Conditional cash transfers to promote male circumcision uptake in middle and low income countries: review

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Abstract

Background: *Voluntary medical male circumcision (VMMC) reduces female-to-male HIV transmission by approximately 60% and is a recommended HIV prevention strategy in countries with high HIV prevalence and low levels of male circumcision. Mathematical models have illustrated that VMMC scale-up across Sub-Saharan Africa could prevent up to 6 million new HIV infections and 3 million deaths by 2025. Compared to the epidemic impact of scaling up ART to 90-90-90 levels, VMMC scale-up demonstrated additional reductions in HIV incidence and lower long-term annual program costs in models applied to several Sub-Saharan African countries. Therefore, low income countries are facing several challenges among which economic factors such as lost wages and opportunity costs of time are likely to be important barriers for VMMC uptake. Conditional cash transfers have shown its efficacy in many studies conducting low and middle countries where economic factors are impacting negatively on VMMC.*

Objectives: to assess the effectiveness of cash transfers to improve voluntary medical male circumcision.

Methods: We searched eligible studies through each database from January 2017 to April 2017. We used the key words added with Boolean operators to search studies. The following databases were assessed: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (PubMed), Scopus, CINAHL and Web of Science (WOS).

We also searched ongoing RCTs through: ClinicalTrials.gov (www.clinicaltrials.gov/) and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (apps.who.int/trialsearch/).

We included randomized control trials that evaluated the impact of conditional cash transfers on male circumcision. All included studies were selected in low and middle income countries. JT identified studies through different database. JT and LM independently assessed eligible studies that met inclusion criteria. We used the statistical package RevMan 5.3 provided by Cochrane. As heterogeneity among included studies was not important, we conducted meta-analysis. We reported the typical (if at least two trials were included) odds ratio. All values were reported with their 95% CIs.

Results : the main result has shown that conditional cash transfer was 4.78 times more likely to improve VMMC compared to the control group (OR 4.78 95%CI 4.17 to 5.48, 6286 participants, 6 studies, P< 0.00001). Heterogeneity: Chi² = 8.97, df = 5 (P = 0.11); I² = 44%. The evidence was graded high.

Conclusion: based on the results, we can conclude that conditional cash transfer is beneficial in improving VMMC. The quality of evidence was judged high so this review could play an important role in VMMC policy in middle and low income countries.

Key words: VMMC; conditional cash transfer; HIV

Background

Description of the condition

Despite access to safe voluntary medical male circumcision (VMMC) and the proof of its effectiveness in reducing acquisition of HIV and other sexually transmitted infections, uptake remains suboptimal in many countries in sub-Saharan Africa(SSA) (Lilleston 2017). VMMC provides direct protection against male HIV acquisition by removing the foreskin which is rich in HIV target cells (Donoval 2006; Kigozi 2009; Lilleston 2017). The potential effect of VMMC on population-level HIV incidence depends on this biologic effect, the level of VMMC coverage, risk profiles of men accepting VMMC, and whether behavioral disinhibition occurs following circumcision (Lilleston 2017). VMMC reduces female-to-male HIV transmission by approximately 60% (Weiss 2000; Bailey 2007; Bazant 2016) and is a recommended HIV prevention strategy in countries with high HIV prevalence and low levels of male circumcision (Bazant 2016).

Compared to the epidemic impact of scaling up ART to 90-90-90 levels, VMMC scale-up demonstrated additional reductions in HIV incidence and lower long-term annual program costs in models applied to Lesotho, Malawi, South Africa, and Uganda (Kripke 2016). In the first (90-90-90) scenario, combined scale-up of ART and VMMC affords greater reductions in HIV incidence than would be achieved by ART scale-up alone in all four countries (Kripke 2016).

Mathematical models have estimated that VMMC scale-up across SSA could prevent up to 6 million new HIV infections and 3 million deaths by 2025 (Weiss 2000; Kibira 2017). VMMC has been rolled out in 14 African countries starting in 2009, and WHO estimates that 11.7 million men have been circumcised as of December 2015(Gray 2007; Kibira 2017). Heterosexual transmission of HIV is still the biggest contributor to the HIV epidemic in sub SSA where over 70 % of the estimated global 35 million HIV positive people live (Wanyama 2009; UNAIDS 2014). Male circumcision reduces HIV heterosexual transmission risk from infected women to men, prevalence of high risk human papilloma virus and incidence of Herpes simplex virus two in men and, genital ulcers in female partners of circumcised HIV negative men (Nurminen 1997; Auvert 2009; Kibira 2017). This is the reason why the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) issued guidance urging countries with high HIV prevalence and low

male circumcision rates to incorporate voluntary medical male circumcision (VMMC) into their HIV prevention programs (Bailey 2007; Kikaya 2016). When we consider individual interpersonal factors that are influencing VMMC uptake; several barriers among which socio-cultural and socio-economic could impact negatively on VMMC. The main goal of this review was to analysis whether conditional cash transfer could ameliorate VMMC uptake in high HIV prevalence countries.

Description of the intervention

Existing literature on demand for VMMC highlights several factors that may be inhibiting VMMC take-up. First, opportunity costs of foregone wages during the recovery period (Westercamp 2007; Lissouba 2011; Wilson 2017) and transportation costs associated with the counseling session/procedure (Chinkhumba 2011) seem to be large impediments to receiving VMMC. Second, individuals are concerned about pain associated with the procedure and recovery period (Westercamp 2007; Westercamp 2010; Lissouba 2011; Plotkin 2011) Third, men are concerned that VMMC reduce sexual performance and pleasure (Westercamp 2007; Lissouba 2011; Plotkin 2011) Fourth, the fact that explaining to individuals that VMMC reduces the acquisition of HIV and other sexually transmitted infection (STI)s seems to increase the acceptability of VMMC (Westercamp 2007,Herman-Roloff 2011; Plotkin 2011; Wilson 2017)suggests that individuals may be uninformed about possible benefits of VMMC (Wilson 2017).

How the intervention might work

Thirumurthy conducted a trial in which the use of formative research to identify optimal communication strategies to overcome barriers to uptake of VMMC among men aged 20–34 years was analyzed (Thirumurthy 2014). In this trial, barriers found were perceptions of low risk for HIV infection among older men, myths regarding loss of sexual prowess postcircumcision, as well as service delivery side barriers, including complaints on inconvenient VMMC service hours (Thirumurthy 2014). Therefore, the duration of time that the compensation offer remained valid was 2 months because this study sought to rapidly determine the acceptability, feasibility, and short-term effectiveness of conditional cash transfers (Thirumurthy 2014).

As VMMC programs mature in most countries, the focus is now on how to sustain the HIV prevention gains realized from VMMC (UNICEF 2014; Luo 2016; Chilimampunga 2017). As part of initiatives to prepare for the sustainability phase, pilot implementation of early infant male circumcision (EIMC) is already underway in most of the 14 VMMC priority countries including Botswana, Kenya, Lesotho, Rwanda, South Africa, Swaziland, Tanzania, Uganda, Zambia, and Zimbabwe (Amuri 2016; Mavhu 2017; Chilimampunga 2017). Although its impact on HIV will take longer to realize, EIMC is ultimately likely to be more effective at preventing HIV acquisition than adult MC as the procedure is carried out well before the individual becomes sexually active, avoiding the risk associated with sex during the healing period (Plank 2010; Mavhu 2017 ;Chilimampunga 2017). However, conditional cash transfers could overcome some socio-economic barriers and then improve VMMC uptake.

Why it is important to do this review

Statistical modeling suggests scaling up VMMC services can substantially change the trajectory of the HIV epidemic; it is projected a 30 to 50% reduction in HIV incidence can be achieved within 10 years in areas where HIV is hyperendemic, is spread primarily through heterosexual transmission, and where most men (80% or more) are not already circumcised (Hargrove 2009; Kaufman 2016). Therefore, resource-limited countries are facing several challenges among which economic factors such as lost wages and opportunity costs of time are likely to be important barriers for VMMC uptake and other health behaviors (Kripke 2016). To alter HIV in hyperendemic regions, fast-track sets both treatment and primary prevention are the main components of HIV battle. If achieved, HIV incidence may drastically decrease over the next five years, reducing HIV to manageable levels by 2020 in order to make the 2030 goal attainable (Kripke 2016). Moreover, the Fast-Track Strategy goals are predicated upon reaching equally essential coverage targets for primary prevention, including 80% male circumcision prevalence in priority settings in SSA by 2020 (Kripke 2016). The UNAIDS Fast-Track report (UNAIDS 2014; Kripke 2016) further clarified fast-track requirements, including an additional 27 million male circumcisions (roughly 90% of males ages 10–29) in priority countries (Kripke 2016). Randomized controlled trials have shown that voluntary medical male circumcision (VMMC) reduces males' risk of HIV acquisition by about 60% (Weiss 2008; Kripke 2016), and follow-on studies have shown that

this level of protection increases over time to reach 74% (Gray 2012; Kripke 2016).

Different interventions appeared more effective in areas with low coverage than areas with high VMMC coverage, suggesting that understanding the coverage of VMMC was extremely important to policy makers and programme planners in designing different interventions in specific settings. Conditional cash transfers have shown its efficacy in many studies conducting low and middle countries where economic factors are impacting negatively on VMMC. Then, Conditional cash transfers could play a turnover role in improving VMMC in resource limited countries.

Objectives: To assess the effectiveness of cash transfers to improve voluntary medical male circumcision.
Methods

Criteria for considering studies for this review

Types of studies: we included different randomized control designs (parallel RCTs, cluster RCTs and cross-over RCTs) that assessed conditional cash transfers to enhance VMMC.

Types of participants: Adults male in high HIV incidence middle and low income countries.

Types of interventions: Interventions included compensation for opportunity costs of time lottery-based rewards

Types of outcome measures

Primary outcomes: VMMC rate

Secondary outcomes: this review did not include any secondary outcome.

Search methods for identification of studies: We attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress).

Electronic searches

We searched eligible through each database, using the key words added with Boolean operators. Database were assessed from 1988 to May 2017

- Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE (PubMed).
- Scopus.
- CINAHL.
- Web of Science (WOS).

We also searched ongoing RCTs through:
- ClinicalTrials.gov (www.clinicaltrials.gov/).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (apps.who.int/trialsearch/).

We used the following search strategy: ((circumcisions, male) OR (VMMC) OR (male circumcision)) AND ((adolescent) OR (adolescent*) OR (teen*) OR (young adult) OR (young adult*) OR (youth*) OR (homeless youth) AND ((Motivation) OR (Token Economy) OR (incentives) OR (conditional cash) OR (cash transfer)).

Data extraction and management

We developed data extraction form. For studies that fulfilled inclusion criteria, two review authors (JT and LM) independently abstracted the following information, which we provided in the 'Characteristics of included studies' table.
- Study design
- Study dates (if dates are not available then this will be reported as such)
- Study settings and country
- Participant inclusion and exclusion criteria
- Participant details and baseline demographics
- The number of participants by study and by study arm
- Details of relevant experimental and comparator interventions such as device type, name and method of dissection
- Definitions of outcome, and method and timing of outcome measurement, as well as any relevant subgroups
- Declarations of interest by primary trial authors

In case of any disagreements, we discussed to find consensus, or, if necessary, JLT was consulted. We provided information, including the trial identifier, about included, excluded and potentially relevant ongoing studies in the 'Characteristics studies' table.

Assessment of risk of bias in included studies

JT and LM independently assessed the risk of bias of each included cluster RCTs. We resolved discrepancies by consensus or by discussing with third review author.

We assessed risk of bias using the Cochrane 'Risk of bias' assessment tool. In addition, we assessed typical domains for cluster RCTs.
- Random sequence generation (selection bias).
- Allocation concealment (selection bias).
- Blinding of participants and personnel (performance bias).
- Blinding of outcome assessment (detection bias).
- Incomplete outcome data (attrition bias).
- Selective reporting (reporting bias).
- This tool includes additional items to assess the risk of selection bias and subsequent confounding ("were baseline outcome measurements similar?" and "were baseline characteristics similar?"), as well as an additional item to consider the likelihood of contamination ("was the study adequately protected against contamination?").

We judged the 'Risk of bias' in each domain as 'low risk', 'high risk' or 'unclear risk'. And then, we evaluated individual bias items as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011).

Unit of analysis issues
We expressed dichotomous data as odd ratios with 95% confidence intervals (CIs).

Dealing with missing data
We contacted the authors of included studies to obtain key missing data as needed.

Assessment of heterogeneity
We identified heterogeneity (inconsistency) through visual inspection of the forest plots to assess the amount of overlap of CIs, and the I^2 statistic, which quantifies inconsistency across studies, to assess the impact of heterogeneity on the meta-analysis; we interpreted the I^2 statistic as follows.
- 0% to 40%: may not be important.
- 30% to 60%: may indicate moderate heterogeneity.
- 50% to 90%: may indicate substantial heterogeneity.

- 75% to 100%: considerable heterogeneity.

We find heterogeneity of 44 %; we attempted to determine possible reasons for it by examining individual study and subgroup characteristics.

Assessment of reporting biases

Only six trials were included in the meta-analysis for VMMC outcome, we did not use the funnel plots to assess reporting bias.

Data synthesis

We used the statistical package RevMan 5.3 provided by Cochrane (RevMan 2014). As heterogeneity among included studies was not important, we conducted meta-analysis. We reported the typical (if at least two trials were included) odds ratio. All values were reported with their 95% CIs.
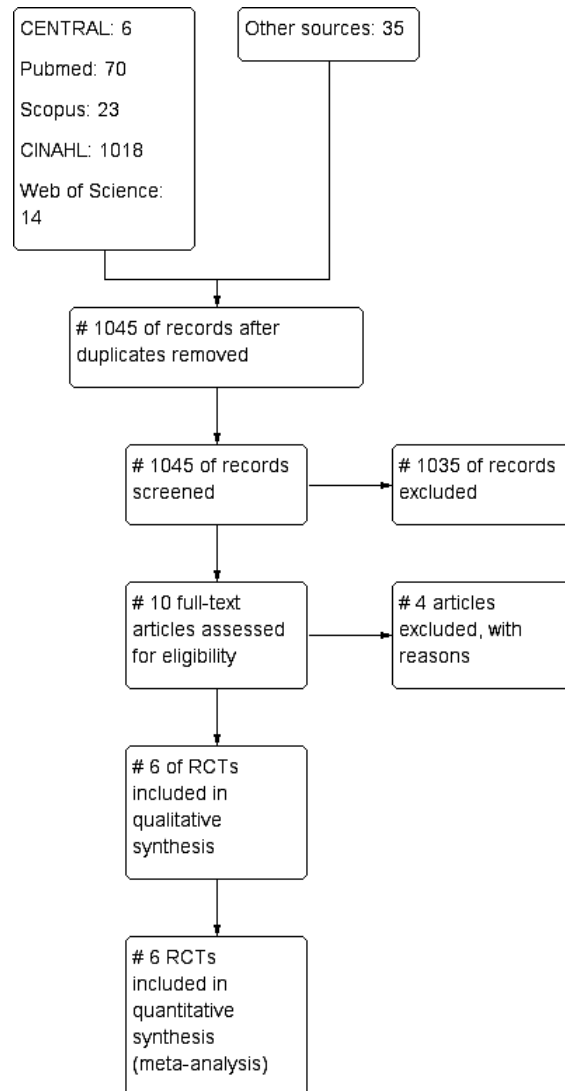
Subgroup analysis and investigation of heterogeneity

We did not conduct subgroup analysis as we found moderate heterogeneity between studies.

Results

Description of studies

We obtained 1045 titles and abstracts from the electronic search of databases after removal of duplicates. Following discussion between JT and LM, we obtained 10 potentially eligible articles. Six RCTs met our inclusion criteria. We screened the abstracts of these studies and deemed three irrelevant. Among them, six were included meta-analysis. Five were clearly irrelevant to this review and were excluded with reasons (see figure 1).

CENTRAL: 6

Pubmed: 70

Scopus: 23

CINAHL: 1018

Web of Science: 14

Other sources: 35

1045 of records after duplicates removed

1045 of records screened

1035 of records excluded

10 full-text articles assessed for eligibility

4 articles excluded, with reasons

6 of RCTs included in qualitative synthesis

6 RCTs included in quantitative synthesis (meta-analysis)

Included studies

The trials identified and included in this review all randomized individual participants and reported only dichotomous outcomes. All six trials were conducted in low- and middle-income countries. The studies investigated the use of incentives in improving VMMC. Six included studies included a combination of interventions among which cash in values of USD 5 to USD 20, food vouchers and lottery. The characteristics of included studies were described in Characteristics of included studies.

Excluded studies

We excluded trials for the following reasons: qualitative study, descriptive study, literature review study and other types of intervention. Excluded studies were described in the table of Characteristics of excluded studies.

Risk of bias in included studies

We have summarized our 'Risk of bias' judgements for each included trial in Figure 2 and Figure 3.

Allocation (selection bias)

We considered the generation of the randomization sequence adequate in nine trials Bazant 2016; Thirumurthy 2014; Thirumurthy 2016; Wilson 2017and unclear risk in the remainder Marshall 2017; Zanolini 2016. Allocation concealment was judged to be adequate inThirumurthy 2014; Thirumurthy 2016; Wilson 2017 and unclear risk in Bazant 2016; Marshall 2017; Zanolini 2016

Blinding (performance bias and detection bias)

Three trials had adequate low risk of performance bias Thirumurthy 2014; Thirumurthy 2016; Wilson 2017 and other three were unclear Bazant 2016; Marshall 2017; Zanolini 2016. All trials reported low risk of outcome assessment.

Incomplete outcome data (attrition bias)
All included trials reported low risk of attrition bias.

Selective reporting (reporting bias)
Three trials reported low risk of reporting bias Bazant 2016; Thirumurthy 2014; Thirumurthy 2016 and other three were unclear Marshall 2017; Wilson 2017; Zanolini 2016.

Other potential sources of bias

The other potential sources of bias included the baseline characteristics, baseline outcome measurements, contamination and confounders. The baseline characteristics were the same in five trials Marshall 2017; Thirumurthy 2014; Thirumurthy 2016; Wilson 2017; Zanolini 2016; only one had different baseline characteristics. The baseline outcome measurements were the same in five trials Marshall 2017; Thirumurthy 2014; Thirumurthy 2016; Wilson 2017; Zanolini 2016 and unclear in

Bazant 2016. The contamination was well controled in Thirumurthy 2014; Thirumurthy 2016; Wilson 2017, unclear in Bazant 2016 and high risk of bias in Zanolini 2016. Lastly, confounders were adjusted in five trials Marshall 2017; Thirumurthy 2014; Thirumurthy 2016; Wilson 2017; Zanolini 2016 and one trial remain high risk of confounders Bazant 2016.

Effects of interventions

Cash transfer was 4.78 times more likely to improve VMMC compared to the control group (OR 4.78 95%CI 4.17 to 5.48, 6286 participants, 6 studies, P< 0.00001). Heterogeneity: Chi² = 8.97, df = 5 (P = 0.11); I² = 44%

Study or Subgroup	Cash transfer group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bazant 2016	124	388	21	278	8.3%	5.75 [3.51, 9.41]
Marshall 2017	425	522	296	522	27.4%	3.35 [2.53, 4.43]
Thirumurthy 2014	34	377	6	370	2.7%	6.01 [2.49, 14.50]
Thirumurthy 2016	28	308	4	299	1.8%	7.38 [2.55, 21.29]
Wilson 2017	429	1000	121	1000	34.4%	5.46 [4.35, 6.85]
Zanolini 2016	594	848	123	374	25.4%	4.77 [3.68, 6.20]
Total (95% CI)		3443		2843	100.0%	4.78 [4.17, 5.48]
Total events	1634		571			

Heterogeneity: Chi² = 8.97, df = 5 (P = 0.11); I² = 44%
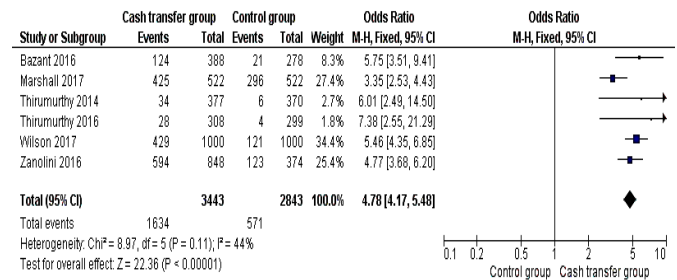Test for overall effect: Z = 22.36 (P < 0.00001)

Figure 2: Forest plot of comparison: Cash transfers versus control group; outcome: rate of VMMC rate.

Discussion

We graded the review based on risk of bias (see figure 2 &3), inconsistency, indirectness, imprecision, publication bias, large effect, plausible confounding and dose response gradient. We found that cash transfer increased significantly VMMC compared to the control group with high quality evidence (see table 1). However, the study used a dynamic; high-volume outreach model of VMMC should include different community based intervention to increase coverage of VMMC. This is the standard VMMC delivery model in the study regions that could increase VMMC significantly when target population is facing socio-economic issues. Considering several factors that could impact negatively on VMMC, different actors among which the Ministry of Health, church leaders, community members and stakeholders need to act concomitantly. These messages should target non-circumcised men and their sexual partners. Educating men undergoing circumcision also needs to be strengthened to avoid sexual risk taking post circumcision

(Kibira 2017). The strength of this study is its high quality of evidence and may influence policy makers.

The overall quality could be judge as high (see Summary of findings table 1).

We minimized potential bias in the review process by following standardized international guidelines (Higgins 2011)(see figure 2 and 3).

Figure 2: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Conditional cash transfers for VMMC						
Patient or population: Adults male in high HIV incidence countries						
Settings: Kenya, South Africa, Tanzania, Zambia						
Intervention: Conditional cash transfers						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Conditional cash transfers				
VMMC rate	**Study population**		**OR 4.78** (4.17 to 5.48)	6286 (6 studies)	⊕⊕⊕⊕ **high**	
	201 per 1000	**546 per 1000** (512 to 579)				
	Moderate					
	98 per 1000	**342 per 1000** (312 to 373)				
*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval; OR: Odds ratio;						

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

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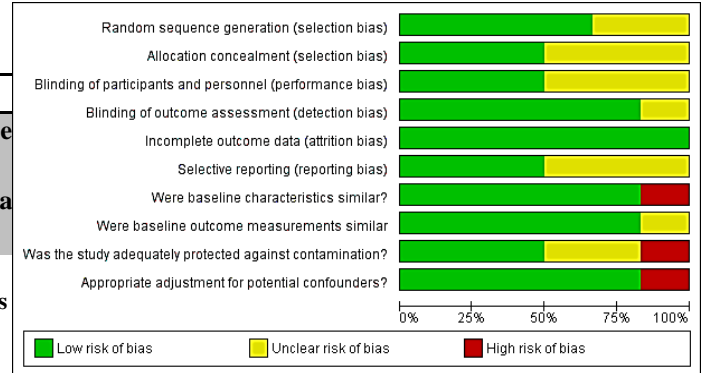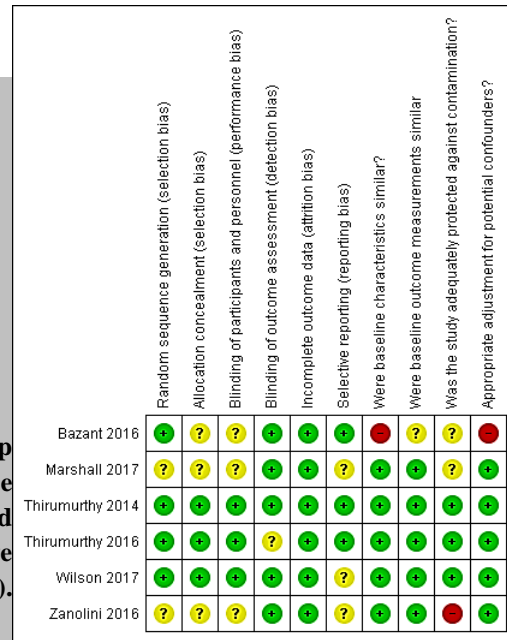**Very low quality: We are very uncertain about the estimate.**

Authors' conclusions

Research on the effectiveness of conditional cash transfer to promote male VMMC has proved high evidence is complete. This study could play an important role in improving VMMC in high HIV epidemic high. Furthermore, Intervention at an individual level consisted of combining motivational interviews with the offer of financial compensation in cases

where participants decided to undergo circumcision. Following informed consent, a first motivational interview was given by a "male circumcision adviser." (Marshall 2017). Lastly, counseling women on VMMC could increase significantly VMMC because most women correctly reported the need for a circumcised man to protect himself from sexually transmitted infections, including HIV, and the proportion of women reporting this opinion increased slightly with time (Maraux 2017).

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