents.

Types of interventions

We included any intervention that aimed to reduce the risk of HIV or other sexually transmitted infections (STIs) or pregnancy among adolescents, and was primarily conducted in schools or linked to schools or school attendance, with or without a community component. Some were curriculum-based educational interventions primarily delivered by adults (teachers, or other adults) or peers (peer educators), or included additional features to change the school or community environment (for example, by changing school policies or improving health services). Other interventions focused on encouraging adolescents to stay at school by providing incentives (cash or other material transfers).

Types of outcome measures

Clinical/biological outcomes:

- HIV prevalence;
- STI prevalence;
- Pregnancy prevalence.

Behavioural self-reported outcomes:

- use of male condoms at first sex;
- use of male condoms at most recent (last) sex;
- incidence of sexual initiation (sexual debut).

Search methods for identification of studies

Electronic searches

We developed the search strategy with the assistance of the HIV/AIDS Review Group Information Specialist and developed a comprehensive search strategy in an attempt to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress). We searched the following bibliographic databases for the years 1990 to 7 April 2016 using the search terms presented in the Appendices: MEDLINE (Appendix 1), Embase (Appendix 2), CENTRAL (the Cochrane Central Register of Controlled Trials) (Appendix 3), the World Health Organization (WHO) International Clinical Trials Registry Platform (apps.who.int/trialsearch; Appendix 4), and ClinicalTrials.gov (clinicaltrials.gov). We also searched the following conference databases: AIDS Education Global Information System (AEGIS) (www.aegis.com), and NLM GATEWAY (gateway.nlm.nih.gov/gw).

Searching other resources

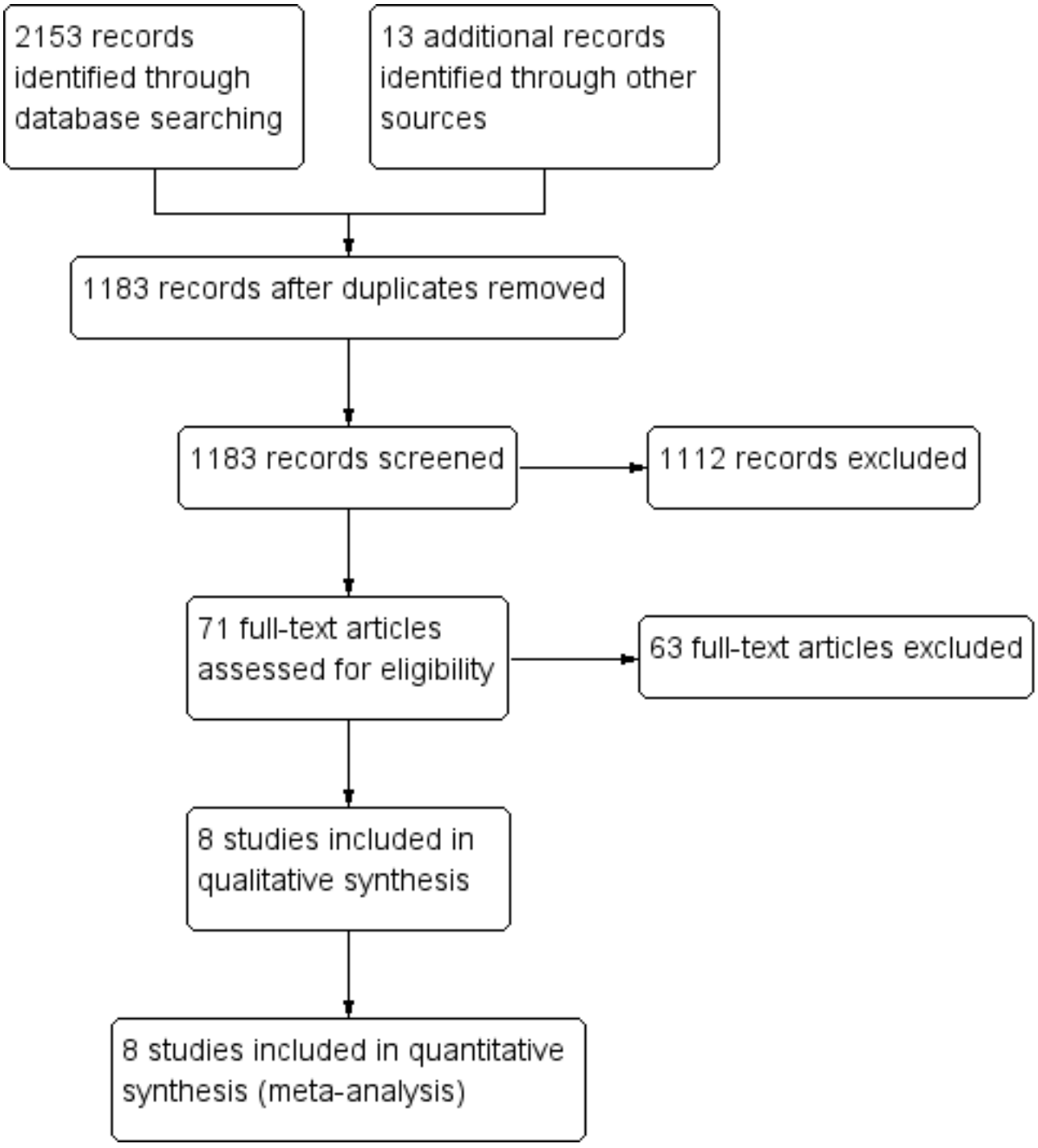
We also searched libraries of relevant organizations and international agencies: the Centers for Disease Control and Prevention (CDC), UNAIDS, the WHO, and the National Health Service (NHS) Centre for Reviews and Dissemination (CRD). We handsearched the reference lists of all relevant papers, including systematic reviews and reviews of reviews. We contacted researchers, research institutions, relevant government departments, and organizations that were known to conduct school-based HIV intervention research or were known to us to identify further published and unpublished studies. Where we were unable to obtain sufficient data from the published articles, we contacted the study authors to request further information about ongoing trials, raw data, and unpublished work.

Data collection and analysis

Selection of studies

Two review authors (AMJ and either DS, CM, AH, or AK) independently reviewed all titles and abstracts identified in the search for relevant trials for the review. We obtained full-text articles for all studies that both review authors recorded as potentially relevant for the review. If the two review authors did not agree initially, we obtained the full-text article and consulted a third review author to make the decision. We listed all full-text articles that we excluded and their reasons for exclusion in a 'Characteristics of excluded studies' table. Also, we constructed a PRISMA diagram to illustrate the study selection process (Figure 2).

Figure 2. Study flow diagram.



Data extraction and management

Two review authors (AMJ and either DS, CM, AH, or AK) independently extracted data on study design (location, context, theoretical framework, dates, duration of follow-up), participants (age, gender, language, ethnicity), interventions (type and complexity of the intervention and all the component parts, length of training of teachers or facilitators, content and duration of the intervention, intensity of the intervention), and methodological quality (method of randomization, attrition, sample size, adjustments for assignment bias, appropriateness of analysis for cluster RCTs, potential confounders, and protection against contamination), using a standardized data extraction form designed specifically for the purpose.

For the meta-analysis of the trials the effect measure we used for inference was the relative risk of the outcome. Some of the included trials reported this measure, but other trials reported odds ratios. To convert the information from these studies into a relative risk framework, we used frequencies of observed outcomes and

odds ratio effect estimates and corresponding confidence limits to estimate the design effect (DE) and intraclass correlation (ICC) for each study overall. We did this by estimating the variance of the odds ratio under the assumption of independence from the raw frequencies, extracting the variance of the odds ratio from the confidence limits adjusted for clustering, and then calculating the design effect as the ratio of the variance (clustered) over the variance (independence). We followed the guidelines from the *Cochrane Handbook for Systematic Reviews of Interventions* to reduce the size of each trial to its 'effective sample size' (Rao 1992). We then solved the corresponding ICC from the standard design effect equation (DE = 1+(m-1)*ICC, where m is the average cluster size). We used this information to adjust the standard error of the relative risk estimate for clustering (McKenzie 2014). If the ICC or design effect was not reported, we assumed the ICC to be 0.1, as in a previous review of school-based studies (Walsh 2015).

For Stephenson 2008 GBR, we estimated the DE from the unweighted effect measures and confidence intervals (CIs) reported. We then applied this estimated DE to the weighted estimates and CIs reported.

We managed trials with multiple publications as one study. One trial incorporated three interventions that were meta-analysed separately (Duflo 2015 KEN). We entered eligible trials into Review Manager (RevMan) 5.3 (Review Manager 5.3). Where methods, data or analyses were unclear, we contacted the trial authors for clarification. We resolved any discrepancies and disagreements by discussion amongst the review author team. There were a few disagreements, generally as a result of differing interpretations of the texts or tables, and we resolved these by going back to the original or supporting papers, or back to the review authors to resolve.

We assessed the quality of evidence using the GRADE approach (GRADEpro 2014).

Assessment of risk of bias in included studies

We independently examined the components of each included trial for risk of bias using the Cochrane 'Risk of bias' assessment tool (Higgins 2011), and incorporated those items specifically related to cluster-RCTs. This included information on random sequence generation, recruitment bias, baseline imbalance, allocation concealment, blinding (of participants, personnel, and the outcome assessors), incomplete outcome data, selective outcome reporting, and other sources of bias. We assessed the methodological components of the trials and classified them as being at either high, low, or unclear risk of bias. Again, we resolved any differences of opinion by discussion.

Measures of treatment effect

We reported all outcomes using risk ratios (RR) with 95% CIs.

Dealing with missing data

We aimed to conduct a complete-case analysis so that we included all individuals with a recorded outcome in the analysis. If missing information was a problem, or we needed more details on reported measures, we sought further clarification from study investigators. All included trials reported at least one of the main outcome measures. However, one trial did not include the data in the final published paper and we were unable to get this data for inclusion in the review despite contacting the trial authors (Jemmott 2015 ZAF).

Assessment of heterogeneity

We assessed statistical heterogeneity between trials by inspecting the forest plots to detect overlapping CIs and by calculating the I^2 statistic using RevMan 5.3 (Higgins 2003). We also conducted a Chi^2 test for heterogeneity at the P=0.1 level.

Assessment of reporting biases

When we reported the results of the included trials, we used the intention-to-treat results for the meta-analysis. We did not construct funnel plots to look for evidence of publication bias because there were too few trials included in each analysis.

Data synthesis

Two review authors, AMJ and CL, analysed data using RevMan 5.3 (Review Manager 5.3). Given that the included trials used a variety of interventions, where it was appropriate to combine trials in a meta-analysis we used a random-effects model, since this is a conservative approach based on fewer assumptions than the fixed-effect approach. We stratified the primary analysis by gender and performed a subgroup analysis by type of intervention (primarily curriculum-based versus incentive-based, and incentive-based plus curriculum) where this was possible. Where trials reported incidence rates (for example, Ross 2007 TZA), we estimated the total number of infections reported and added this to the baseline infections to get an overall prevalence of infections at the endpoint of the trial. Where trials reported the inverse outcome we inverted the reported numbers. For Henderson 2007 GBR we estimated the number of respondents who were evaluated for using a condom at last sex and we then used this as the number of sexually active participants in the trial.

Subgroup analysis and investigation of heterogeneity

We conducted subgroup analyses for young women and young men separately. We also conducted subgroup analyses for type of intervention (for example, education-based interventions and incentives to stay at school).

'Summary of findings' tables

We used a 'Summary of findings' table to interpret the results and to provide key information about the certainty of evidence for included trials in the comparison, magnitude of effect of the interventions examined, and included available data on the main outcomes. We used the GRADE profiler, GRADEpro 2014, to import data from RevMan 5.3 (Review Manager 5.3). We based the display on a recent trial of what review users prefer (Carrasco-Labra 2015).

RESULTS

Description of studies

Results of the search

The search identified 1183 unique references after we removed duplicates. After screening the abstracts, we excluded 1112 articles, and we assessed the remaining 71 full-text articles formally for eligibility against the inclusion criteria (see Figure 2).

Included studies

We included eight cluster-randomized trials in this review; 281 communities and 55,157 participants were enrolled. The cluster size ranged from 18 to 461 participants. One trial was conducted in Latin America (Chile, Cabezón 2005 CHL), two trials in Europe (England (Stephenson 2008 GBR), and Scotland (Henderson 2007 GBR)), and five in sub-Saharan Africa (Malawi (Baird 2012 MWI), Zimbabwe (Cowan 2010 ZWE), Kenya (Duflo 2015 KEN), South Africa (Jemmott 2015 ZAF), and Tanzania (Ross 2007 TZA). Of those conducted in Africa, two were in rural areas (Cowan 2010 ZWE; Ross 2007 TZA), and three were in both rural and urban areas (Baird 2012 MWI; Duflo 2015 KEN; Jemmott 2015 ZAF).

All included trials were published between 2005 and 2015, with reported follow-ups ranging from 18 months (Baird 2012 MWI), to seven years (Duflo 2015 KEN; Stephenson 2008 GBR).

Seven of the eight trials included a specific sexual and reproductive health educational component in the intervention and were based on a range of theoretical frameworks (Cabezón 2005 CHL; Cowan 2010 ZWE; Duflo 2015 KEN; Henderson 2007 GBR; Jemmott 2015 ZAF; Ross 2007 TZA; Stephenson 2008 GBR). These interventions focused specifically on changing knowledge, attitudes, behaviours, and norms related to sexual and reproductive health. The educational component ranged in intensity from three, one-hour sessions in one school year (Stephenson 2008 GBR), to 36 sessions of 40 minutes over three school years (Ross 2007 TZA). Three trials incorporated trained peer educators into their intervention (Cowan 2010 ZWE; Ross 2007 TZA; Stephenson 2008 GBR), two incorporated nurse or health worker training to encourage 'youth friendly services' (Cowan 2010 ZWE; Ross 2007 TZA), and one included a parental training component (Cowan 2010 ZWE). Drama (including video dramas), games, or role play were incorporated into five of the intervention programmes (Cowan 2010 ZWE; Henderson 2007 GBR; Jemmott 2015 ZAF; Ross 2007 TZA; Stephenson 2008 GBR). Four of the seven trials reported some mention of gender roles (Cowan 2010 ZWE; Henderson 2007 GBR; Ross 2007 TZA; Stephenson 2008 GBR). Condoms were not given freely to participants in any of the trials, but were demonstrated to students in two trials (Henderson 2007 GBR; Stephenson 2008 GBR), and sold and marketed to young people in one trial (Ross 2007 TZA) (see Table 1: Description of educational interventions).

One trial, and a trial within one of the studies, had no specific educational component, and used only a conditional or unconditional cash transfer as the intervention (Baird 2012 MWI), or two free school uniforms over a period of 18 months (Duflo 2015 KEN). These interventions were an attempt to influence the 'upstream factors' that affect reproductive health outcomes, such school attendance, poverty, and inequality (see Table 2: Description of incentive interventions).

Biological outcomes such as HIV, herpes simplex virus 2 (HSV2) (and other sexually transmitted infections (STIs)), were measured by dried blood spots and laboratory tests (Baird 2012 MWI; Cowan 2010 ZWE; Duflo 2015 KEN; Ross 2007 TZA), or blood sera and urine tests (Jemmott 2015 ZAF), and participants were provided treatment, counselling, and follow-up as necessary. Current pregnancy was measured by urine sample (Ross 2007 TZA), or school reports with follow-up home visits (Duflo 2015 KEN), whilst pregnancy at follow-up was measured by linkage to health service records (Henderson 2007 GBR; Stephenson 2008 GBR), or school reports (Cabezón 2005 CHL; Duflo 2015 KEN), with follow-up home visits (Duflo 2015 KEN).

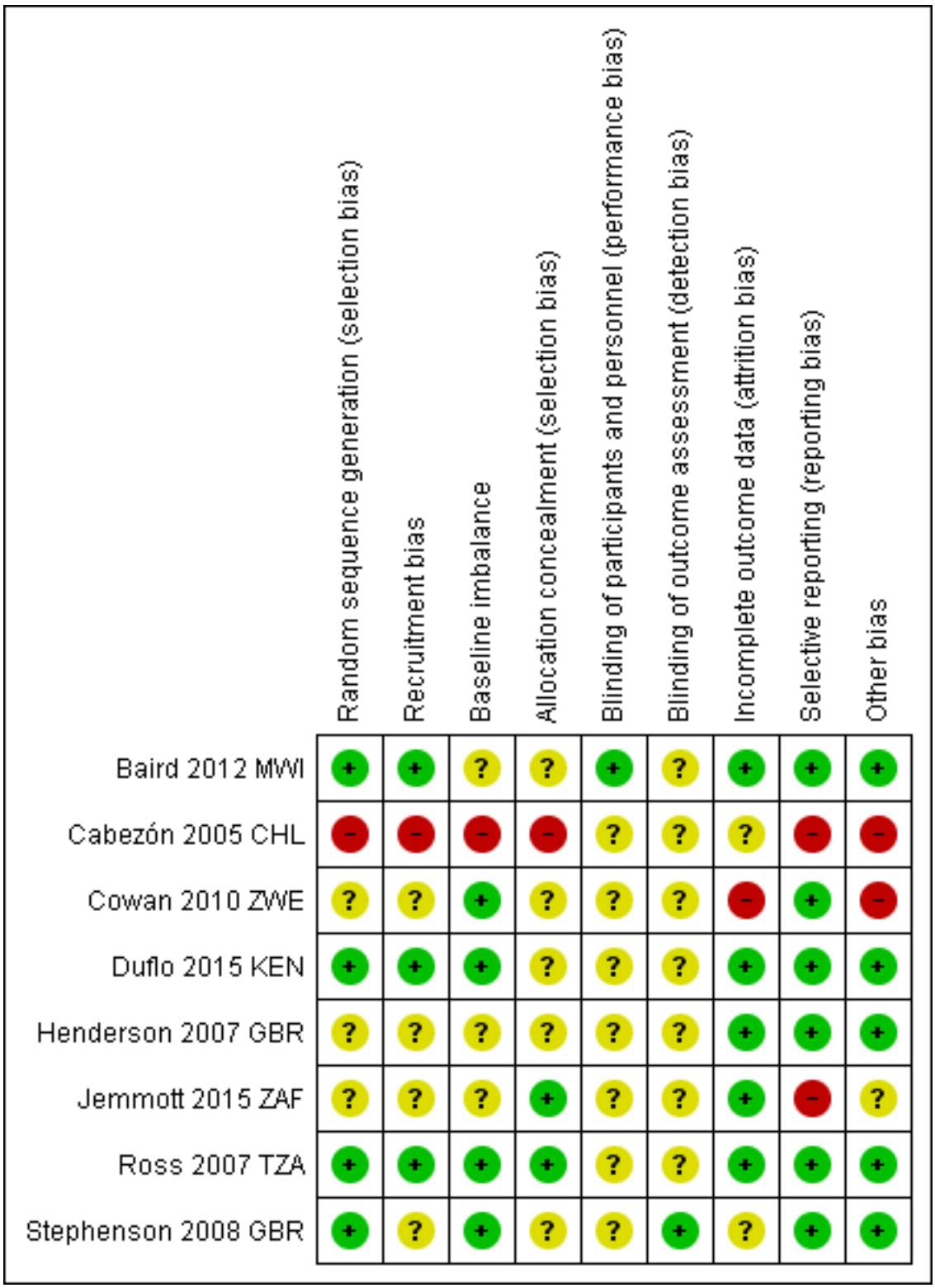
Excluded studies

We excluded 63 studies (see the 'Characteristics of excluded studies' table); a further five trials are ongoing, or have been completed, but have not reported their results in peer-reviewed publications (see the 'Characteristics of ongoing studies' table).

Risk of bias in included studies

We have summarized the 'Risk of bias' assessments in Figure 3.

Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study.



Allocation

Random sequence generation

Baird 2012 MWI, Duflo 2015 KEN, Ross 2007 TZA, and Stephenson 2008 GBR utilized a computer-generated random sequence and we deemed them to be at low risk of bias. We judged Cabezón 2005 CHL to be at high risk of bias, as classes were alternately selected by choosing a letter of the class from a bag, and the remaining trials were at unclear risk due to inadequate description of methods (Cowan 2010 ZWE; Henderson 2007 GBR; Jemmott 2015 ZAF).

Recruitment bias

We considered Baird 2012 MWI, Duflo 2015 KEN and Ross 2007 TZA to be at low risk of recruitment bias as individuals were recruited and baseline surveys were completed before the randomization of enumeration areas. We judged Cowan 2010 ZWE, Henderson 2007 GBR, Jemmott 2015 ZAF and Stephenson 2008 GBR to be at unclear risk of recruitment bias, as clusters were randomized first and then individuals were recruited from those clusters. Cabezón 2005 CHL only requested informed consent from parents of girls in the intervention group, and we therefore deemed it to be at high risk of recruitment bias.

Baseline imbalance

Cowan 2010 ZWE, Duflo 2015 KEN, Ross 2007 TZA, and Stephenson 2008 GBR all reported baseline measurements of outcomes between intervention and control participants and there were no baseline imbalances reported, therefore we judged them to be at low risk of bias. We deemed Baird 2012 MWI, Henderson 2007 GBR and Jemmott 2015 ZAF to be at unclear risk of bias for baseline imbalance. Baird 2012 MWI reported that, at baseline, schoolgirls in the intervention group were more likely to report unprotected sexual intercourse than those in the control group. Furthermore, the main outcome measures, HIV and HSV2, were not measured at baseline. Henderson 2007 GBR reported a slight gender imbalance at baseline and also an imbalance in those who reported sexual activity between the intervention and control groups. Jemmott 2015 ZAF reported 'some imbalance' at baseline, but provided no further details. We deemed Cabezón 2005 CHL to be at high risk of bias as there was baseline imbalance in the incidence of pregnancy between the intervention and control groups in the 1997 cohort, with no pregnancies in the intervention group and six in the control group.

Allocation concealment

We judged both Jemmott 2015 ZAF and Ross 2007 TZA to be at low risk of bias for allocation concealment as they reported concealing allocation up to the point of assignment. We judged Baird 2012 MWI, Cowan 2010 ZWE, Duflo 2015 KEN, Henderson 2007 GBR, and Stephenson 2008 GBR to be at an unclear risk of bias for allocation concealment, as the trial authors did not describe this in any detail. We judged one trial to be at a high risk of bias for allocation concealment (Cabezón 2005 CHL), as classes were chosen alternately and therefore assignment was unlikely to have been concealed adequately.

Blinding

Baird 2012 MWI and colleagues mentioned that they did not mask students to their assignment, and it became apparent that some participants had friends or acquaintances in other groups. However as it was not an educational intervention but rather a cash transfer incentive-based programme there was no chance of 'contamination'. Furthermore, although participants were aware of whether they were receiving cash, how much, and whether it was conditional or not, they were not aware that the primary outcomes were related to HIV/STI prevalence. Baird 2012 MWI did not mask the investigators that conducted statistical analyses and did not describe blinding of the assessors who gathered samples. Overall, we deemed the trial as at an unclear risk of bias for performance and detection bias. Only Stephenson 2008 GBR described the process of blind matching of participants to routine National Health Service (NHS) data, and therefore we judged it to be at low risk of bias for the purposes of this Cochrane Review for detection bias, but unclear for performance bias. It is often difficult to blind participants and personnel in cluster-RCTs within schools and communities, as a number of trial authors noted (Henderson 2007 GBR; Jemmott 2015 ZAF; Stephenson 2008 GBR). Trial authors did not report blinding of participants or personnel (Cabezón 2005 CHL; Cowan 2010 ZWE; Henderson 2007 GBR; Jemmott 2015 ZAF; Ross 2007 TZA), or said that it was not possible to blind teachers who attended a training course to deliver the intervention (Duflo 2015 KEN; Henderson 2007 GBR). Therefore, we judged these trials to be at an unclear risk of bias (Cabezón 2005 CHL; Cowan 2010 ZWE; Duflo 2015 KEN; Henderson 2007 GBR; Jemmott 2015 ZAF; Ross 2007 TZA).

Incomplete outcome data

We judged Baird 2012 MWI, Duflo 2015 KEN, Henderson 2007 GBR, Jemmott 2015 ZAF and Ross 2007 TZA to be at low risk of bias for this domain, as loss to follow-up was similar in both intervention and control groups amongst those selected for follow-up, and these trials performed intention-to-treat analyses. We deemed Henderson 2007 GBR to be at low risk of bias for objective outcomes, as follow-up was equal across both trial arms (99.6% intervention, 99.5% control). A small level of attrition may have occurred due to women attending private clinics (less than 2% terminations) or having terminations in England or Wales (2.7%). There is no reason to expect this would differ across trial arms. However, we deemed Henderson 2007 GBR to be at high risk of bias for self-reported outcomes due to a very low rate of response (41% control, 38% intervention). A systematic under-representation of school leavers may have biased the result towards the null hypothesis. We deemed Ross 2007 TZA to be at low risk of bias due to similar attrition rates across control (72%) and intervention (74%) arms. Stephenson 2008 GBR conducted an intention-to-treat analysis. Missing data for objective measures meant that 28% of the control girls and 21% of the trial girls (P value 0.21) could not be matched with abortion data. It is possible that this may have biased the result towards the null hypothesis, but this risk appears to be small. Cabezón 2005 CHL reported that loss to follow-up was 'similar' across intervention and control groups, but provided no data to support this, so we judged the trial to be at an unclear risk of bias. Cowan 2010 ZWE reported that interim survey results revealed a high rate of outmigration (46%) from the original cohort, so the design of the trial was altered and resulted in a cross-sectional study. As a result, the proportion of the original cohort members included in the final survey was unlikely to have been more than 7%. This very high loss to follow-up left all outcome measures and the study prone to a high risk of bias.

Selective reporting

We judged six trials to be at low risk of bias (Baird 2012 MWI; Cowan 2010 ZWE; Duflo 2015 KEN, Henderson 2007 GBR; Ross 2007 TZA; Stephenson 2008 GBR), as the trial authors reported all of the outcomes stated in their methods section. We judged Cabezón 2005 CHL to be at high risk of bias as the measurement of pregnancy rates was obtained from school records, and it is unlikely that all pregnancies were reported. Jemmott 2015 ZAF did not include complete details of the outcome data related to the biological outcomes measured (HIV, HSV2 and other STIs) in the published paper and so we judged it to be at high risk of bias.

Other potential sources of bias

We considered Baird 2012 MWI, Duflo 2015 KEN, Henderson 2007 GBR, Ross 2007 TZA, and Stephenson 2008 GBR to have a low risk of bias for this domain, as we found no other potential sources of bias. Jemmott 2015 ZAF did not describe their method of choosing schools that were eligible in sufficient detail, so we deemed the trial to be at an unclear risk of bias. We judged Cabezón 2005 CHL to be at high risk of bias. As abortion in Chile is illegal, it is unlikely that pregnancy and abortion would be reported fully to schools. Cowan 2010 ZWE reported that it became difficult to implement the programme in schools for political reasons, and that this coincided with a fall in school attendance for economic reasons and substantial outmigration from the country. Therefore we judged this trial as having a high risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Educational interventions versus no intervention; **Summary of findings 2** Incentive-based programmes versus no intervention; **Summary of findings 3** Combined incentive-based and educational interventions versus no intervention

Comparison 1: School-based educational interventions versus no intervention

Six trials evaluated school-based educational interventions and reported biologically confirmed outcomes (Cabezón 2005 CHL; Cowan 2010 ZWE; Duflo 2015 KEN; Henderson 2007 GBR; Ross 2007 TZA; Stephenson 2008 GBR). One additional trial reported that these outcomes were measured, but did not report the data (Jemmott 2015 ZAF). We have requested the data from the trial authors but have received no response. Duflo 2015 KEN was a four-arm trial in which one trial arm received an educational intervention that we included in Comparison 1. This trial also included an incentive programme, the results of which we have reported in Comparison 2, as well as a combined incentive and educational programme that is reported in Comparison 3.

HIV incidence and prevalence

Only Ross 2007 TZA measured HIV incidence. The incidence of HIV was low with no statistically significant differences between intervention and control groups in young women (16/1448 intervention group versus 24/1492 control group), or young men (3/2076 intervention group versus 2/2024 control group).

Three trials measured HIV prevalence at the end of follow-up (Cowan 2010 ZWE; Duflo 2015 KEN; Ross 2007 TZA). In these trials, there were no demonstrable effects on the prevalence of HIV in young women or young men, or both sexes combined (RR 1.03, 95% CI 0.80 to 1.32; three trials, 14,163 participants; Analysis 1.1). Although the effect estimate is close to no effect, the 95% confidence interval (CI) is wide, and larger studies may be necessary to fully exclude the possibility of small effects.

Note that although Ross 2007 TZA did not measure HIV prevalence, we were able to calculate prevalence based on the reported baseline prevalence and the incidence rate. This is based on the assumption that those who had HIV at baseline (or subsequently developed HIV during the study) were still living with HIV at the end of the study.

Other sexually transmitted infections

Three trials measured and reported HSV2 prevalence at the end of follow-up. Across all three trials there were no demonstrable effects in either young women, young men, or both sexes combined (RR 1.04, 95% CI 0.94 to 1.15; three trials, 17,445 participants; Analysis 1.2).

Only Ross 2007 TZA measured and reported the prevalence of syphilis at the end of follow-up. Although the prevalence was lower in the intervention group, the 95% CI is wide and includes the possibility of no effect for young women, young men, and both sexes combined (RR 0.81, 95% CI 0.47 to 1.39; one trial, 6977 participants; Analysis 1.3).

Pregnancy

Three trials measured short-term pregnancy prevalence through either urine testing (Cowan 2010 ZWE; Ross 2007 TZA), or school reports and home visits (Duflo 2015 KEN) of female participants within the trial. There were no apparent effects in individual trials or all trials combined (RR 0.99, 95% CI 0.85 to 1.16; three trials, 8280 participants; Analysis 1.4).

Four trials measured long-term pregnancy prevalence. Two trials measured this outcome using health service data with biologically confirmed pregnancies (Henderson 2007 GBR; Stephenson 2008 GBR), while the other two trials relied on school reports and records (Cabezón 2005 CHL; Duflo 2015 KEN). There was an apparent reduction in long-term pregnancy prevalence (RR 0.55, 95% CI 0.34 to 0.91; Analysis 1.5). Of these trials, only Cabezón 2005 CHL reported an effect that reached standard levels of statistical significance, and this effect was consistent for both cohorts, (RR 0.20, 95% CI 0.11 to 0.35 and RR 0.18, 95% CI 0.08 to 0.39). However, we deemed this trial to be at a high risk of bias and when this study was excluded there was no effect on long-term pregnancy prevalence for the remaining trials (RR 0.93, 95% CI 0.81 to 1.08; three trials, 11, 612 participants).

Self-reported measures of behaviour change

Six trials also collected data on secondary measures of self-reported behaviour change (Cowan 2010 ZWE; Duflo 2015 KEN; Henderson 2007 GBR; Jemmott 2015 ZAF; Ross 2007 TZA; Stephenson 2008 GBR). Across these trials there was no demonstrable effect on the number of young people reporting their first sexual encounter during the trial period (RR 0.96, 95% CI 0.91 to 1.01; four trials, 22,623 participants; Analysis 1.6). There was also no evidence of an effect on the proportion of young people using a condom during their first sexual encounter (RR 1.00, 95% CI 0.98 to 1.01; two trials, 8015 participants; Analysis 1.7), or using a condom during their most recent sexual encounter (RR 1.00, 95%

CI 0.97 to 1.03; six trials, 18,795 participants; Analysis 1.8). Although the exact outcome measurement varied between trials, statistical heterogeneity between trials was low.

Comparison 2: Incentive programmes versus no intervention

Two trials evaluated incentive-based programmes to encourage school attendance (Baird 2012 MWI; Duflo 2015 KEN).

HIV prevalence

There were no demonstrable effects on the prevalence of HIV in young women or men in either trial, or in the trials combined (RR 1.23, 95% CI 0.51 to 2.96; two trials, 3805 participants; Analysis 2.1). However, the prevalence of HIV was low, and consequently the trials are underpowered to exclude clinically important effects with confidence.

Baird 2012 MWI measured HIV prevalence amongst girls attending school, and those who had dropped out. However, the trial was not powered to detect effects in school dropouts, and because our analysis was aimed primarily at school-based interventions, we have only included the schoolgirl cohort in all of our analyses. In the published paper Baird reported that the effect of HIV prevalence was statistically significant (HIV tests were positive in 7/490 intervention schoolgirls and 17/799 control schoolgirls at follow-up).

Other sexually transmitted diseases

Both trials reported HSV2 prevalence at the end of the trial. Of these, Baird 2012 MWI reported a reduction in HSV2 prevalence in young women (RR 0.30, 95% CI 0.11 to 0.85), based on 5/488 intervention schoolgirls testing positive compared to 27/796 control schoolgirls. However, it is important to note that Baird did not measure, or report HSV2 prevalence at baseline. No effect was apparent in young women or young men in the other trial (Duflo 2015 KEN), or when we combined the two trials (RR 0.98, 95% CI 0.72 to 1.36; two trials, 7229 participants; Analysis 2.2).

Only Baird 2012 MWI assessed the prevalence of syphilis, and the prevalence was too low to demonstrate effects (1/491 intervention schoolgirls versus 4/800 control schoolgirls; Analysis 2.3).

Pregnancy

Both trials measured short-term pregnancy prevalence. Overall, pregnancy was reduced by around a quarter in those who received incentives (116/2014 intervention versus 151/2186 control; RR 0.76, 95% CI 0.58 to 0.99; two trials, 4200 participants; Analysis 2.4). The effect size was consistent across trials, but with wide CIs which include no effect.

Only Duflo 2015 KEN measured the incidence of pregnancy throughout the long-term follow-up period up to seven years, and did not demonstrate an effect (604/1521 intervention versus 583/1370 control; RR 0.89, 95% CI 0.73 to 1.08; one trial, 2891 participants; Analysis 2.5).

Self-reported measures of behaviour change

Both trials collected data on secondary measures of self-reported behaviour change. There was a reduction in the proportion of young people reporting their first sexual encounter (sexual debut) during the trial period (RR 0.83, 95% CI 0.73 to 0.95; two trials, 7177 participants; Analysis 2.6). Only Duflo 2015 KEN, reported on the proportion using a condom during their most recent sexual encounter and demonstrated no reduction (RR 0.98, 95% CI 0.85 to 1.12; one trial, 4265 participants, Analysis 2.7).

Comparison 3: Combined incentive and educational programmes

Duflo 2015 KEN was a four-arm trial that also included a trial arm in which participants received both free school uniforms and a programme of sexual and reproductive health education.

HIV prevalence

There were no demonstrable effects on HIV prevalence (RR 1.53, 95% CI 0.45 to 5.13; 1 trial, 2506 participants; Analysis 3.1).

Other sexually transmitted diseases

The prevalence of herpes simplex virus infection was lower in those receiving an incentive and educational programme combined compared to controls (RR 0.82, 95% CI 0.68 to 0.99; one trial, 5899 participants, Analysis 3.2), and this reduction was mainly in young women (RR 0.76, 95% CI 0.62 to 0.93).

Pregnancy

No effect was demonstrated either on the proportion of young women pregnant in the short-term (RR 0.90, 95% CI 0.67 to 1.19; one trial, 2782 participants; Analysis 3.3), or the incidence of pregnancy at the long-term follow up (RR 0.90, 95% CI 0.73 to 1.12; one trial, 2801 participants; Analysis 3.4).

Self-reported measures of behaviour change

The proportion of young people reporting their sexual debut during the trial was lower in those receiving the intervention (RR 0.84, 95% CI 0.73 to 0.97; one trial, 6102 participants; Analysis 3.5), but there was no effect demonstrated on the proportion of adolescents using a condom during their most recent sexual encounter (RR 1.02, 95% CI 0.89 to 1.17; one trial, 4193 participants; Analysis 3.6).

DISCUSSION

Summary of main results

Sexual and reproductive health educational programmes

In these trials, the educational programmes evaluated had no demonstrable effect on the prevalence of HIV (*low certainty evidence*), or other sexually transmitted infections (Herpes Simplex virus prevalence: *moderate certainty evidence*; Syphilis prevalence: *low certainty evidence*). There was also no apparent effect on the number of young women who were pregnant at the end of the trial (*moderate certainty evidence*).

Material or monetary incentive-based programmes to promote school attendance

In these two trials, the incentives used had no demonstrable effect on the prevalence of HIV (*low certainty evidence*). Compared to controls, the prevalence of Herpes Simplex virus infection was lower in young women receiving a monthly cash incentive to stay in school, but not in young people given free school uniforms (*very low certainty evidence*). Only one trial evaluated the effects on syphilis and the prevalence was too low to confidently detect or exclude effects (*very low certainty evidence*). However, the number of young

women who were pregnant at the end of the trial was lower among those who received incentives (*low certainty evidence*).

Combined material or monetary incentive-based and educational programmes

One trial used a combined approach; this showed there was no demonstrable effect on the prevalence of HIV (*low certainty evidence*). Compared to controls, the prevalence of HSV infection was lower for those receiving free school uniforms to stay in school and an educational programme (*low certainty evidence*). The provision of a combined programme had no demonstrable effect on the number of young women who were pregnant at both short- and long-term follow-up (*low certainty evidence*).

Overall completeness and applicability of evidence

The trials included in this review evaluated educational programmes that incorporated many of the specific characteristics that have previously been recommended for well-designed adolescent sexual and reproductive health interventions (Kirby 2006). However, despite this, they failed to demonstrate any reduction in the prevalence of STIs or adolescent pregnancy. It is only possible to theorize about the potential reasons for this, but three factors may be important.

Firstly, the trials could simply be underpowered for the detection of small but clinically important effects. This could certainly be true for the lack of effect on HIV. Even in geographical settings where HIV is more common than elsewhere, the incidence during adolescence is relatively low and very large trials would be required to exclude small effects with confidence (see Table 3). For more common outcomes though, such as HSV2 and pregnancy, the trials are adequately powered to detect effects, and the effect estimate is close to zero with narrow 95% confidence intervals (CIs). Importantly, if the interventions are not reducing these more common outcomes, they are unlikely to be having an impact on HIV.

Secondly, despite the effort that went in to designing these educational programmes, they may still have failed to address some areas critical to effecting change. For instance, it is unclear to what extent the programmes incorporated discussion of exploitation or violence, or whether the messages were adapted appropriately for both the male and female students. Furthermore, none gave condoms freely to participants. It is therefore not possible to say that educational programmes would never work, only that these programmes did not, despite extensive efforts to develop multifaceted approaches through formative consultation with young people themselves (Henderson 2007 GBR; Ross 2007 TZA; Stephenson 2008 GBR).

The third possible explanation is that educational programmes alone do not address the wider structural issues that influence sexual health outcomes, sexual behaviour and risk taking; the availability and affordability of schools and health services, contraceptive choice and condoms, poverty, and cultural gender norms. Indeed it is this third factor which has led some to develop and promote interventions which prioritize school attendance and educational achievement.

This review included two trials that promoted school attendance through cash transfers, and free school uniforms respectively (Baird 2012 MWI; Duflo 2015 KEN). Further trials are currently ongoing (Pettifor 2016), or have not yet reported their results (NCT01187979; NCT01233531). The two early trials have had some positive, but conflicting findings, which should temper enthusiasm for this approach until the results of these additional trials have been published. Baird 2012 MWI found a reduction in HSV2 prevalence in girls given monthly cash incentives, while Duflo 2015 KEN did not reproduce this effect with free school uniforms. Similarly, while both cash incentives and free school uniforms were associated with a reduction in adolescent pregnancies, a third trial arm in Duflo 2015 KEN, which received both free school uniforms and an educational intervention, did not have a lower incidence of pregnancy. This is counter-intuitive and further trials will help us to understand why.

Quality of the evidence

We assessed the quality or certainty in the evidence using the GRADE approach, which we have presented in the 'Summary of findings' tables (Summary of findings for the main comparison; Summary of findings 2).

For educational programmes we have moderate certainty that these programmes do not have an impact on either STIs or pregnancy. As described above, we downgraded the certainty for indirectness, as we are unable to extrapolate the findings of these few trials in specific settings confidently to all educational programmes everywhere. For the finding of no effect on HIV prevalence we further downgraded the evidence to low certainty under 'imprecision', as the prevalence of HIV was generally low in these trials and very large trials would be needed to exclude fully the possibility of small but clinically important effects.

For incentive-based programmes, our level of certainty is low or very low due to the limited number of trials available (which affects both precision and directness) and the inconsistencies in the findings of the two available trials. There are currently several more trials of incentive-based programmes underway, and we would expect that certainty about the presence or absence of effects will be increased in future editions of this review.

Potential biases in the review process

We used only peer-reviewed trials in this review. It is unlikely that we missed papers that were unpublished that included biological outcomes, as this is a relatively new innovation in adolescent sexual and reproductive health research and it is likely that they would be published. Most intervention studies of this kind use self-reported measures only.

The missing data from Jemmott 2015 ZAF are unlikely to have affected the overall findings, however, the findings on pregnancy at long-term follow-up were sensitive to the exclusion of Cabezón 2005 CHL. The potential for a high risk of bias in this study suggests that the study authors' conclusions should be treated with caution.

All eight of the cluster-randomized controlled trials (cluster-RCTs) reported that they took account of the cluster randomization. However, not all of them included the intraclass correlation (ICC) or design effect. Therefore, we recalculated the standard errors reported and use these in our meta-analyses.

We have only included RCTs. Before-and-after studies are often used for public health interventions, but when we deemed that there were enough RCTs for this analysis, we decided that the

inclusion of studies with less robust designs was unlikely to add anything further.

Agreements and disagreements with other studies or reviews

The conclusions of this Cochrane Review are consistent with previous published reviews of curriculum-based educational programmes. The Health Technology Assessment Centre's systematic review of school-based interventions to prevent STIs including HIV included RCTs and assessed sexual risk behaviour outcomes (Shepherd 2010). The review authors identified few statistically significant effects on behaviour in the included studies. Where there were significant effects, they often only applied to a subgroup of the participants (boys only or girls only, or only the subgroup who became sexually active during the study period). This led them to conclude that "school-based behavioural interventions for the prevention of STIs in young people can bring about improvements in knowledge and increased self-efficacy, but the interventions did not significantly influence sexual risk-taking behaviour or infection rates". The recent suggestion that the UK Govenment's Teenage Pregnancy Strategy which incorporated school-based programmes and health service interventions has been effective in reducing adolescent pregnancy (Hadley 2016) is promising but needs further evidence from controlled studies, preferably with randomized designs, as temporal trends can confuse and mislead.

There now seems to be consensus that in sub-Saharan Africa few curriculum-based educational programmes have been shown to be effective, and many of the evaluations have a high risk of bias (Michielsen 2010; Paul 2008). The most recent systematic review of programmes for adolescents and young people based in schools and other settings, found 28 experimental studies, only 11 of which were RCTs, and many of which were judged to be of sub optimal quality (Michielsen 2010). This paucity of strong evidence regarding the effects of educational programmes in sub-Saharan Africa on adolescent HIV, STI and pregnancy prevention is also consistent with the assessments of earlier reviews (Flisher 2008; Gallant 2004; Kirby 2007; Magnussen 2004; Michielsen 2010; Paul 2008), in that programmes that aimed at delaying sexual debut among adolescents and young people have been shown to have limited effectiveness. Our current knowledge of what works remains limited, especially for marginalized adolescents (Chandra-Mouli 2015).

The finding that incentive-based programmes that encourage school attendance may reduce pregnancy in adolescents confirms the results of a previous study which suggests that leaving school early was associated with early pregnancy (Imamura 2007).

AUTHORS' CONCLUSIONS

Implications for practice

There is a continued need to provide health services that cater for the sexual and reproductive health needs of adolescents by providing a range of contraceptive choices and condoms and to include them in decision-making around services that can most fully meet their needs. Schools may be a good place in which to provide sexual and reproductive health services, but there is little evidence that curriculum-based educational programmes alone, as they are currently configured and without the provision of contraception and condoms, are effective in reducing risk behaviours for adolescents and improving their health outcomes. It is likely that the wider role of health service provision and availability, gender norms, sexual exploitation and intimate partner violence, poverty and inequality also need to be acknowledged and addressed and that programmes for girls and boys might need to be configured differently.

Incentive-based interventions that focus on keeping young people in secondary school have had some promising — though conflicting — early results, and further trials are ongoing to investigate this.

Implications for research

Some of the trials included in this review were large, complex, well-designed, and well-conducted trials whose participants were followed up on a medium- to long-term basis. The cost of these trials has been significant, yet they have not been able to show effectiveness for educational curriculum-based interventions on biologically measured adolescent sexual and reproductive health outcomes. The implications for research are significant. The only trial that showed promise in reducing the prevalence of herpes simplex virus 2 (HSV2) was the conditional cash transfer intervention (Baird 2012 MWI); while the only two trial interventions that reduced pregnancy were the incentive-based interventions to maintain school attendance (Baird 2012 MWI; Duflo 2015 KEN).

Increasingly it is being realized that structural determinants of health, such as the provision of continuing secondary education or training, are important issues to address for improving adolescent sexual and reproductive outcomes, especially for girls. We need to begin to acknowledge this fully in our work when designing high quality interventions.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Baird 2012 MWI

Methods	Trial design: cluster-randomized controlled trial (cluster-RCT)
	Unit of randomization: enumeration areas
	Number of clusters: 176
	Data collection: the primary outcomes were collected by home-based voluntary counselling and testing (VCT)
	Length of follow-up: impact assessed at 12 months, and biological outcomes measured at 18 months

Baird 2012 MWI *(Continued)*

	Adjustment for clustering: yes
Participants	Target group: 'never married' girls aged 13 to 22 years (schoolgirls and those who had dropped out of school) Sample size: 3796 Exclusions: none stated
Interventions	Intervention group: • Did the target group receive sexuality education? No, there was no specific sexuality education component. • How many sessions? N/A. • Who delivered the sessions? N/A. • What was the content of the session? N/A. • What additional components were there? Cash transfers were given as monthly payments of USD 1 to USD 5 to the participant and USD 4 to USD 10 to her family to encourage participants to stay in education (conditional) or with no conditions attached. • Were condoms distributed free? No. Control group: no intervention
Outcomes	Included in this review: • prevalence of HIV at 18 months; • prevalence of HSV2 at 18 months; • prevalence of syphilis; • self-reported sexual debut. Not included in this review: • school enrolment; • self-reported marriage; • self-reported pregnancy; • knowledge of HIV/AIDS.
Notes	Country: Malawi Setting: Zomba district (rural) Study dates: 2007 to 2009 Study sponsors: Global Development Network, Bill and Melinda Gates Foundation, National Bureau of Economic Research Africa Project, World Bank's Research Support Budget, and several World Bank trust funds (Gender Action Plan, Knowledge for Change Program, and Spanish Impact Evaluation fund)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “the 176 geographic enumeration areas were randomly assigned (1:1) to intervention (cash transfer programme) or control groups (no programme)." p.1322 Quote: "the intervention group were further randomly assigned with computer-generated random numbers to one of two groups: one received conditional cash transfer offers and the other unconditional cash transfer offers." p. 1322

Baird 2012 MWI *(Continued)*

		Comment: stratified random sampling was described. Method of stratification described.
Recruitment bias	Low risk	Comment: a stratified random sample of 176 enumeration areas was chosen from 550 enumeration areas in the district. Individuals were recruited and baseline surveys completed before randomization of enumeration areas.
Baseline imbalance	Unclear risk	Quote: "Baseline characteristics in the intervention and control groups were similar." p. 1325 Comment: the intervention group were more likely to have unprotected sexual intercourse at baseline (16% intervention schoolgirls vs 11% control schoolgirls and 61% vs 57% of those dropped out of school). Biological outcomes (HIV, HSV2 and syphilis prevalence) were not reported at baseline. Authors report that this is because HIV testing was rare in Malawi at the start of the study and that it would constitute a separate intervention.
Allocation concealment (selection bias)	Unclear risk	Comment: not reported sufficiently.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Study participants were not masked to their assignment but did not know what the comparison groups were because they were assigned at the enumeration area level.” p.1322, and “Study participants could not think that cash transfers were intended to reduce risky sexual behaviour and HIV or that they were tied to good behaviour in terms of sexual activity.”p.1323 Comment: participants were aware of whether they were receiving cash, how much, and whether it was conditional or not. They were not, however, aware that the primary outcomes were in fact related to STI prevalence, although some students had friends and acquaintances in the other groups. Source: p.1322, p.1323 Procedures.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Trained counsellors who did home-based counselling and rapid testing for HIV, HSV-2 and syphilis were masked to the participant's group. Statistical analyses were done by the investigators who were not masked to the treatment status of the participants." p.1322
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “The percentage of study participants lost to follow up did not differ between control, conditional, and unconditional groups, and was lower than that reported for similar studies” and “133 (7%) baseline schoolgirls and 86 (10%) baseline dropouts were lost to follow up at 12 months" and that "none of the enumeration areas had complete loss to follow up rates were similar for 18 month visit (figure 2). Of the 1777 individuals selected for biological testing, 71 (4%) were lost to follow up because of either refusal to get tested (n = 51) or not being located by the data collection teams." Loss to follow up was similar amongst all groups. There was successful follow up of: 255/265 (96%) selected (90% of 283 total) CCT schoolgirls offered cash arm, 235/236 (99.6%) selected (46% of 506 total) UCT schoolgirls offered cash arm, 210/226 (96%) selected (48% of 436 total) dropouts offered cash arm. 799/827 (97%) selected (53% of 1495 total) control schoolgirls. 207/223 (93%) selected (46% of 453 total) schoolgirl controls. Source: p.1324 'Statistical analysis paragraph 2 p.1327 Discussion paragraph 2 p.1325 Results paragraph 2

Baird 2012 MWI *(Continued)*

		p.1324 figure 2
Selective reporting (reporting bias)	Low risk	Comment: all outcomes stated in methods were reported.
Other bias	Low risk	Comment: no other source of bias identified.

Cabezón 2005 CHL

Methods	Trial design: cluster-RCT Unit of randomization: classes in secondary schools Number of clusters: 13 Data collection: pregnancies that were term, preterm or miscarried were registered by the school administration Length of follow-up: 3 years Adjustment for clustering: no
Participants	Target group: girls aged 15 to 16 years attending an all-girls' high school Sample size: 1259 Exclusions: none stated
Interventions	The intervention • Did the target group receive sexuality education? Yes. • How many sessions? 14 sessions of 45 minutes each. • Who delivered the sessions? Teachers who were not specifically biology or sexuality education teachers. • What was the content of the sessions? TeenSTAR programme, stressing abstinence, fertility awareness, and psychological and personal aspects of sexuality. Contraceptive use was not recommended. • What additional components were there? None. • Were condoms distributed free? No. Control group: no intervention
Outcomes	Outcomes included in this review: • pregnancy prevalence. Not included in this review: • no other outcomes reported.
Notes	Country: Chile Setting: one school in a suburban area. Study dates: 1997 to 2000 Study sponsors: not stated
Risk of bias	

Cabezón 2005 CHL *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Among 10 classes five were alternatively selected". p.65. Quote: "These 8 classes were chosen blindly, taking the letter of the class from a bag to be intervention group in the 1998 cohort, thus leaving 2 classes as control group in this cohort." p.65.
Recruitment bias	High risk	Comment: only intervention group parents were asked to sign a consent form.
Baseline imbalance	High risk	Comment: there was baseline imbalance in pregnancy incidence between the groups in 1997, with none in the intervention group and 6 in the control group. p.66 Table 3.
Allocation concealment (selection bias)	High risk	Comment: unlikely as classes were chosen alternately.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: blinding not described.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: blinding not described.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "During the 4-year follow up period the dropout rates from school were similar in the three studied cohorts." p. 67.
Selective reporting (reporting bias)	High risk	Quote: "Measurement of pregnancy rates is difficult because it is not possible to know if there were any induced abortions in the control or study groups." p. 68.
Other bias	High risk	Comment: as abortion in Chile is illegal it is unlikely that pregnancy and abortion was fully reported to schools.

Cowan 2010 ZWE

Methods	Trial design: cluster-RCT Unit of randomization: a 'community' comprising a health clinic, its catchment population and its secondary schools Number of clusters: 30 Data collection: a representative survey of 18-22 year olds in study communities 4 years after the intervention. This included a questionnaire, HIV-1, HSV2, and a pregnancy test Length of follow-up: 4 years Adjustment for clustering: yes
Participants	Target group: Form 2 pupils (median age 15 years) Sample size: 6791

Cowan 2010 ZWE *(Continued)*

	Exclusions: none stated
Interventions	The intervention • Did the target group receive sexuality education? Yes. • How many sessions? Not clear. Reported as an "in-school 3-year curriculum and 1-year 24 session out-of school programme". • Who delivered the sessions? 'Professional peer educators' (PPEs) - i.e. school leavers who were selected, trained, and supervised and worked in the community for 8 to 10 months. • What was the content of the sessions? HIV prevention activities using adapted 'MEMA kwa Vijana' programme with additional materials from 'Talktime', 'Mopani', 'Auntie Stella' and 'Young People We Care' which included self-awareness, communication, self-belief and gender. • What additional components were there? A 22-session community programme targeting parents and community stakeholders aimed at improving communication between parents and children and support for adolescent reproductive health. A 5-day residential training programme for clinic nurses to improve accessibility for adolescents. • Were condoms distributed free? No. Control group: no intervention (delayed intervention until 2007)
Outcomes	Outcomes included in this review: • HIV prevalence; • HSV2 prevalence; • current pregnancy; • self-reported sexual debut; • use of condoms at last sex. Outcomes not included in this review: • knowledge and attitudes around sexual behaviour; • reported sexual behavior including multiple sexual partners; • use of pregnancy prevention methods with first, last, or any partner; • self reported symptoms of STDs.
Notes	Country: Zimbabwe Setting: rural districts Study dates: 2003 to 2007 Study sponsors: National Institute of Mental Health, DfID Zimbabwe

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “Restricted randomisation was used to ensure balance between arms of the study.” Source: p1237 (Cowan 2008). Comment: random allocation, stratification criteria detailed, but method of randomization was not explained.
Recruitment bias	Unclear risk	Comment: clusters were randomized first and then individuals were recruited from those clusters.
Baseline imbalance	Low risk	Quote: "There was excellent balance between early and deferred intervention [*author's note*: i.e. between intervention and control] arms in terms of rates

Cowan 2010 ZWE *(Continued)*

		of HIV-1 infection and other behavioural and socio-demographic variables." Source: p.1240 (Cowan 2008).
Allocation concealment (selection bias)	Unclear risk	Comment: allocation concealment not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no blinding described.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no blinding described.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: “During our interim survey in 2006, we found there had been considerable outmigration (46%).Those who remained were of lower risk than those who had left” p. 2542 “The age of the [original] cohort spanned 11 years, the age of participants surveyed at the end of the trial spanned 5 years.” “The proportion of original cohort members being included in the final survey was unlikely to be more than 7%.” p.2543. Comment: there was a very low follow-up rate of the original cohort. Cross-sectional analysis of clusters was completed, but with few of original participants. As a result any effect of the intervention is likely to be diluted by following up members of the cluster who did not receive the intervention.
Selective reporting (reporting bias)	Low risk	Comment: all outcomes stated in the Methods were reported.
Other bias	High risk	Quote: "It became difficult to implement the programme in schools for political reasons. This coincided with a fall in school attendance for economic reasons." p.2551. A reported decline in HIV incidence in Zimbabwe resulted in a change in study design in order to increase the power of the study. As a result, the final cross-sectional survey included six enumeration areas from each community (each community contained approximately 50 enumeration areas), so approximately 12% of eligible 18-22 year olds were sampled. As a result of outmigration the proportion of the original cohort members being included was unlikely to be more than 7%.

Duflo 2015 KEN

Methods	Trial design: cluster-RCT Unit of randomization: schools Number of clusters: 328 Data collection: unannounced 'roll call' visits were made over 5 years. Biomarker data (HIV and HSV2) were measured at 7 years. Length of follow-up: 7 years Adjustment for clustering: yes
Participants	Target group: 6th grade students (13 to 14 years old)

Duflo 2015 KEN *(Continued)*

	Sample size: 19,289 students in 6th grade in 2003, enrolled in primary schools Exclusions: none stated
Interventions	The intervention (3 intervention groups: 1. Stand-alone education subsidy, 2. Stand-alone education, 3. a joint programme of subsidy plus education). • Did the target group receive sexuality education? Yes, the Kenyan government's UNICEF HIV/AIDS curriculum. • How many sessions? No details given about exposure or timing. • Who delivered the sessions? Trained class teachers. • What was the content of the session? The focus was on abstinence until marriage. • What additional components were there? Health clubs to deliver HIV information outside the classroom. The 'stand-alone education subsidy' was free school uniforms that were given at the onset of the school year and 18 months later. • Were condoms distributed free? No. Control group: no intervention.
Outcomes	Included in this review: • prevalence of HIV at 7 years; • prevalence of HSV2 at 7 years; • self/peer-reported pregnancy; • self-reported sexual debut; • self-reported condom used at last sex. Not included in this review: • school enrolment; • self-reported marriage; • knowledge of HIV/AIDS.
Notes	Country: Kenya Setting: Butere-Mumias and Bungoma Study dates: 2003 to 2010 Study sponsors:the Hewlett Foundation, the MacArthur Foundation, the National Institutes of Health, the Nike Foundation, the Partnership for Child Development, and the World Bank

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "Schools were stratified and assigned to one of four arms using a random number generator." p.2673.
Recruitment bias	Low risk	Comment: all schools in the geographical area were included and agreed to participate. Clusters were randomized first and then individuals were included from those clusters. However students were enrolled before the announcement of the educational subsidy programme and only those on the original baseline enrolment group were eligible for free uniforms.
Baseline imbalance	Low risk	Quote: "Differences across treatment groups are small in magnitude and only 4 of 65 p-values estimated are smaller than 0.10, suggesting that the randomization was effective at creating balance between the groups."

Duflo 2015 KEN *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: allocation concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: blinding of students not described. Blinding of teachers was not possible.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: 'roll calls' were used for the pregnancy outcomes. It was unclear if the assessors were blinded to allocation of the schools and therefore the individuals attending them. The HIV and HSV2 testing was completed by a mobile clinic and later, for those who had not responded, 'field officers' and 'lab technicians'. Again it was unclear if these assessors were blinded to allocation of the individuals/schools.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: there was no loss of clusters in the trial.
Selective reporting (reporting bias)	Low risk	Comment: all outcomes stated in the methods were reported.
Other bias	Low risk	Comment: no other source of bias was identified.

Henderson 2007 GBR

Methods	Trial design: cluster-RCT Unit of randomization: schools Number of clusters: 25 Data collection: Data collection was via linkage of individual participants' details to NHS conception and termination data, aggregated by school. Length of follow-up: 4.5 years. Adjustment for clustering: yes Cluster-RCT to assess the impact of a theoretically-based sexuality education programme in 25 (13 intervention, 12 control) secondary schools in the east of Scotland. The approach taken was stated as 'harm reduction' so that those already sexually active would be encouraged to use condoms. Incentives were offered to schools including teacher training, supply cover, or, for schools in the control arm, an equivalent cash amount that could be spent on personal and social education but not sexuality education.
Participants	Target group: 3rd year secondary school students aged 13-15 years Sample size: 4196 Exclusions: Roman Catholic schools
Interventions	The intervention • Did the target group receive sexuality education? Yes, SHARE (Sexual Health and Relationships: Safe, Happy and Responsible). • How many sessions? 20 sessions; 10 sessions in 3rd year, aged 13-14 years and 10 in the 4th year, aged 14-15 years.

Henderson 2007 GBR *(Continued)*

- Who delivered the sessions? Trained class teachers.
- What was the content of the session? Advice to delay sexual intercourse until they were ready and always use a condom until they planned to have children.
- What additional components were there? Access to health services.
- Were condoms distributed free? No.

Control group: usual practice.

Outcomes	Included in this review: • current pregnancy; • has been pregnant; • self-reported sexual debut; • self-reported use of condom at first sex; • self-reported use of condom at last sex. Not included in this review: • any self-reported evidence of sex unprotected against STDs; • mean score for condom use; • self-reported most recent intercourse with oral contraception, with or without a condom; • self-reported unwanted pregnancies.
Notes	Country: Scotland Setting: state schools in east Scotland Study dates: 1993 to 1996 Study sponsors: UK Medical Research Council and Health Education Board for Scotland

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A balanced randomisation took into account socioeconomic characteristics of the school populations…" Comment: stratification of random sampling described. Method of random generation not described. Source: p.2 Recruitment and randomisation of schools
Recruitment bias	Unclear risk	Comment: clusters were randomized first and then individuals were recruited from those clusters.
Baseline imbalance	Unclear risk	Comment: slight imbalance in gender reported by authors. Also there was a difference in those students who had reported sexual intercourse at baseline. Source: p.3 online (Wight 2002)
Allocation concealment (selection bias)	Unclear risk	Comment: allocation concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: blinding of students was not described. Blinding of teachers was not possible, as teachers were sent on a SHARE training course.

Henderson 2007 GBR *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "We submitted records of surname, forename, date of birth, and postcode(s) for women in the trial (excluding withdrawals) for linkage to the NHS data. Comment: biological outcome data from NHS databases, gathered independently of trial personnel, but blinding of study assessors not described. Source: p.2 Follow up and statistical analysis
Incomplete outcome data (attrition bias) All outcomes	Low risk	Biological outcomes: Quote: "There may have been a small level of attrition across both arms because of women attending private health care (less than 2% of terminations), moving from Scotland during the study period (1% average annual migration out of Scotland), or having their terminations in England or Wales (2.7% of all terminations performed on Scottish residents). On balance, the comparison between this study and national rates suggests that the linkage was broadly effective." Comment: 99.6% participants in intervention arm analysed, 99.5% participants in control arm analysed (flow diagram p.2). Very high follow-up rate, loss to follow-up not significantly different across trial arms (9/2071 intervention arm vs 10/2135 control arm). Intention-to-treat analysis performed. Source: p.3 Discussion first paragraph, and p.2 flow diagram. Outcome group: self-reported outcomes Quote: "One school considered the baseline survey to be too explicit for pupils aged 13-14 years but took part in all other aspects of the study" "a new work experience scheme increased this [leaving school] to 27%. The response rate was lower for school leavers (41% control, 38% intervention). Non-response among those still in school was primarily among persistent absentees, but a small proportion refused to participate (2%). The response rates were similar in each arm of the trial." Comment: follow-up data available for 2987/4233 (71%) control pupils, and 2867/4197 (68%) intervention pupils. High loss to follow-up, spread approximately equally across both groups. Systematic under-representation of school leavers could possibly have introduced bias towards the null as data is missing regarding long-term effects. Source: p.3 Participant follow up, p.2 flow chart
Selective reporting (reporting bias)	Low risk	Comment: all outcomes stated in methods were reported.
Other bias	Low risk	Comment: no other source of bias identified.

Jemmott 2015 ZAF

Methods	Trial design: cluster-RCT Unit of randomization: schools Number of clusters: 18 (9 matched pairs) Data collection: questionnaire surveys at 3, 6, 12, 42, and 54 months. Blood test and urine sample for STIs at 54 months Length of follow-up: 54 months

Jemmott 2015 ZAF *(Continued)*

	Adjustment for clustering: yes
Participants	Target group: Grade 6 pupils (median age not stated but range 9 to 18 years) Sample size: 1057 Exclusions: none stated
Interventions	The intervention • Did the target group receive sexuality education? Yes. • How many sessions? 12 sessions given over 6 days. • Who delivered the sessions? Adult facilitators with 8 days' training. • What was the content of the session? 'Let us protect our future' programme with small group mixed gender sessions involved games, brainstorming, role-playing, group discussions and comic work-books with a series of characters and storylines.Participants were given assignments to take home and to complete with parents. • What additional components were there? Incentives were given to encourage participants to attend follow-up (notebooks, pens, cap, jacket). • Were condoms distributed free? No. Control group: no intervention.
Outcomes	Outcomes included in this review: • self-reported condom use at last sex. Outcomes not included in this review: • HSV-2 prevalence (data not available); • self-reported unprotected vaginal intercourse in the 3 months prior to final data collection (54 months); • self-reported sexual experience (e.g. vaginal sex, multiple partners, heterosexual anal sex, consistent condom use, frequency of condom use, talking to parents about condoms and about not having sex); • potential mediators/theoretical constructs of the HIV risk-reduction intervention targeted.
Notes	Country: South Africa Setting: urban/semi-rural areas of Eastern Cape Study dates: 2004 to 2010 Study sponsors: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Schools were randomized firstly from 35 eligible schools but the method for this was not described. It was not clear how the matching was done for the18 schools chosen. The authors did say that randomization was done using a computer-generated random number sequence within pairs where one of the pair would be allocated to the HIV/STI risk reduction intervention and one to the control group. p. 611.
Recruitment bias	Unclear risk	Comment: clusters were randomized first and then individuals were recruited from those clusters.
Baseline imbalance	Unclear risk	Comment: there was some imbalance at baseline.

Jemmott 2015 ZAF *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "School personnel, potential participants and recruiters were masked to the schools' randomized intervention assignment." p.611.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The nature of the intervention precluded masking the facilitators and participants to the group assignment during the interventions." p.611.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: blinding was not described. Source: Measures: p.615. No description of blinding of laboratory technicians to the allocation status of the samples
Incomplete outcome data (attrition bias) All outcomes	Low risk	It appears that the authors had a very high follow-up rate. The participant flow diagram (p.616) suggests that the study had a 99.2% follow-up at 54 months (1049/1057).
Selective reporting (reporting bias)	High risk	Data for the biological outcomes was not included in table 2 (p.617) so could not be included in the meta-analysis. The authors were contacted directly and asked for the data but this has not been sent to date.
Other bias	Unclear risk	Method of choosing schools that were eligible was not sufficiently described.

Ross 2007 TZA

Methods	Trial design: cluster-RCT Unit of randomization: communities Number of clusters: 20 Data collection: survey at 1 and 3 years after enrolment. HIV/HSV2 and pregnancy test at 3 years Length of follow-up: 3 years Adjustment for clustering: yes
Participants	Target group: Year 5 to 7 primary school pupils (14 to 18 years old) Sample size: 9645 Exclusions: none stated
Interventions	The intervention: • Did the target group receive sexuality education? Yes. • How many sessions? 12 x 40 minute sessions per year for 2 years. • Who delivered the sessions? Teachers with peer assistants. • What was the content of the session? Aimed to provide knowledge and skills to delay sexual debut, reduce sexual risk-taking and increase appropriate use of health services. • What additional components were there? Health workers were trained for 1 week in the provision of youth-friendly sexual and reproductive health services and supervised quarterly. Community mobilization activities included annual youth health weeks, interschool competitions and performances, and quarterly video shows. • Were condoms distributed free? No, but they were promoted and sold by 4-5 peer assistants per village.

Ross 2007 TZA *(Continued)*

	Control group: no intervention.
Outcomes	Outcomes included in this review: • HIV incidence; • HSV2 prevalence; • syphilis prevalence; • current pregnancy; • self-reported sexual debut; • self-reported condom use at last sex. Outcomes not included in this review: • other self-reported sexual behaviour such as more than 1 partner during the past 12 months.
Notes	Country: Tanzania Setting: rural areas of Mwanza region Study dates: 1998 to 2002 Study sponsors: The European Commission, Development Cooperation Ireland, UK Medical Research Council, Department for International Development (DFID)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Restricted randomisation was used to balance HIV and chlamydia prevalence between the two trial arms” Comment: stratified randomization of communities described; stratification explained. Source: p.1944 Methods (Ross 2007 TZA).
Recruitment bias	Low risk	Comment: individuals were recruited first and then randomized to clusters.
Baseline imbalance	Low risk	Quote: "The baseline characteristics of the intervention and comparison groups were generally similar (Table 2). Slight baseline imbalances in ethnic group and lifetime number of partners were adjusted for in all analyses of trial outcomes. There were substantial differences between male and female participants, so outcomes were analyzed separately for sex." p.1947.
Allocation concealment (selection bias)	Low risk	Quote: "A system of constrained randomisation was used to allocate communities to the two study arms,ensuring adequate balance on important factors. There were 28,000 ways of allocating half the communities in each stratum to the intervention arm. A computer program tested whether each of these allocations satisfied balance criteria, including: (i) mean HIV prevalence in each study arm within 0.075% of overall mean; (ii) mean prevalence of Chlamydia trachomatis (CT) in each arm within 0.1% of overall mean; (iii) one of two communities neighbouring gold mines allocated to each arm; (iv) even distribution of intervention communities over the four project districts. A total of 953 allocations satisfied these criteria, and one was randomly chosen at a meeting attended by senior government officials" Source: p.436 (Hayes 2005).
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no blinding described.

Ross 2007 TZA *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: blinding was not described. Source: p.1946 Impact evaluation final paragraph. There is no description of the authors blinding the laboratory technicians to the allocation status of the samples.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "7040 (73%) of the 9645 eligible cohort members were seen at the final survey. Follow up rates were similar in the intervention (72%) and comparison (74%) communities, higher among male (77%) than female (69%) participants (P<0.001)" "HIV incidence was much lower than predicted based on a previous survey of 15-19 year olds in the same communities… those who were lost to follow up may have been at a higher risk than those followed up." Comment: similar attrition across intervention and comparison groups Source: p.1497 Completeness of follow up p.1949 Table 2 p.1951 Discussion
Selective reporting (reporting bias)	Low risk	Comment: all outcomes stated in Methods were reported.
Other bias	Low risk	Comment: no other source of bias identified.

Stephenson 2008 GBR

Methods	Trial design: cluster-RCT Unit of randomization: schools Number of clusters: 27 Data collection: survey questionnaires were completed in the classroom at baseline, and after 6 and 18 months. Those who were still in school also completed a questionnaire at 54 months after baseline. Those who had left school were provided with a questionnaire by post, by home visit or by GP. Primary outcome measures were abortion and live births age 20 as determined by linkage to routine NHS data. Length of follow-up: 7 years Adjustment for clustering: yes
Participants	Target group: Year 9 pupils, (13 to 14 years old) Sample size: 9508 (eligible and followed up for biological outcomes), 8766 for other outcomes Exclusions: 8 schools were excluded due to distance from London where the research team was located.
Interventions	The intervention • Did the target group receive sexuality education? Yes. • How many sessions? 3 x 1 hour sessions in Year 9. • Who delivered the sessions? Trained peer educators.

Stephenson 2008 GBR *(Continued)*

	• What was the content of the session? Sessions focused on sexual communication and condom use, knowledge about pregnancy, STIs (including HIV), contraception, and local sexual health services. • What additional components were there? None. • Were condoms distributed free? No. Control group: usual teacher-led sexual and relationships education (SRE).
Outcomes	Outcomes included in this review: • current pregnancy; • has been pregnant; • self-reported condom use at first sex; • self-reported condom use at last sex. Outcomes not included in this review: • self-reported sexual intercourse and use of contraceptives at first and last sex; • regretted or pressured sex at first and last sex; • quality of relationship with current partner; • self-reported STI diagnosed by a doctors or nurse; • attendance at clinic for advice about sex; • knowledge of emergency contraceptive pill; • ability to identify local sexual health services.
Notes	Country: England. Setting: rural and urban schools in central and southern England Study dates: 1998-2005 Study sponsors: UK Medical Research Council

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Schools were ranked and divided into three risk strata of approximately equal size. Randomisation of schools occurred within strata, using a computer-generated sequence of allocation of block size ten for each”. Comment: randomization method adequately described, criteria for stratification given. Source: p.1581 Randomisation
Recruitment bias	Unclear risk	Comment: clusters were randomized first and then individuals were recruited from those clusters.
Baseline imbalance	Low risk	Quote: "The two groups were well balanced with respect to demographic data and proportion reporting sexual intercourse at baseline (table 1)." Source: p.342 (Stephenson 2004).
Allocation concealment (selection bias)	Unclear risk	Comment: allocation concealment not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: “blinding of participants to type of sex education was not possible”. Comment: blinding of participants was not possible.

Stephenson 2008 GBR *(Continued)*

		Source: p.1585 Discussion.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: biological outcome measures. Quote: "Following list-cleaning of the trial register through National Health Register (NHS) central register, girls were matched to routine data on live births from two sources: (1) registration of births (2) registration of maternities. Girls were matched to routine data derived from statutory abortion notification…" "Matching to routine sources was blinded". Comment: biological outcomes were measured independently of trial co-ordinators. Source: p.1580 Outcomes p.1585 Discussion
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome group: biological outcomes. Quote: "Primary analysis was by intention to treat." There was "more missing data in the trial register for abortion matching (postcode and date of birth) than for live birth matching (NHS number only). Any bias from under matching of abortions is likely to be toward underestimation of abortion data in the control arm, since the control arm had more missing data than the intervention arm". "missing postcode for 25% of girls (28% control, 21% intervention, p=0.21)". Comment: 100% of all eligible girls were followed up, and an intention-to-treat analysis performed. Missing data for abortions was higher in the control group but the P value was 0.21. It is possible that this might have biased the results towards the null hypothesis, but this appears to be a small risk. Source: p.1581 Statistical methods p.1583 CONSORT diagram. p.1585 Discussion p1584 Evaluation of outcomes Outcome group: self reported measures. Quote: "Parents did not provide consent for 183 (1·9%) of year 9 pupils (1·5% from control, 2·3% from intervention schools) to take part in the research. Two schools (one from each arm) withdrew because of staff changes without knowing their random allocation. One school was unable to implement the intervention, but contributed to follow-up. Differential loss to follow-up between intervention and control schools was largely attributable to loss of one large school after a parent's objection to the questionnaire, although completion rates differed significantly at first follow-up. Source: p.342 (Stephenson 2004). Quote: "Questionnaires at age 18y were completed by significantly more (p=0.001) intervention pupils (52.3% overall: 61.3% girls, 43.7% boys) than control pupils (38.1% overall: 45.4% girls, 31.4% boys)." "pupils at higher risk of pregnancy are likely to be harder to follow up". Comment: high rate of loss to follow-up, different between control and intervention arm.

Stephenson 2008 GBR *(Continued)*		
		Source: p.1584 Evaluation of outcomes paragraph 2, CONSORT diagram p.1583, p.1585 Discussion.
Selective reporting (reporting bias)	Low risk	Comment: all outcomes stated in Methods were reported.
Other bias	Low risk	Comment: no other source of bias identified.

Abbreviations: HIV: human immunodeficiency virus, HIV-1: human immunodeficiency virus-1, HSV2: herpes simplex virus-2, N/A: not applicable, STD: sexually transmitted disease; STI: sexually transmitted infection.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aninanya 2015	No biological outcomes
Bauermeister 2015	No biological outcomes
Beattie 2015	Protocol/early report
Borawski 2015	No biological outcomes
Chhabra 2007	Not an RCT
Coyle 2004	No biological outcomes
Cupp 2013	No biological outcomes
de Walque 2012	Not school-based
Dente 2005	Not an RCT
Di Noia 2007	No biological outcomes
DiClemente 2004	No biological outcomes
DiIorio 2007	Not school-based
Dittus 2014	No biological outcomes
Espada 2015	No biological outcomes
Estrada 2015	No biological outcomes
Gaydos 2008	No biological outcomes
Gray 2007	Not an RCT
Grossman 2013	Not an RCT
Guse 2012	Systematic review
Hawk 2013	Not school-based

Study	Reason for exclusion
Hidalgo 2015	No biological outcomes
Hill 2014	Not RCT
Jemmott 2010	No biological outcomes
Jewkes 2008	Not school-based.
Kennedy 2014	Not school-based
Kirby 1997	No biological outcomes
Langley 2015	No biological outcomes
Li 2008	Not an RCT
Markham 2012	No biological outcomes
Marsch 2015	No biological outcomes
Mathews 2015	No biological outcomes
Mavedzenge 2011	Systematic review
Mellanby 2000	Not an RCT
Michielsen 2010	Systematic review
Morales 2016	No biological outcomes
Morrison 2007	Not an RCT
Namisi 2013	No biological outcomes
Newby 2013	Protocol/early report
Oringanje 2016	Systematic review
Paul-Ebhohimhen 2008	Systematic review
Pedlow 2003	Systematic review
Peskin 2015	No biological outcomes
Pettifor 2015	Protocol/early report
Picot 2012	Systematic review
Prado 2007	Not school-based
Raiford 2014	Not school-based
Reyna 2014	No biological outcomes
Rohrbach 2015	No biological outcomes

Study	Reason for exclusion
Ross 2010	Systematic review
Sanci 2015	Not school-based
Shahmanesh 2008	Systematic review
Shepherd 2010	Systematic review
Simmons 2015	Not school-based
Spoth 2014	Not school-based
Stanton 2015	No biological outcomes
Stephenson 1998	Not an RCT
Tingey 2015	Protocol/early report
Tortolero 2010	No biological outcomes
Underhill 2007	Systematic review
Wang 2014	No biological outcomes
Weiss 2008	Not an RCT
Zhang 2015	Not an RCT
Zimmerman 2008	Not an RCT

Abbreviations: RCT: randomized controlled trial.

Characteristics of ongoing studies *[ordered by study ID]*

ISRCTN56270821

Trial name or title	Preventing sexual risk behavior and partner violence among adolescents in Cape Town
Methods	Cluster-RCT in 42 participating high schools in Western Cape Province
Participants	Males and females in Grade 8 attending public high schools in the Western Cape Province (between 3000 and 4000 adolescents).
Interventions	The intervention consists of 4 components: • after-school clubs to prevent sexual risk behaviour and partner violence and to promote healthy relationships; • a school-based health service; • local police officers' involvement in a school safety programme; • a photography project to involve students in improving the school safety programme.
Outcomes	The primary outcomes are: 1. sexual debut; 2. number of partners; 3. consistent use of condoms

ISRCTN56270821 *(Continued)*

	Secondary outcomes are 1. live births and terminations of pregnancy among female participants, as counts per school, over a 3-year time period; 2. intimate partner violence perpetration and victimization
Starting date	January 2013
Contact information	Catherine Mathews, South African Medical Research Council
Notes	www.controlled-trials.com/ISRCTN56270821

NCT01187979

Trial name or title	Reducing HIV in adolescents (RHIVA): a proof of concept cluster randomized controlled trial to evaluate the impact of a cash incentivised prevention intervention to reduce HIV infection in high school learners in rural KwaZulu-Natal, South Africa
Methods	The impact of the cash incentivised intervention will be assessed using a matched pair, cluster-RCT design. The 14 selected high schools in the Vulindlela School Circuit will be matched in pairs. The matched pairs of schools will be the unit of randomization. Baseline measurements, using a standardized tool (structured questionnaire and biological specimens) will be undertaken simultaneously in each matched pair and will include all eligibly enrolled and consenting learners in the respective schools. On completion of baseline measurements in each matched pair of schools, the randomization code for the pair will be revealed and the intervention will be implemented in the intervention school. All schools will receive the same prevention intervention but only the intervention school will receive the cash incentives. Follow-up measurements will be undertaken approximately 12 and 24 months after implementation of the intervention using a similar standardized assessment tool to that used at baseline.
Participants	4000 Grade 9 and 10 male and female students (aged 13+ years) in 14 schools
Interventions	Behavioural: cash incentives paid to learners for reaching predetermined milestones Behavioural: standard department of education life skills curriculum
Outcomes	Primary: HIV incidence Secondary: academic performance, substance use patterns, pregnancy, contraceptive use, participation in extra-curricular activities, HIV risk-reduction behaviour. Linked HIV and substance use testing will be undertaken in all learners and pregnancy testing in female learners. Other secondary endpoints will be assessed using a structured questionnaire.
Starting date	September 2010
Contact information	Dr Quarraisha Abdool Karim, Centre for the AIDS Programme of Research in South Africa
Notes	www.clinicaltrials.gov/ct2/show/NCT01187979?term=abdool+karim&rank=4

NCT01233531

Trial name or title	Effects of cash transfer for the prevention of HIV in young South African women
Methods	Individually randomized, parallel controlled trial. The overall purpose of this study is to determine whether providing cash transfers to young women and their household, conditional on school attendance, reduces young women's risk of acquiring HIV. The overall goal of the Conditional Cash

NCT01233531 *(Continued)*

	Transfer (CCT) intervention is to reduce structural barriers to education, with the goal of increasing school attendance of young women, thereby decreasing their HIV risk.
Participants	Females 13 to 20 years enrolled in grades 8, 9, 10, or 11 at the beginning of the study at schools at the study site
Interventions	Monthly cash transfer payments for attending school In the intervention, young women and their households will be randomized in 1:1 ratio to receive monthly cash transfer payments, conditional on the young woman attending school, or to the control arm. Young women will be recruited at the beginning of grades 8 through 11 in the first year of the study.
Outcomes	Primary: HIV incidence Secondary: HSV2 incidence, HSV incidence
Starting date	March 2011
Contact information	Audrey Pettifor, University of North Carolina
Notes	www.clinicaltrials.gov/ct2/show/NCT01233531?term=hptn+068&rank=1

NCT02455583

Trial name or title	An assessment of an HIV prevention intervention (Project AIM) on youth sexual intentions, sexual behaviours and HSV-2 incidence and prevalence in junior secondary schools in Eastern Botswana
Methods	Stratified, cluster-RCT
Participants	Males and females enrolled in Form 1 in one of 50 selected schools who are fluent and literate in English or Setswana
Interventions	Form 1 learners at 25 intervention schools will receive the Project AIM intervention (14 sessions of 40 minutes delivered twice a week) and LIVING (standard of care)).
Outcomes	Primary: difference in HSV2 incidence between the intervention and control arm at 24 months Secondary: self-reported sexual and sexual-risk related behaviour measured by sexual initiation, number of sexual partners and frequency of alcohol use, sexual intercourse, and condom use; sexual thoughts measured by frequency of thoughts about engaging in sexual activity, attitudes towards education and frequency of thoughts and feelings about the future and hopelessness; attitudes towards partner concurrency, transactional sex and sexual risk communication with a partner; intention to engage in sexual activity
Starting date	September 2014
Contact information	Kim S Miller, Centers for Disease Control and Prevention Nontobeko S Tau, Botswana Ministry of Education and Skills Development
Notes	clinicaltrials.gov/ct2/show/NCT02455583

NCT02665091	
Trial name or title	Impact of peer education program on HIV/AIDS related sexual behaviours of secondary school students in rural communities, India: a quasi-experimental study
Methods	Individually RCT
Participants	Young people 14 to 18 years old
Interventions	Peer education programme
Outcomes	Primary: knowledge score of HIV Secondary: willingness to have HIV testing, willingness to participate in HIV counselling services and frequency of use of condoms
Starting date	February 2015
Contact information	Hitesh Nayak, NMP Medical Research Institute
Notes	clinicaltrials.gov/ct2/show/record/NCT02665091

Abbreviations: HIV: human immunodeficiency virus; HSV: herpes simplex virus; HSV2: herpes simplex virus-2.

DATA AND ANALYSES

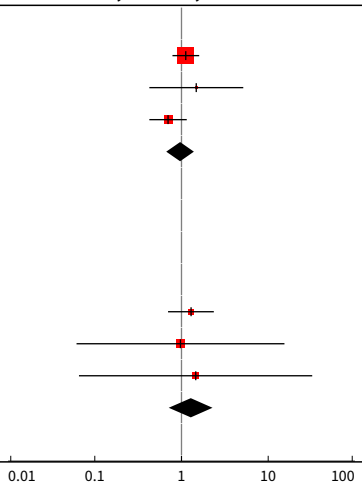
Comparison 1. Educational interventions versus no intervention

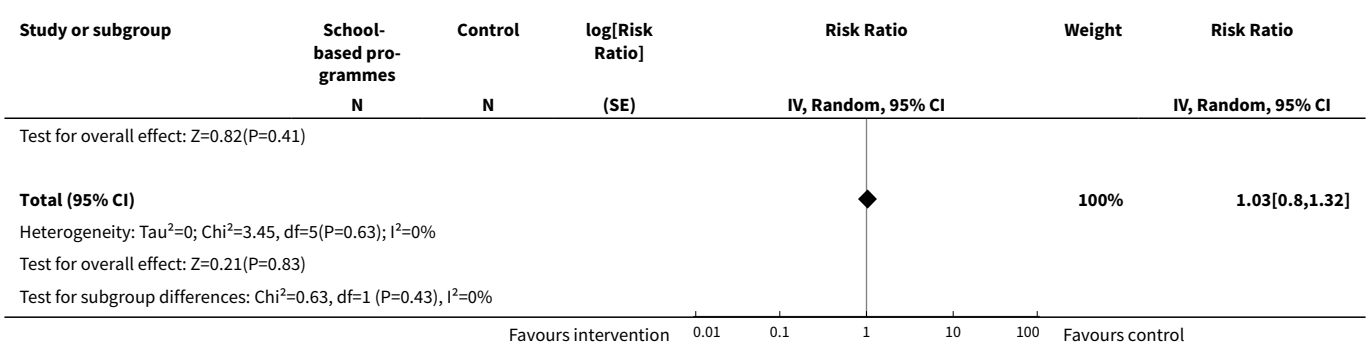
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HIV prevalence	3	14163	Risk Ratio (Random, 95% CI)	1.03 [0.80, 1.32]
1.1 HIV prevalence young women	3	6680	Risk Ratio (Random, 95% CI)	0.96 [0.67, 1.39]
1.2 HIV prevalence young men	3	7483	Risk Ratio (Random, 95% CI)	1.28 [0.71, 2.28]
2 HSV2 prevalence	3	17508	Risk Ratio (Random, 95% CI)	1.04 [0.94, 1.15]
2.1 HSV2 prevalence young women	3	8211	Risk Ratio (Random, 95% CI)	1.05 [0.92, 1.20]
2.2 HSV2 prevalence young men	3	9297	Risk Ratio (Random, 95% CI)	1.02 [0.88, 1.19]
3 Syphilis prevalence	1	6977	Risk Ratio (Random, 95% CI)	0.81 [0.47, 1.39]
3.1 Syphillis prevalence young women	1	2877	Risk Ratio (Random, 95% CI)	0.86 [0.42, 1.76]
3.2 Syphillis prevalence young men	1	4100	Risk Ratio (Random, 95% CI)	0.74 [0.32, 1.72]
4 Pregnancy prevalence (short-term)	3	8280	Risk Ratio (Random, 95% CI)	0.99 [0.85, 1.16]
5 Pregnancy prevalence (long-term)	4	12345	Risk Ratio (Random, 95% CI)	0.55 [0.34, 0.91]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Self-reported sexual debut	4	22623	Risk Ratio (Random, 95% CI)	0.96 [0.91, 1.01]
6.1 Young women	3	8126	Risk Ratio (Random, 95% CI)	1.00 [0.94, 1.06]
6.2 Young men	3	8475	Risk Ratio (Random, 95% CI)	0.95 [0.85, 1.06]
6.3 Self-reported sexual debut young women and young men	1	6022	Risk Ratio (Random, 95% CI)	0.95 [0.82, 1.09]
7 Self-reported use of condom at first sex	2	8015	Risk Ratio (Random, 95% CI)	1.00 [0.98, 1.01]
7.1 Used condom at first sex young women	2	4365	Risk Ratio (Random, 95% CI)	0.99 [0.97, 1.01]
7.2 Used condom at first sex young men	2	3650	Risk Ratio (Random, 95% CI)	1.00 [0.98, 1.02]
8 Self-reported use of condom at last sex	6	18795	Risk Ratio (Random, 95% CI)	1.00 [0.97, 1.03]
8.1 Used condom last sex young women	4	7444	Risk Ratio (Random, 95% CI)	1.01 [0.95, 1.07]
8.2 Used condom at last sex young men	4	6412	Risk Ratio (Random, 95% CI)	1.00 [0.93, 1.07]
8.3 Used condom at last sex women and men	2	4939	Risk Ratio (Random, 95% CI)	1.01 [0.91, 1.12]

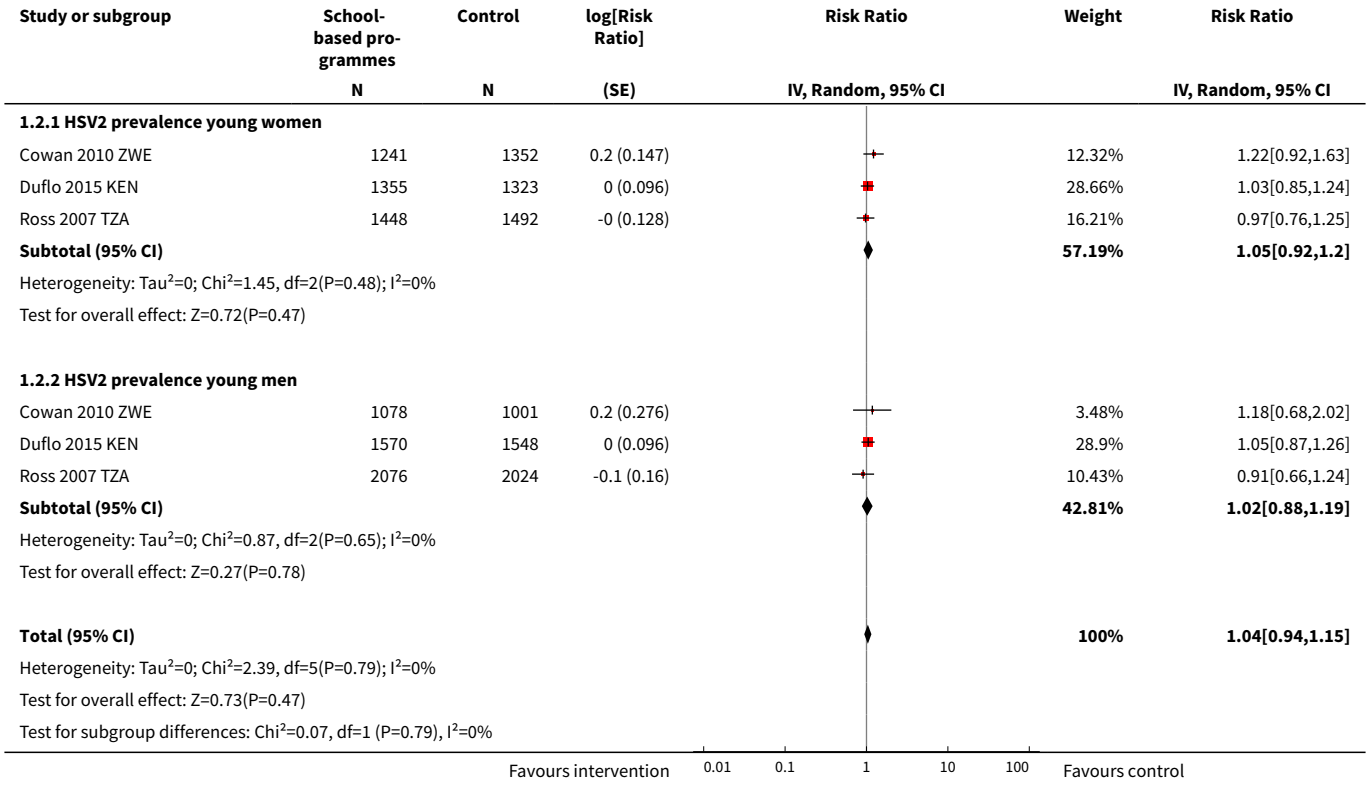
Analysis 1.1. Comparison 1 Educational interventions versus no intervention, Outcome 1 HIV prevalence.

Study or subgroup	School-based programmes N	Control N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 HIV prevalence young women						
Cowan 2010 ZWE	1241	1352	0.1 (0.181)		50.85%	1.12[0.79,1.6]
Duflo 2015 KEN	578	569	0.4 (0.636)		4.13%	1.48[0.43,5.16]
Ross 2007 TZA	1448	1492	-0.4 (0.253)		26.13%	0.7[0.43,1.15]
Subtotal (95% CI)					**81.11%**	**0.96[0.67,1.39]**
Heterogeneity: Tau^2=0.03; Chi^2=2.76, df=2(P=0.25); I^2=27.56%						
Test for overall effect: Z=0.2(P=0.84)						
1.1.2 HIV prevalence young men						
Cowan 2010 ZWE	1078	1001	0.3 (0.31)		17.38%	1.29[0.7,2.36]
Duflo 2015 KEN	666	648	-0 (1.408)		0.84%	0.97[0.06,15.37]
Ross 2007 TZA	2076	2014	0.4 (1.58)		0.67%	1.46[0.07,32.21]
Subtotal (95% CI)					**18.89%**	**1.28[0.71,2.28]**
Heterogeneity: Tau^2=0; Chi^2=0.04, df=2(P=0.98); I^2=0%						

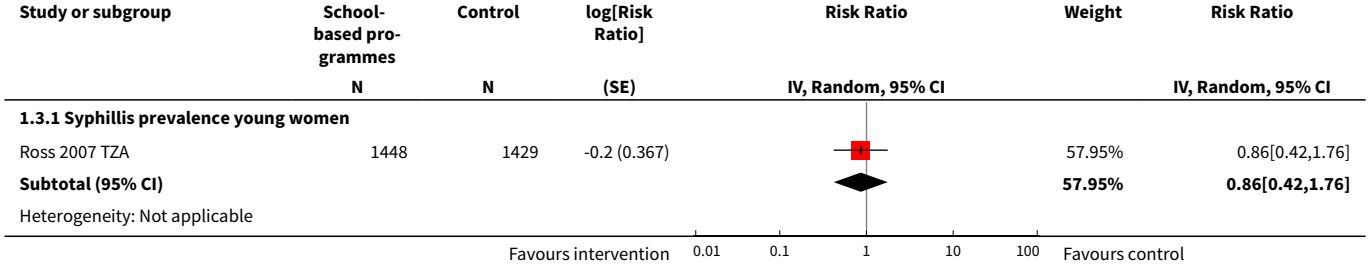


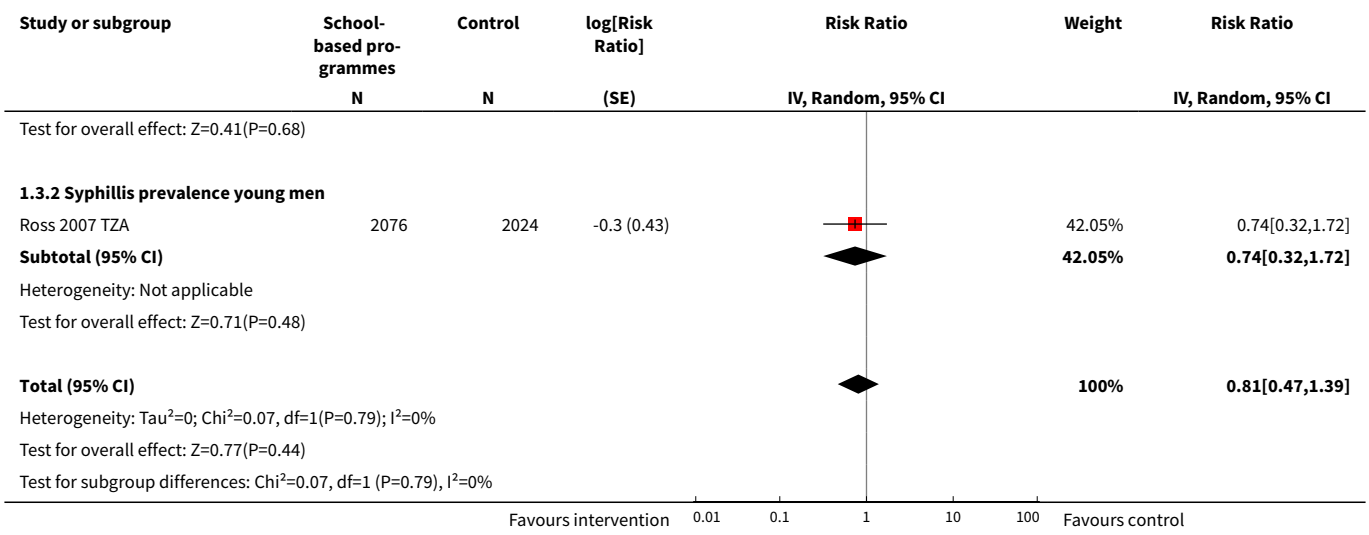


Analysis 1.2. Comparison 1 Educational interventions versus no intervention, Outcome 2 HSV2 prevalence.

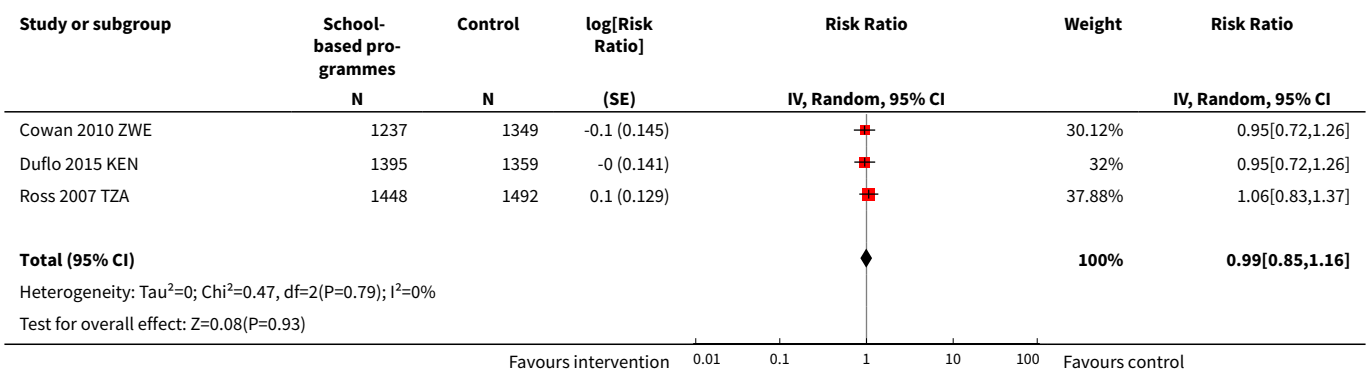


Analysis 1.3. Comparison 1 Educational interventions versus no intervention, Outcome 3 Syphilis prevalence.

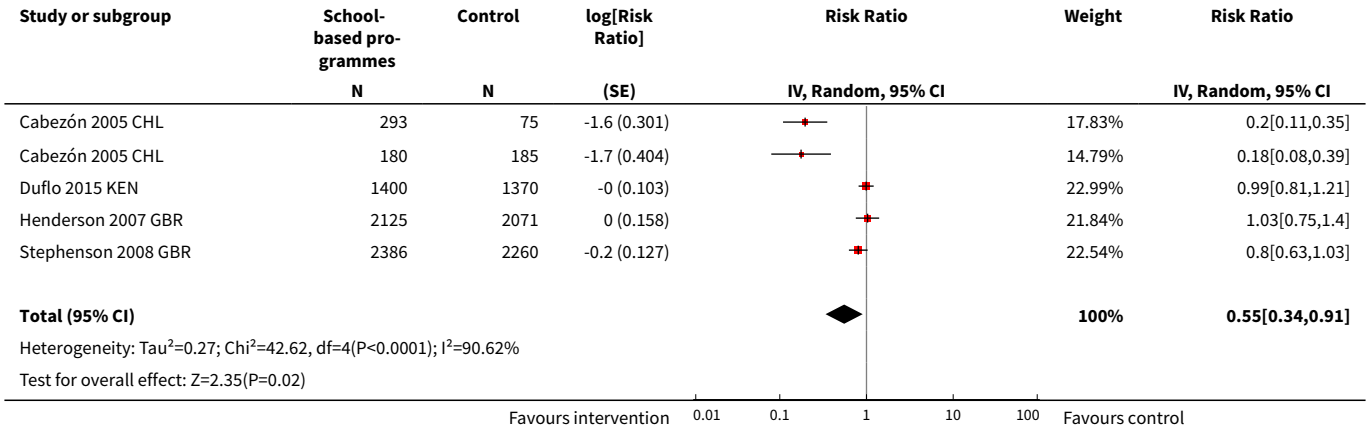




Analysis 1.4. Comparison 1 Educational interventions versus no intervention, Outcome 4 Pregnancy prevalence (short-term).

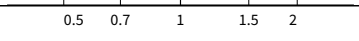


Analysis 1.5. Comparison 1 Educational interventions versus no intervention, Outcome 5 Pregnancy prevalence (long-term).



Analysis 1.6. Comparison 1 Educational interventions versus no intervention, Outcome 6 Self-reported sexual debut.

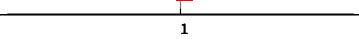
Study or subgroup	School-based programmes N	Control N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.6.1 Young women						
Cowan 2010 ZWE	1217	1289	0 (0.07)		10.84%	1.01[0.88,1.15]
Henderson 2007 GBR	1330	1350	-0 (0.066)		11.69%	0.96[0.85,1.1]
Ross 2007 TZA	1448	1492	0 (0.039)		22.39%	1[0.93,1.08]
Subtotal (95% CI)					**44.93%**	**1[0.94,1.06]**
Heterogeneity: Tau^2=0; Chi^2=0.28, df=2(P=0.87); I^2=0%						
Test for overall effect: Z=0.16(P=0.87)						
1.6.2 Young men						
Cowan 2010 ZWE	1038	974	0 (0.064)		12.12%	1.03[0.91,1.17]
Henderson 2007 GBR	1117	1246	-0 (0.112)		4.9%	0.98[0.79,1.23]
Ross 2007 TZA	2076	2024	-0.1 (0.031)		27.9%	0.89[0.84,0.94]
Subtotal (95% CI)					**44.93%**	**0.95[0.85,1.06]**
Heterogeneity: Tau^2=0.01; Chi^2=4.79, df=2(P=0.09); I^2=58.23%						
Test for overall effect: Z=0.91(P=0.36)						
1.6.3 Self-reported sexual debut young women and young men						
Duflo 2015 KEN	3028	2994	-0.1 (0.073)		10.14%	0.95[0.82,1.09]
Subtotal (95% CI)					**10.14%**	**0.95[0.82,1.09]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%						
Test for overall effect: Z=0.73(P=0.47)						
Total (95% CI)					**100%**	**0.96[0.91,1.01]**
Heterogeneity: Tau^2=0; Chi^2=9.1, df=6(P=0.17); I^2=34.07%						
Test for overall effect: Z=1.45(P=0.15)						
Test for subgroup differences: Chi^2=0.76, df=1 (P=0.68), I^2=0%						



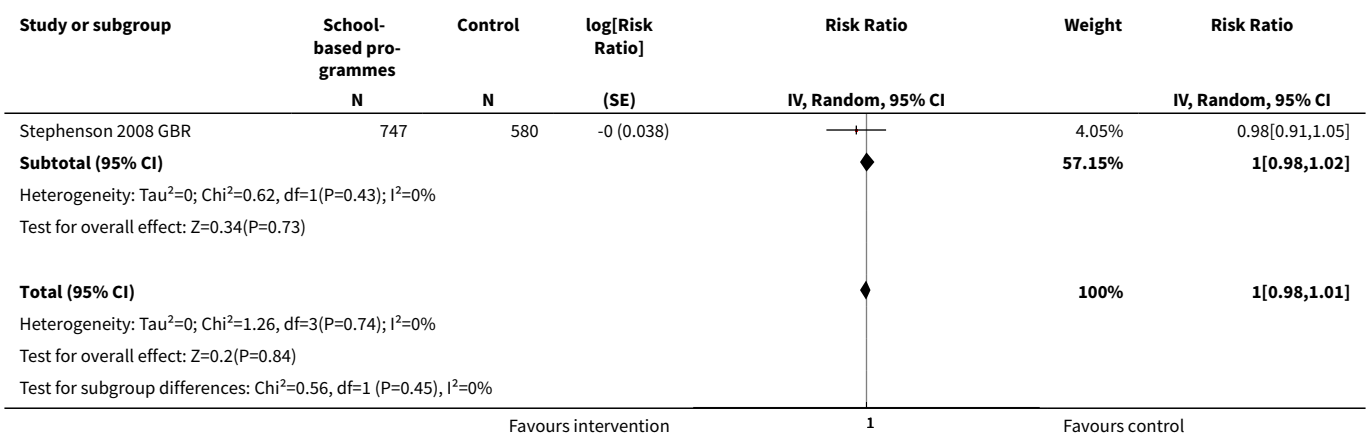
Favours intervention — Favours control

Analysis 1.7. Comparison 1 Educational interventions versus no intervention, Outcome 7 Self-reported use of condom at first sex.

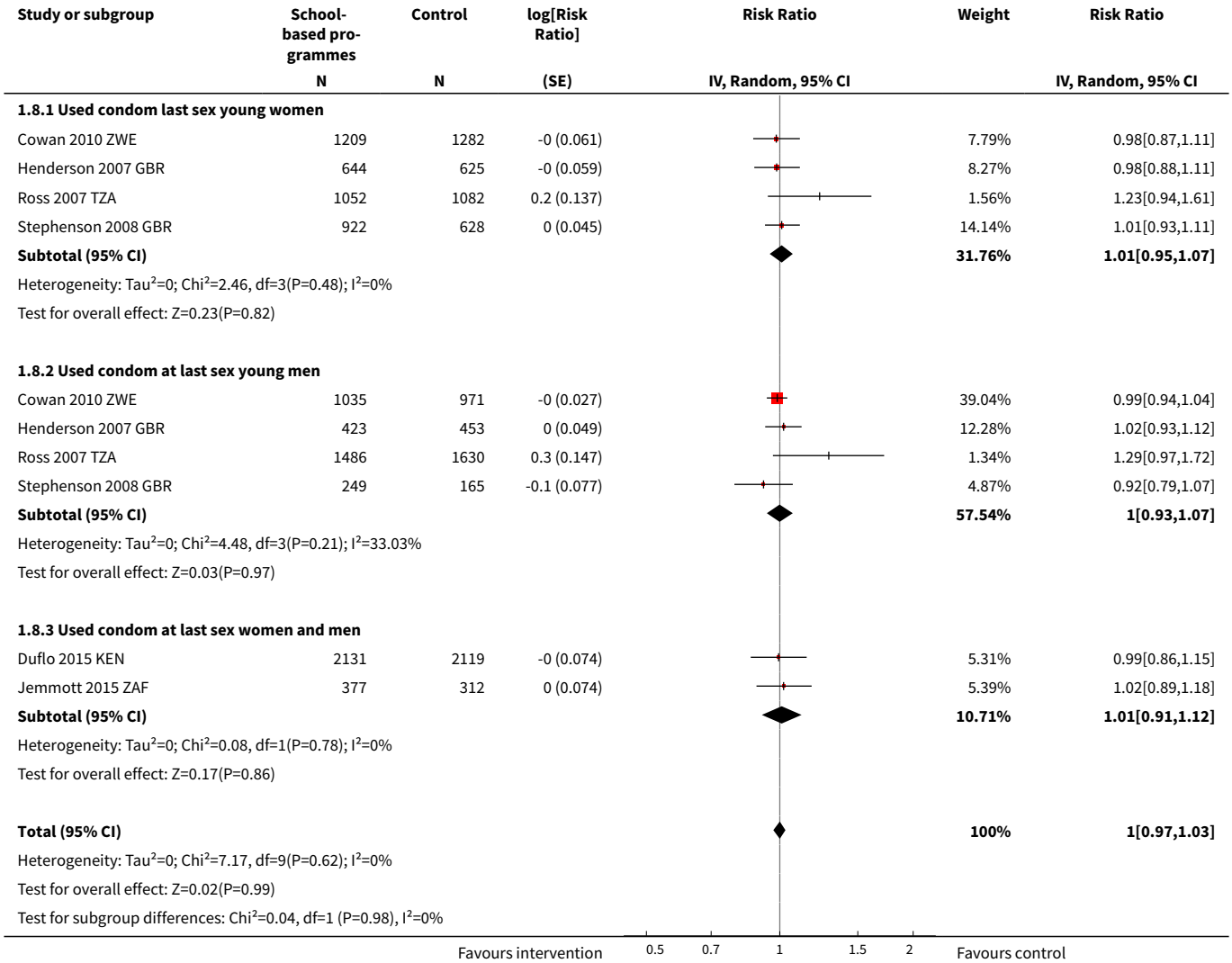
Study or subgroup	School-based programmes N	Control N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
1.7.1 Used condom at first sex young women						
Henderson 2007 GBR	1309	1320	-0 (0.013)		36.75%	0.99[0.97,1.02]
Stephenson 2008 GBR	989	747	-0 (0.031)		6.1%	0.98[0.93,1.05]
Subtotal (95% CI)					**42.85%**	**0.99[0.97,1.01]**
Heterogeneity: Tau^2=0; Chi^2=0.08, df=1(P=0.78); I^2=0%						
Test for overall effect: Z=0.69(P=0.49)						
1.7.2 Used condom at first sex young men						
Henderson 2007 GBR	1099	1224	0 (0.01)		53.1%	1.01[0.99,1.03]



Favours intervention — Favours control



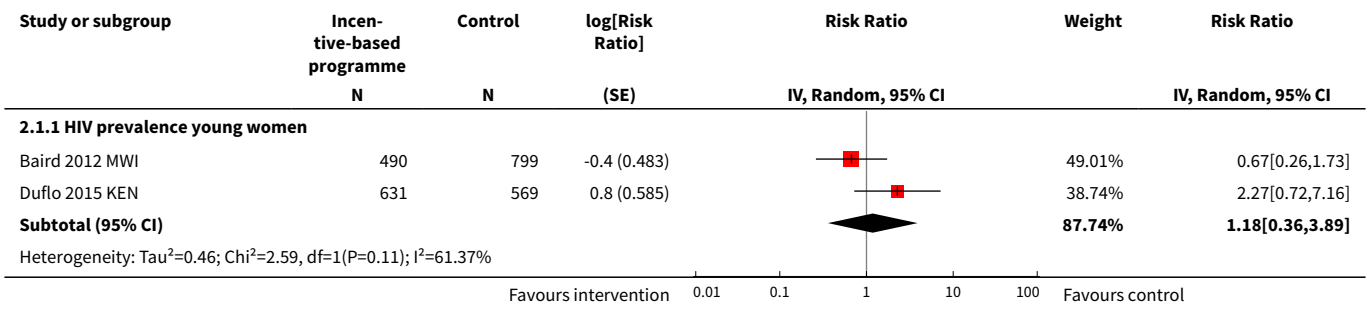
Analysis 1.8. Comparison 1 Educational interventions versus no intervention, Outcome 8 Self-reported use of condom at last sex.

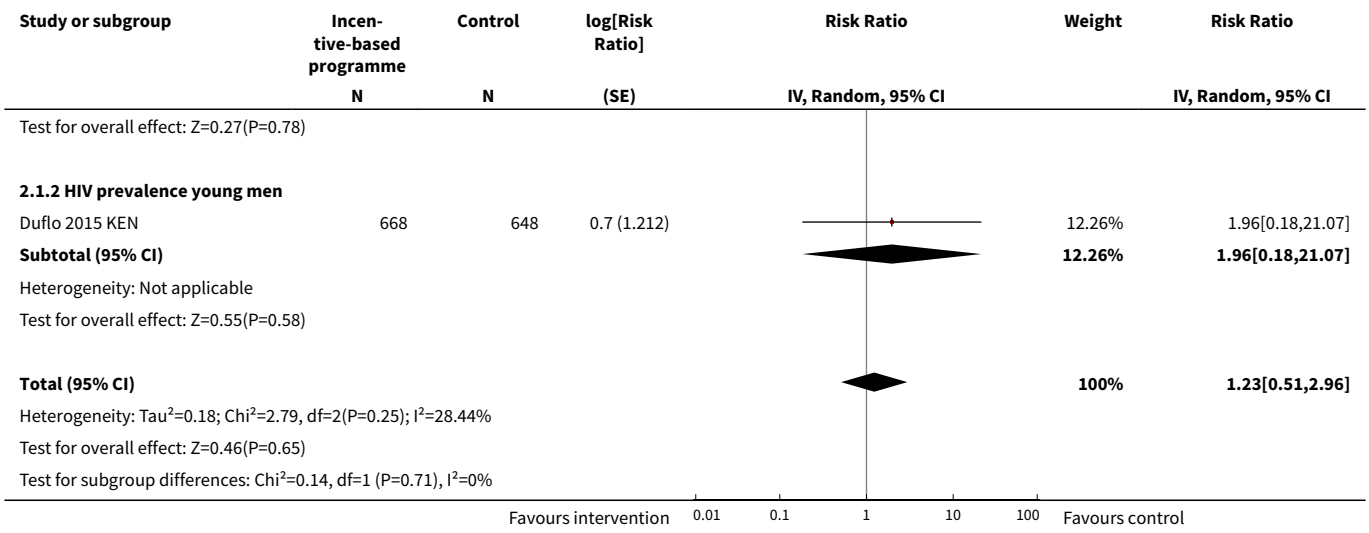


Comparison 2. Incentive-based interventions versus no intervention

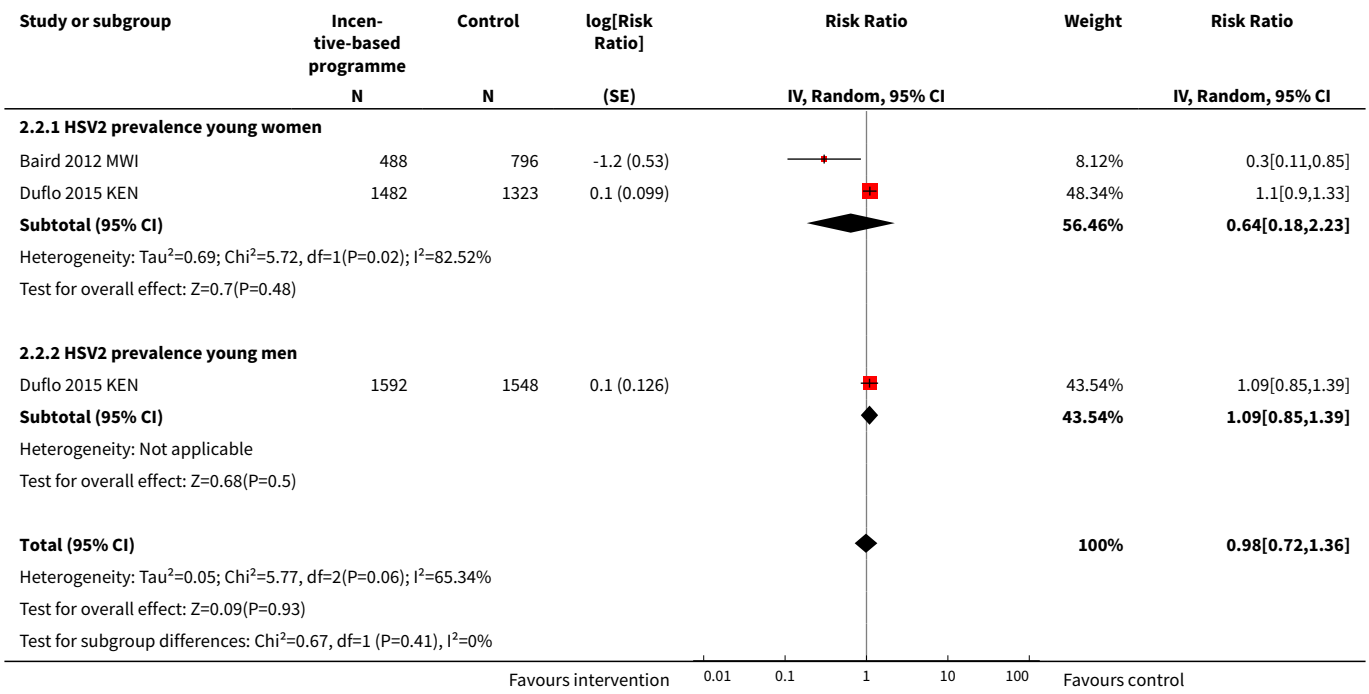
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HIV prevalence	2	3805	Risk Ratio (Random, 95% CI)	1.23 [0.51, 2.96]
1.1 HIV prevalence young women	2	2489	Risk Ratio (Random, 95% CI)	1.18 [0.36, 3.89]
1.2 HIV prevalence young men	1	1316	Risk Ratio (Random, 95% CI)	1.96 [0.18, 21.07]
2 HSV2 prevalence	2	7229	Risk Ratio (Random, 95% CI)	0.98 [0.72, 1.36]
2.1 HSV2 prevalence young women	2	4089	Risk Ratio (Random, 95% CI)	0.64 [0.18, 2.23]
2.2 HSV2 prevalence young men	1	3140	Risk Ratio (Random, 95% CI)	1.09 [0.85, 1.39]
3 Syphilis prevalence	1	1291	Risk Ratio (Random, 95% CI)	0.41 [0.05, 3.27]
3.1 Syphillis prevalence young women	1	1291	Risk Ratio (Random, 95% CI)	0.41 [0.05, 3.27]
4 Pregnancy prevalence (short-term)	2	4200	Risk Ratio (Random, 95% CI)	0.76 [0.58, 0.99]
5 Pregnancy prevalence (long-term)	1	2891	Risk Ratio (Random, 95% CI)	0.89 [0.73, 1.08]
6 Self-reported sexual debut	2	7177	Risk Ratio (Random, 95% CI)	0.83 [0.73, 0.95]
6.1 Young women	1	1016	Risk Ratio (Random, 95% CI)	0.68 [0.41, 1.13]
6.2 Self-reported sexual debut young women and young men	1	6161	Risk Ratio (Random, 95% CI)	0.85 [0.74, 0.97]
7 Self-reported use of condom at last sex	1	4265	Risk Ratio (Random, 95% CI)	0.98 [0.85, 1.12]
7.1 Used condom at last sex women and men	1	4265	Risk Ratio (Random, 95% CI)	0.98 [0.85, 1.12]

Analysis 2.1. Comparison 2 Incentive-based interventions versus no intervention, Outcome 1 HIV prevalence.

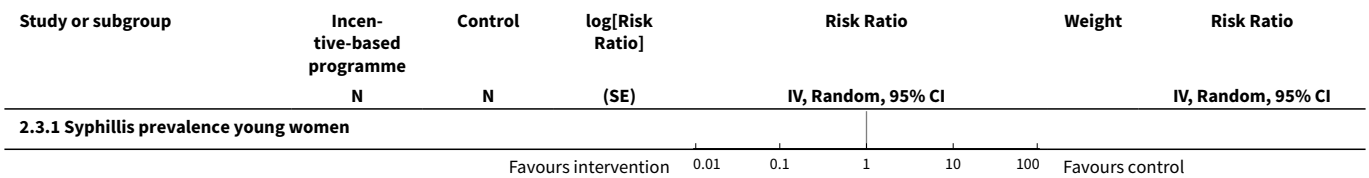


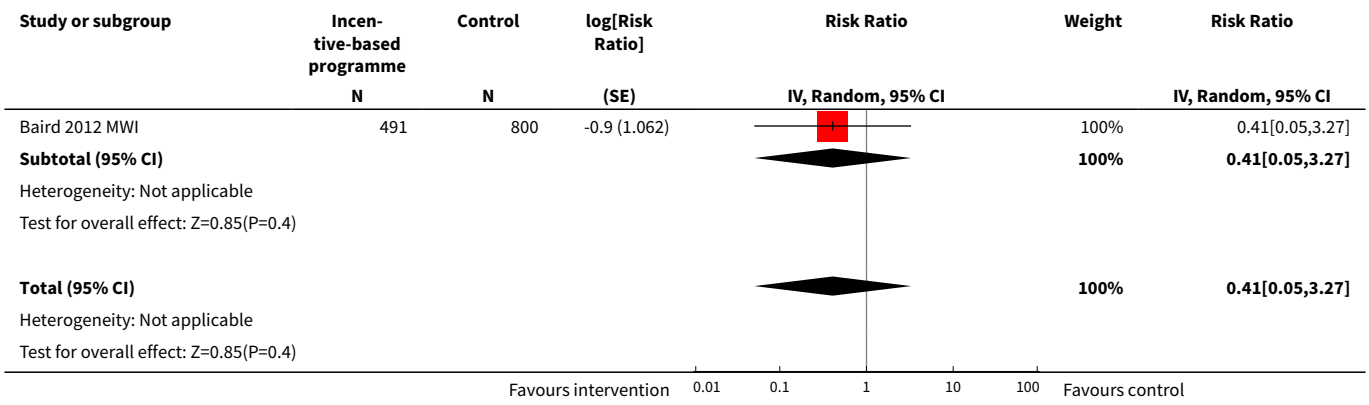


Analysis 2.2. Comparison 2 Incentive-based interventions versus no intervention, Outcome 2 HSV2 prevalence.

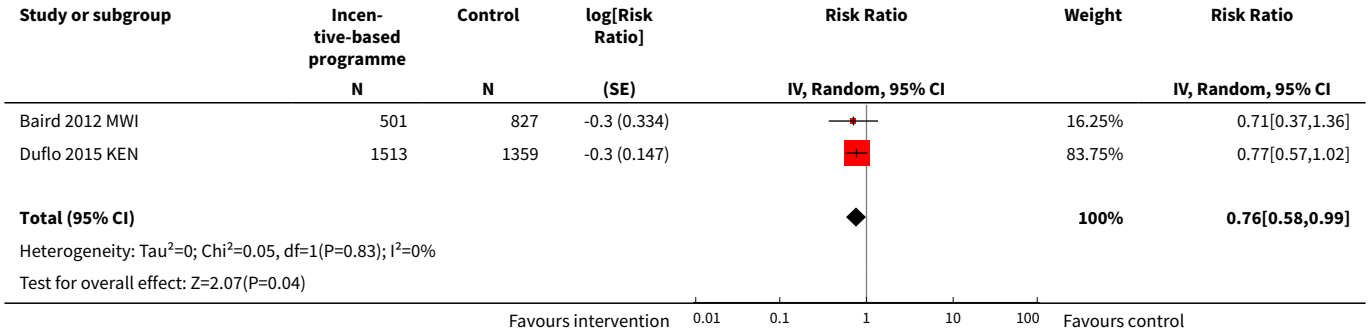


Analysis 2.3. Comparison 2 Incentive-based interventions versus no intervention, Outcome 3 Syphilis prevalence.

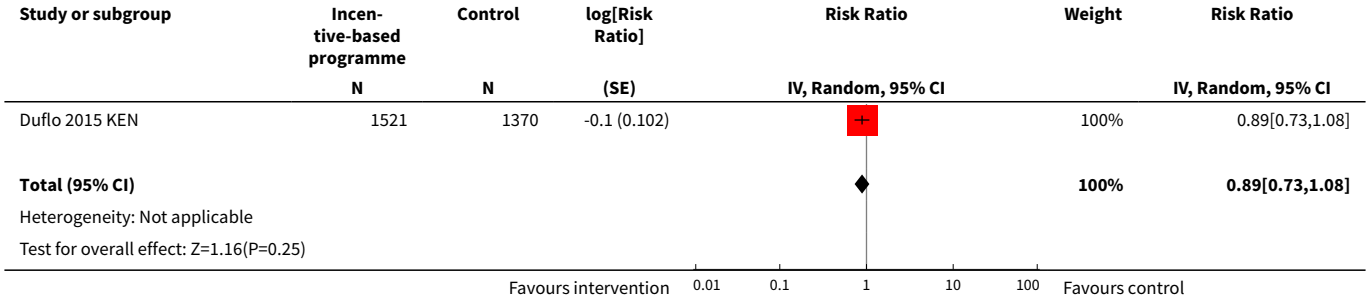




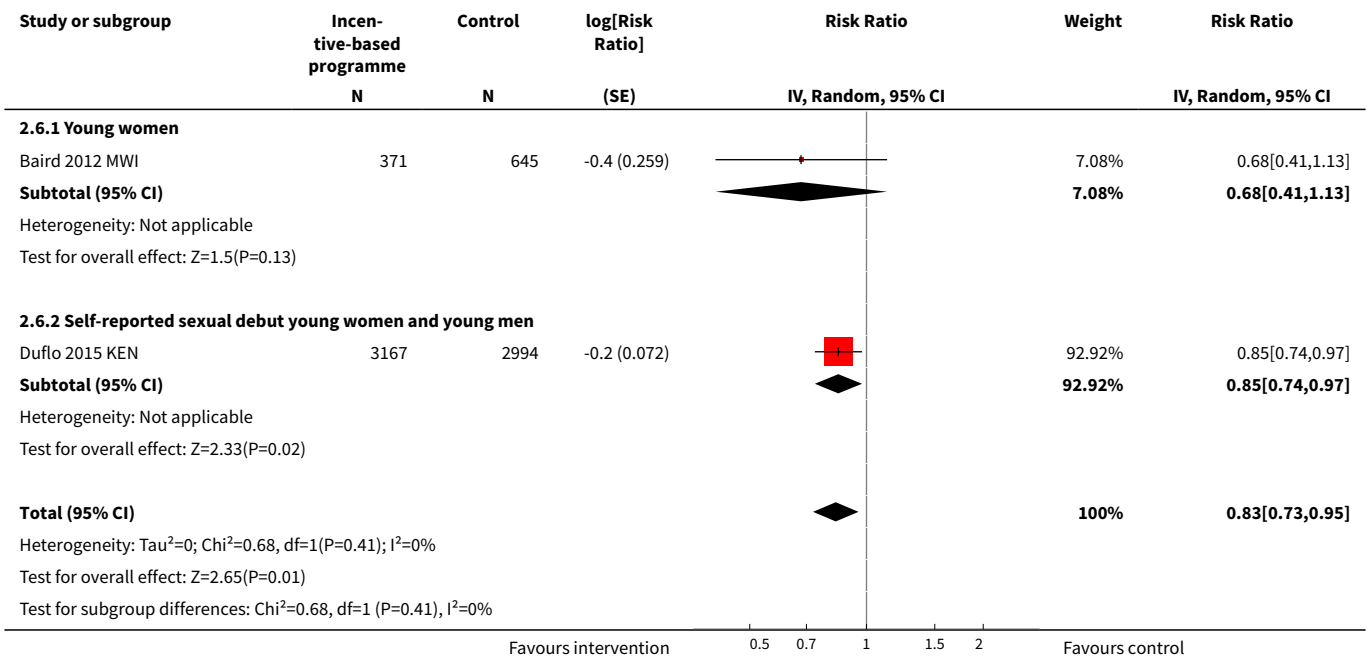
Analysis 2.4. Comparison 2 Incentive-based interventions versus no intervention, Outcome 4 Pregnancy prevalence (short-term).



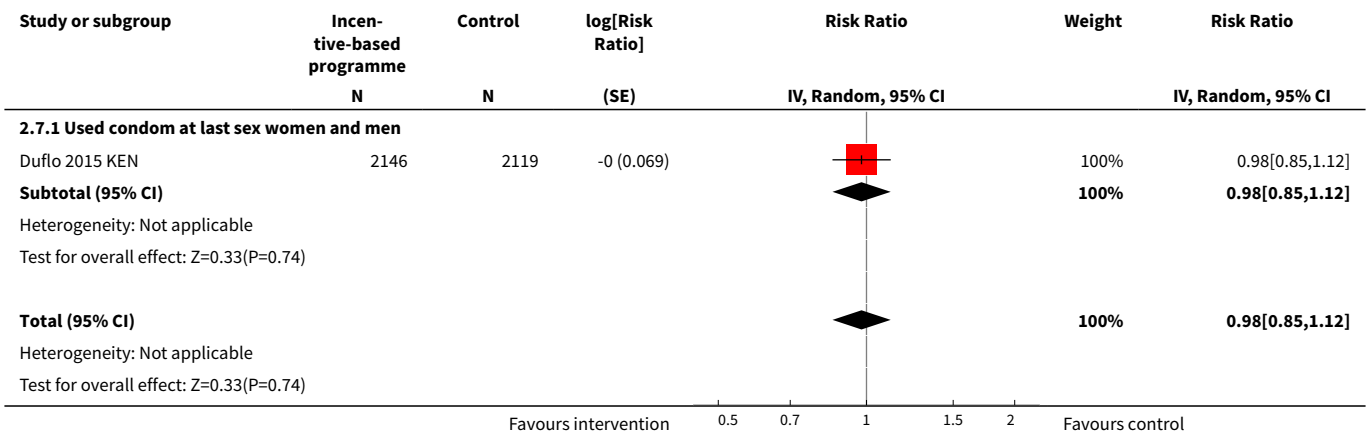
Analysis 2.5. Comparison 2 Incentive-based interventions versus no intervention, Outcome 5 Pregnancy prevalence (long-term).



Analysis 2.6. Comparison 2 Incentive-based interventions versus no intervention, Outcome 6 Self-reported sexual debut.



Analysis 2.7. Comparison 2 Incentive-based interventions versus no intervention, Outcome 7 Self-reported use of condom at last sex.

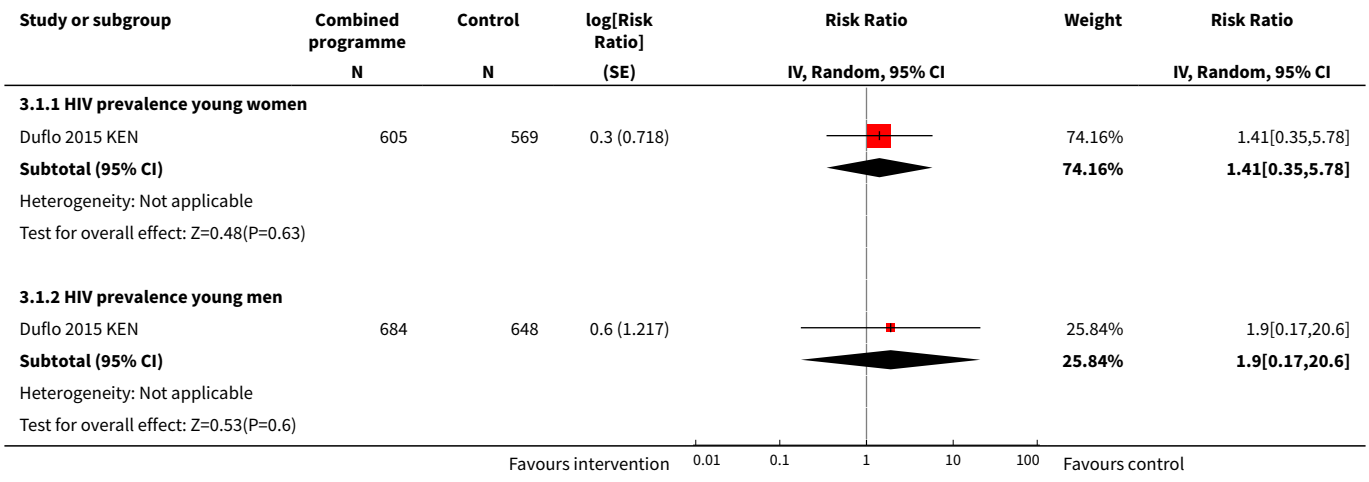


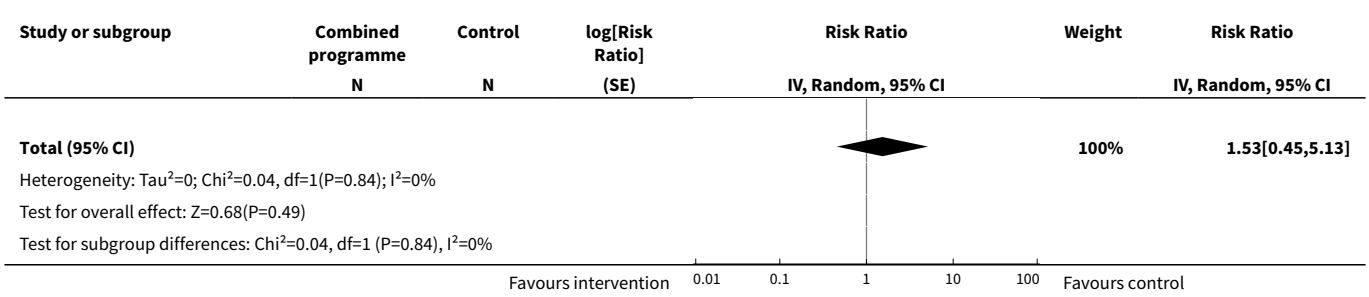
Comparison 3. Combined incentive-based and educational interventions versus no intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HIV prevalence	1	2506	Risk Ratio (Random, 95% CI)	1.53 [0.45, 5.13]

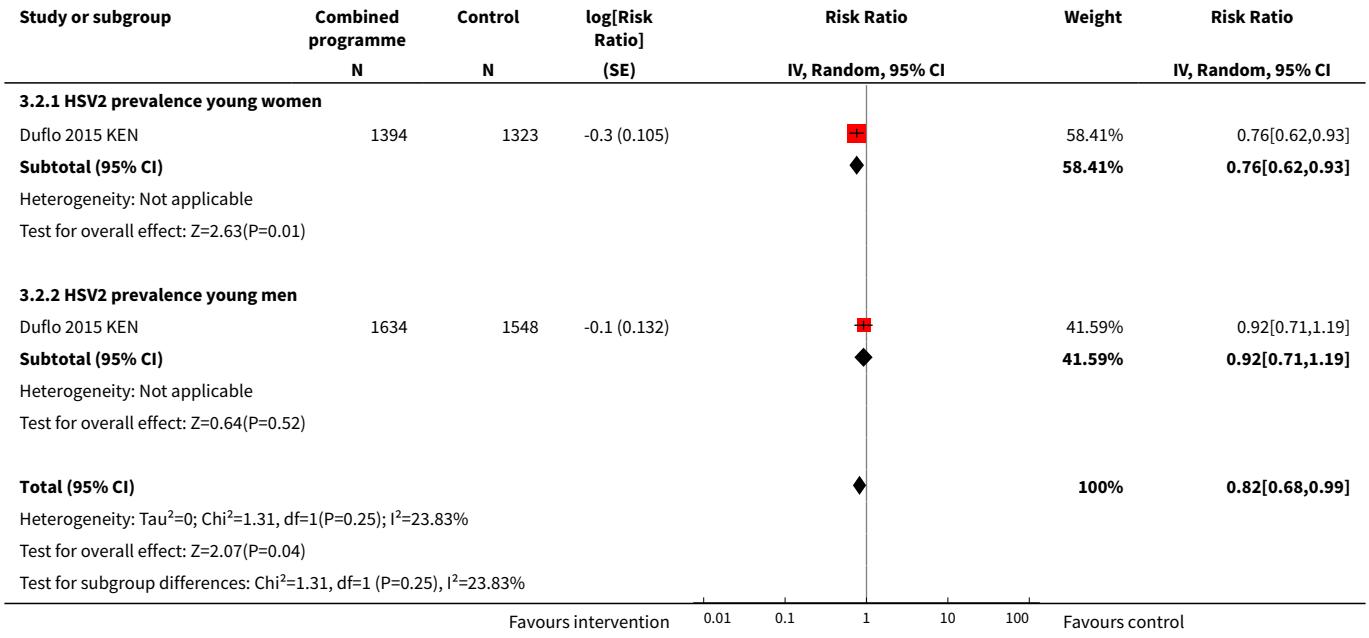
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 HIV prevalence young women	1	1174	Risk Ratio (Random, 95% CI)	1.41 [0.35, 5.78]
1.2 HIV prevalence young men	1	1332	Risk Ratio (Random, 95% CI)	1.90 [0.17, 20.60]
2 HSV2 prevalence	1	5899	Risk Ratio (Random, 95% CI)	0.82 [0.68, 0.99]
2.1 HSV2 prevalence young women	1	2717	Risk Ratio (Random, 95% CI)	0.76 [0.62, 0.93]
2.2 HSV2 prevalence young men	1	3182	Risk Ratio (Random, 95% CI)	0.92 [0.71, 1.19]
3 Pregnancy prevalence (short-term)	1	2782	Risk Ratio (Random, 95% CI)	0.90 [0.67, 1.19]
4 Pregnancy prevalence (long-term)	1	2801	Risk Ratio (Random, 95% CI)	0.90 [0.73, 1.12]
5 Self-reported sexual debut	1	6102	Risk Ratio (Random, 95% CI)	0.84 [0.73, 0.97]
5.1 Self-reported sexual debut young women and young men	1	6102	Risk Ratio (Random, 95% CI)	0.84 [0.73, 0.97]
6 Self-reported use of condom at last sex	1	4193	Risk Ratio (Random, 95% CI)	1.02 [0.89, 1.17]
6.1 Used condom at last sex women and men	1	4193	Risk Ratio (Random, 95% CI)	1.02 [0.89, 1.17]

Analysis 3.1. Comparison 3 Combined incentive-based and educational interventions versus no intervention, Outcome 1 HIV prevalence.

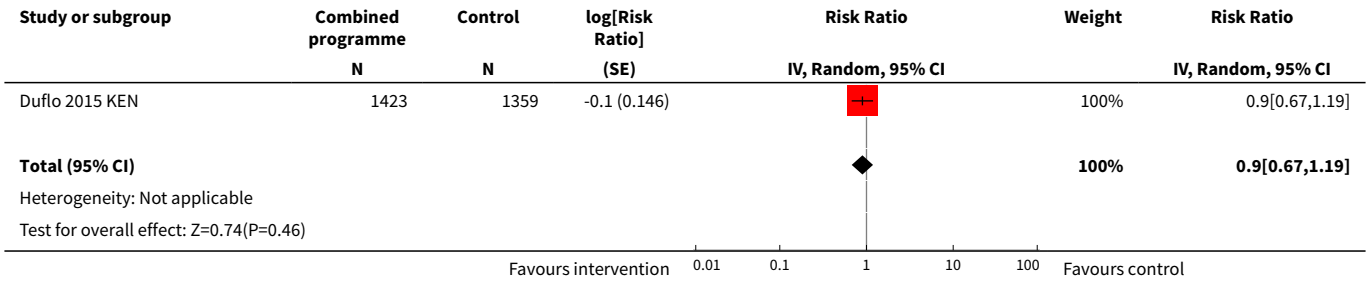




Analysis 3.2. Comparison 3 Combined incentive-based and educational interventions versus no intervention, Outcome 2 HSV2 prevalence.

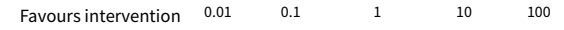


Analysis 3.3. Comparison 3 Combined incentive-based and educational interventions versus no intervention, Outcome 3 Pregnancy prevalence (short-term).



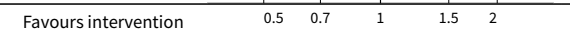
Analysis 3.4. Comparison 3 Combined incentive-based and educational interventions versus no intervention, Outcome 4 Pregnancy prevalence (long-term).

Study or subgroup	Combined programme N	Control N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
Duflo 2015 KEN	1431	1370	-0.1 (0.109)		100%	0.9[0.73,1.12]
Total (95% CI)					**100%**	**0.9[0.73,1.12]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%						
Test for overall effect: Z=0.93(P=0.35)						



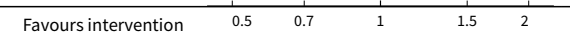
Analysis 3.5. Comparison 3 Combined incentive-based and educational interventions versus no intervention, Outcome 5 Self-reported sexual debut.

Study or subgroup	Combined programme N	Control N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
3.5.1 Self-reported sexual debut young women and young men						
Duflo 2015 KEN	3108	2994	-0.2 (0.071)		100%	0.84[0.73,0.97]
Subtotal (95% CI)					**100%**	**0.84[0.73,0.97]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.43(P=0.02)						
Total (95% CI)					**100%**	**0.84[0.73,0.97]**
Heterogeneity: Not applicable						
Test for overall effect: Z=2.43(P=0.02)						



Analysis 3.6. Comparison 3 Combined incentive-based and educational interventions versus no intervention, Outcome 6 Self-reported use of condom at last sex.

Study or subgroup	Combined programme N	Control N	log[Risk Ratio] (SE)	Risk Ratio IV, Random, 95% CI	Weight	Risk Ratio IV, Random, 95% CI
3.6.1 Used condom at last sex women and men						
Duflo 2015 KEN	2074	2119	0 (0.07)		100%	1.02[0.89,1.17]
Subtotal (95% CI)					**100%**	**1.02[0.89,1.17]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%						
Test for overall effect: Z=0.29(P=0.77)						
Total (95% CI)					**100%**	**1.02[0.89,1.17]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%						
Test for overall effect: Z=0.29(P=0.77)						



ADDITIONAL TABLES

Table 1. Description of educational interventions

Study (Country)	Target group	Target group education				Other components	Outcome measurement
		Duration of intervention	Number of sessions	Delivered by	Content[1]		
Cabezón 2005 CHL (Chile)	Girls (age 15 to 16 years) attending an all girls' high school	1 year	14	Teachers	TeenSTAR programme focusing on abstinence, fertility awareness, and psychological and personal aspects of sexuality.	N/A	3 years
Cowan 2010 ZWE (Zimbabwe)	Form 2 pupils (median age 15 years)	3 years	Unclear 'both in-and-out of school'	A school leaver (peer) who received training and supervision	A focus on developing knowledge and skills around sexual health issues.	A 22-session community-based programme for parents and community stakeholders aimed at improving communication with and community support of teenagers. A strand aimed at nurses and rural clinic workers aiming to improve accessibility of clinics to young people.	4 years
Duflo 2015 KEN (Kenya)	6th grade students (median age 13.5 years)	No details given	No details given	Teachers	Kenyan government's UNICEF/HIV/AIDS curriculum focusing on abstinence until marriage.	Health clubs to deliver HIV information outside the classroom.	2 years 7 years
Henderson 2007 GBR (Great Britain)	13-15 year olds	2 years	20	Teachers	Aimed to reduce unwanted pregnancies, reduce unsafe sex, and improve the quality of sexual relationships.	5-day training for teachers	4.5 years
Jemmott 2015 ZAF (South Africa)	Grade 6 pupils (age range 9 to 18 years)	6 days	12	Adult facilitators with 8 days of training	Mixed-sex sessions involved games, brainstorming, role-playing, group discussions, and comic workbooks with a series of characters and storylines.	Participants were given assignments to take home and to complete with parents.	4.5 years
Ross 2007 TZA (Tanzania)	Primary school students (age	3 years	36	Teachers with peer assistants	Aimed to provide knowledge and skills to delay sexual debut, reduce sexual risk-taking, and in-	Health workers were trained for 1 week in the provision of youth-friendly sexual and re-	3 years

Table 1. Description of educational interventions *(Continued)*

	range 14 to > 18 years)				crease appropriate use of health services.	productive health services and supervised quarterly. Community mobilization activities including annual youth health weeks, inter-school competitions and performances, and quarterly video shows.	
Stephenson 2008 GBR (Great Britain)	Year 9 pupils (age 13 to 14 years)	4 months	3	Peers	Aimed at improving skills in sexual communication and condom use and knowledge of pregnancy, STIs, contraception, and local health services.	N/A	7 years

[1]None of the interventions included free distribution of condoms.
Abbreviations: N/A: not applicable ; STI: sexually transmitted infection.

Table 2. Description of incentive-based interventions

Study ID (Country)	Target group	Incentive-based components				Outcome measurement
		Type	Size	Conditional	Frequency	
Baird 2012 MWI **(Malawi)**	Never married girls (age 13 to 22 years)	Cash	USD 1 to 5 to the participant and USD 4 to 10 to her family	Yes	Monthly	1.5 years
Duflo 2015 KEN **(Kenya)**	6th grade students (median age 13.5 years)	School uniform	—	No	At start of school year and 18 months later	2 years 7 years

Table 3. Optimal information size calculations

Outcome	Assumed risk[1]	Clinically important relative reduction	Sample size required[2,3]
HIV prevalence	10/1000 (1%)	25%	43,576
HIV prevalence	10/1000 (1%)	50%	9344
HSV2 prevalence	110/1000 (11%)	25%	3606
Syphilis prevalence	30/1000 (3%)	25%	14,264
Pregnancy	90/1000 (9%)	25%	4494

[1]The assumed risk is the median control group risk from the included studies.
[2]We based all calculations on 2-sided tests, with a ratio of 1:1, power of 0.8, and confidence level of 0.05.
[3]We performed all calculations using www.sealedenvelope.com/power/binary-superiority.

APPENDICES

Appendix 1. PubMed search strategy

Search	Query
#10	Search (((#7 AND #8))) AND (""[Date - Publication] : ""[Date - Publication])
#9	Search (#7 AND #8)
#8	Search (youth[tiab] OR youths[tiab] OR youngster[tiab] OR teenager[tiab] OR teenagers[tiab] OR teen[tiab] OR teens[tiab] OR adolescent[mh] OR adolescent[tiab] OR adolescents[tiab] OR adolescence[tiab] OR child[mh] OR child[tiab] OR children[tiab] OR young person*[tiab] OR young people[tiab])

(Continued)

#7	Search (#3 AND #4 AND #5 AND #6)
#6	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic"[mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh])
#5	Search (Schools[mh] OR schools[tiab] OR school[tiab] OR community[tiab] OR communities[tiab] OR community networks[mh] OR teacher[tiab] OR teachers[tiab] OR classroom[tiab] OR classrooms[tiab] OR educator[tiab] OR educators[tiab] OR peer[tiab] OR peers[tiab])
#4	Search (sexual behavior[mh] OR sexual behavior[tiab] OR sexual behaviour[tiab] OR sex behavior[tiab] OR sex behaviour[tiab] OR sex education[mh] OR sex education[tiab] OR sex counseling[mh] OR sex counseling[tiab] OR sex counselling[tiab] OR health education/methods[mh] OR health education[tiab] OR health knowledge, attitudes, practice[mh]))
#3	Search (#1 OR #2)
#2	Search (sexually transmitted diseases[mh] OR sexually transmitted disease*[tiab] OR sexually transmissible disease*[tiab] OR sexually transmitted infection*[tiab] OR sexually transmissible infection*[tiab] OR sexually transmitted infectious disease*[tiab] OR sexually transmissible infectious disease*[tiab] OR sexually transmitted disorder*[tiab] OR sexually transmissible disorder*[tiab] OR STI[tiab] OR STIs[tiab] OR STD[tiab] OR STDs[tiab])
#1	Search (HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tiab] OR hiv-1*[tiab] OR hiv-2*[tiab] OR hiv1[tiab] OR hiv2[tiab] OR hiv infect*[tiab] OR human immunodeficiency virus[tiab] OR human immunedeficiency virus[tiab] OR human immuno-deficiency virus[tiab] OR human immune-deficiency virus[tiab] OR ((human immun*[tiab]) AND (deficiency virus[tiab])) OR acquired immunodeficiency syndrome[tiab] OR acquired immunedeficiency syndrome[tiab] OR acquired immuno-deficiency syndrome[tiab] OR acquired immune-deficiency syndrome[tiab] OR ((acquired immun*[tiab]) AND (deficiency syndrome[tiab])) OR "sexually transmitted diseases, Viral"[MeSH:NoExp])

Appendix 2. Embase search strategy

No	Query	Results
#15	#12 AND #13 AND [27-3-2015]/sd NOT [7-4-2016]/sd	81
#14	#12 AND #13	912
#13	'adolescent'/de OR adolescent:ab,ti OR adolescents:ab,ti OR 'adolescence'/de OR adolescence:ab,ti OR 'youth'/de OR youth:ab,ti OR youths:ab,ti OR 'teenager'/de OR teenager:ab,ti OR teenagers:ab,ti OR teens:ab,ti OR 'child'/de OR child:ab,ti OR 'children'/de OR children:ab,ti OR 'minor'/de OR minor:ab,ti OR 'minors'/de OR minors:ab,ti OR 'student'/de OR student:ab,ti OR 'students'/de OR students:ab,ti OR 'young person':ab,ti OR 'young persons':ab,ti OR 'young people':ab,ti	3103461
#12	#3 AND #9 AND #10 AND #11	1691
#11	'school'/de OR school:ab,ti OR 'schools'/de OR schools:ab,ti OR 'community'/de OR community:ab,ti OR communities:ab,ti OR 'teacher'/de OR teacher:ab,ti OR teachers:ab,ti OR classroom:ab,ti OR classrooms:ab,ti OR educator:ab,ti OR educators:ab,ti OR peer:ab,ti OR peers:ab,ti	808453

(Continued)

#10	'sexual behavior'/de OR 'sexual behavior':ab,ti OR 'sexual behaviour'/de OR 'sexual behaviour':ab,ti OR 'sex behavior'/de OR 'sex behavior':ab,ti OR 'sex':ab,ti OR 'sex'/de OR (sex:ab,ti AND behaviour:ab,ti) OR 'sex education'/de OR 'sex education':ab,ti OR 'sex counseling'/de OR 'sex counseling':ab,ti OR 'sex counselling':ab,ti OR 'sexual health'/de OR 'sexual health':ab,ti OR 'sexual education'/de OR 'sexual education':ab,ti OR 'school health education'/de OR 'school health education':ab,ti OR 'attitudes to health':ab,ti OR 'health knowledge, attitudes, practice'/de OR 'health knowledge, attitudes, practice':ab,ti	662610
#9	#4 NOT #8	1598799
#8	#5 NOT #7	5322811
#7	#5 AND #6	1455470
#6	'human'/de OR 'normal human'/de OR 'human cell'/de	17012217
#5	'animal'/de OR 'animal experiment'/de OR 'invertebrate'/de OR 'animal tissue'/de OR 'animal cell'/de OR 'nonhuman'/de	6778281
#4	'randomized controlled trial'/de OR 'randomized controlled trial' OR random*:ab,ti OR trial:ti OR allocat*:ab,ti OR factorial*:ab,ti OR placebo*:ab,ti OR assign*:ab,ti OR volunteer*:ab,ti OR 'crossover procedure'/de OR 'crossover procedure' OR 'double-blind procedure'/de OR 'double-blind procedure' OR 'single-blind procedure'/de OR 'single-blind procedure' OR (doubl* NEAR/3 blind*):ab,ti OR (singl*:ab,ti AND blind*:ab,ti) OR crossover*:ab,ti OR cross +over*:ab,ti OR (cross NEXT/1 over*):ab,ti	1792524
#3	#1 OR #2	517510
#2	'sexually transmitted diseases'/exp OR 'sexually transmitted diseases':ab,ti OR 'sexually transmitted diseases, bacterial'/exp OR 'sexually transmitted diseases, viral'/exp OR (sexually:ab,ti AND transmitted:ab,ti AND disease*:ab,ti) OR (sexually:ab,ti AND transmissible:ab,ti AND disease*:ab,ti) OR (sexually:ab,ti AND transmitted:ab,ti AND infection*:ab,ti) OR (sexually:ab,ti AND transmissible:ab,ti AND infection*:ab,ti) OR (sexually:ab,ti AND transmitted:ab,ti AND infectious:ab,ti AND disease*:ab,ti) OR (sexually:ab,ti AND transmissible:ab,ti AND infectious:ab,ti AND disease*:ab,ti) OR (sexually:ab,ti AND transmitted:ab,ti AND disorder*:ab,ti) OR (sexually:ab,ti AND transmissible:ab,ti AND disorder*:ab,ti) OR sti:ab,ti OR std:ab,ti	105559
#1	'human immunodeficiency virus infection'/exp OR 'human immunodeficiency virus infection':ab,ti OR 'human immunodeficiency virus'/exp OR 'human immunodeficiency virus':ab,ti OR 'human immunedeficiency virus':ab,ti OR 'human immune-deficiency virus':ab,ti OR 'human immuno-deficiency virus':ab,ti OR hiv:ab,ti OR 'hiv+1':ab,ti OR 'hiv+2':ab,ti OR 'acquired immunodeficiency syndrome':ab,ti OR 'acquired immuno+deficiency syndrome':ab,ti OR 'acquired immune+deficiency syndrome':ab,ti OR 'acquired immunedeficiency syndrome':ab,ti	440747

Appendix 3. CENTRAL search strategy

ID	Search

(Continued)

#1	MeSH descriptor: [HIV Infections] explode all trees
#2	MeSH descriptor: [HIV] explode all trees
#3	hiv or hiv-1* or hiv-2* or hiv1 or hiv2 or HIV INFECT* or HUMAN IMMUNODEFICIENCY VIRUS or HUMAN IMMUNEDEFICIENCY VIRUS or HUMAN IMMUNE-DEFICIENCY VIRUS or HUMAN IMMUNO-DEFICIENCY VIRUS or HUMAN IMMUN* DEFICIENCY VIRUS or ACQUIRED IMMUNODEFICIENCY SYNDROME or ACQUIRED IMMUNEDEFICIENCY SYNDROME or ACQUIRED IMMUNO-DEFICIENCY SYNDROME or ACQUIRED IMMUNE-DEFICIENCY SYNDROME or ACQUIRED IMMUN* DEFICIENCY SYNDROME
#4	MeSH descriptor: [Lymphoma, AIDS-Related] this term only
#5	MeSH descriptor: [Sexually Transmitted Diseases, Viral] this term only
#6	#1 or #2 or #3 or #4 or #5
#7	sexually transmitted disease*:ti,ab,kw or sexually transmissible disease*:ti,ab,kw or sexually transmitted infection*:ti,ab,kw or sexually transmissible infection*:ti,ab,kw or sexually transmitted infectious disease*:ti,ab,kw or sexually transmissible infectious disease*:ti,ab,kw or sexually transmitted disorder*:ti,ab,kw or sexually transmissible disorder*:ti,ab,kw or STI:ti,ab,kw or STIs:ti,ab,kw or STD:ti,ab,kw or STDs:ti,ab,kw
#8	MeSH descriptor: [Sexually Transmitted Diseases] explode all trees
#9	#7 or #8
#10	#6 or #9
#11	MeSH descriptor: [Sexual Behavior] explode all trees
#12	MeSH descriptor: [Sex Education] this term only
#13	MeSH descriptor: [Sex Counseling] this term only
#14	MeSH descriptor: [Health Education] this term only
#15	MeSH descriptor: [Attitude to Health] 1 tree(s) exploded
#16	sexual behavior:ti,ab,kw or sexual behaviour:ti,ab,kw or sex behavior:ti,ab,kw or sex behaviour:ti,ab,kw or sex education:ti,ab,kw or sex counseling:ti,ab,kw or sex counselling:ti,ab,kw
#17	#11 or #12 or #13 or #14 or #15 or #16
#18	MeSH descriptor: [Schools] this term only
#19	MeSH descriptor: [Community Networks] explode all trees
#20	school*:ti,ab,kw or community:ti,ab,kw or communities:ti,ab,kw or teacher*:ti,ab,kw or classroom*:ti,ab,kw or educator*:ti,ab,kw or peer*:ti,ab,kw
#21	#18 or #19 or #20
#22	MeSH descriptor: [Adolescent] this term only
#23	MeSH descriptor: [Child] this term only

(Continued)

#24	youth*:ti,ab,kw or teenager*:ti,ab,kw or teen:ti,ab,kw or teens:ti,ab,kw adolescen*:ti,ab,kw or child:ti,ab,kw or children:ti,ab,kw or youngster:ti,ab,kw or young person:ti,ab,kw or young people:ti,ab,kw
#25	#22 or #23 or #24
#26	#10 and #17 and #21 and #25 Publication Year from YEAR to YEAR, in Trials

Appendix 4. WHO ICTRP search strategy

sexually transmitted disease AND sexual behavior AND school OR sexually transmitted disease AND sexual behaviour AND school OR sexually transmitted disease AND sexual behavior AND community OR sexually transmitted disease AND sexual behaviour AND community OR hiv AND sexual behavior AND school OR hiv AND sexual behaviour AND school OR hiv AND sexual behavior AND community OR hiv AND sexual behaviour AND community

HISTORY

Protocol first published: Issue 1, 2007
Review first published: Issue 11, 2016

Date	Event	Description
24 August 2011	Feedback has been incorporated	Feedback from peer-review incorporated into the protocol
29 November 2010	Amended	Revised the protocol
12 November 2008	Amended	Converted to RevMan 5 and re-published without new citation.

CONTRIBUTIONS OF AUTHORS

AMJ and either DS, CM, AK, or AH conducted the searches, independently assessed all papers for inclusion, and extracted the data. AMJ and CL conducted the analyses and CL provided overall statistical advice. AMJ wrote the review and DS, CM, AK, AH, and CL commented on the review drafts and approved the final submission.

DECLARATIONS OF INTEREST

Two review authors (AMJ and CM) are investigators in an ongoing study evaluating the effects of school-based HIV and intimate partner violence prevention intervention programme on biologically measured pregnancy outcome for adolescents.
DS has no known conflicts of interest.
AK has no known conflicts of interest.
AH has no known conflicts of interest.
CL has no known conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- University of York, UK.

  Support for AMJ from October 2012 to date, and AH from January to March 2014.
- Liverpool School of Tropical Medicine, UK.

External sources

- South African Medical Research Council, South Africa.

  Funded the time of AMJ to September 2012 and time of CM and CL.

- Stellenbosch University, South Africa.

  Funded the time of AK.
- South African Cochrane Centre, South Africa.

  Provided academic training for AMJ and CM and support for the review authors, assisted with the searches and procured some of the full-text articles.
- Department for International Development (DFID), UK.

  Grant: 5242

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The only major deviation from the protocol and the review was a change in the title in line with recent guidance from Cochrane, which suggested that a more explanatory title be used. The original registered title was 'School-based interventions to postpone sexual intercourse and promote condom use among adolescents'

INDEX TERMS

Medical Subject Headings (MeSH)

*Contraception; *Pregnancy in Adolescence; *School Health Services; HIV Infections [epidemiology] [*prevention & control] [transmission]; Herpes Genitalis [epidemiology] [*prevention & control] [transmission]; Herpesvirus 2, Human; Program Evaluation; Randomized Controlled Trials as Topic; Reward; Sex Education; Sexually Transmitted Diseases [prevention & control]; Syphilis [epidemiology] [*prevention & control]

MeSH check words

Adolescent; Female; Humans; Male; Pregnancy