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et al.

Identification and measurement of health-related spillovers in impact evaluations

March 2016

Systematic
Review
Summary 3

Health



International
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About this summary

Identification and measurement of health-related spillovers in impact evaluations, 3ie Systematic Review Summary 3, is a summary of the full review, *The identification and measurement of health-related spillovers in impact evaluations: a systematic review*, which is available with all of its appendixes on the 3ie [website](#).

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Identification and measurement of health-related spillovers in impact evaluations

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Summary

1. Introduction

The choice of which global health interventions to fund and implement is increasingly based on rigorous evidence of intervention impact. In order for impact evaluations to measure the full population-level impact of interventions, they must estimate both direct effect on recipients and any indirect or spillover effects on non-recipients. We define spillovers as the effects of an intervention on individuals who did not receive the intervention but were connected to intervention recipients through physical or social proximity. A spillover of an intervention that improves health is positive if it leads to improved health among beneficiaries; a spillover is negative if it harms health.

The expected benefits and costs of a programme are major considerations in deciding whether to continue, stop, change or scale up an intervention. If spillovers are present in the same direction as the treatment effect, studies that only estimate effects on intervention recipients will underestimate the effectiveness of the intervention. In addition, cost-effectiveness calculations that exclude such positive spillovers will underestimate an intervention's benefits. Similarly, if negative spillovers are present (i.e. those in the opposite direction of the treatment effect), studies only estimating effects on intervention recipients will overestimate the intervention's benefits. The methods used to estimate spillovers in existing studies vary widely, making it difficult to compare studies. Standardisation of methods used to estimate and report spillovers would improve the quality of spillover evidence available to policymakers.

We conducted a systematic review focused on health-related spillovers of health interventions targeting populations in low- and middle-income countries. We synthesised results and defined types of spillovers within a unified framework. We also highlighted methodological areas where the field would benefit from further application, development and standardisation of methods and guidance about how to estimate spillovers in impact evaluations.

We hand-searched titles published between 2010 and 2013 in five journals in relevant fields and searched 19 electronic databases for relevant articles published before 2014. Following a review of 34,042 titles, 12,836 abstracts, and 775 full texts, we identified 54 studies that met inclusion criteria. In this report, we describe the interventions evaluated by studies in the review, discuss mechanisms of spillover, summarise the evidence for spillovers included in studies, and discuss implications for research, practice and policy.

2. Mechanisms of spillover

The mechanisms by which spillovers may occur depend on the intervention and outcomes measured, as well as features of the population receiving the intervention. The method of measuring spillovers and the magnitude of spillover estimates depends upon the hypothesised mechanism. In this systematic review, we categorised studies based on the following mechanisms of spillover: geographic proximity, social proximity, learning or imitation, norm shaping, income and substitution effects, general equilibrium effects and relative deprivation.

3. Interventions

The interventions assessed in studies identified through our systematic review included vaccines, mass drug administration for parasite control, health education, cash transfers, HIV and AIDS counselling and treatment, insecticide-treated bednets, school feeding, maternal and child health promotion, and water and sanitation programmes.

4. Findings

In the 54 qualifying studies, the most common interventions were vaccines (n = 22 studies) followed by mass drug administration for infectious disease control (n = 7) and health education (n = 5). A wide range of outcomes was also studied, including disease outcomes, such as cholera (n = 8), trachoma (n = 4) and pertussis (n = 3), and health behaviour outcomes, such as screening for illness (n = 1) and healthcare visits (n = 1). In our assessment of the overall quality of study evidence, 6 of the 54 included studies (11 per cent) had high-quality evidence, 30 (56 per cent) had moderate-quality, 12 (22 per cent) had low-quality, and 6 (11 per cent) had very low-quality evidence. We found evidence that publication bias was present for certain spillover estimates, but not for total or direct effects.

Here, we briefly summarise findings within each intervention category for which at least three studies assessed spillovers:

Vaccines

Twenty-two studies estimated spillover effects of vaccines for cholera, diphtheria, pertussis, *Haemophilus influenzae* type b, pneumococcal conjugate, polio, tuberculosis, typhoid, tetanus, and measles. Most of these studies were of moderate or high quality. The majority of studies evaluating spillovers of vaccines included in this review found evidence of reduced disease among unvaccinated individuals. We found that spillovers of vaccines were larger in studies assessing spillovers on smaller scales. In addition, spillover effects were stronger among studies with higher vaccine coverage. These findings are consistent with what we would expect based on the theory of disease transmission for vaccine-preventable diseases (Halloran *et al.* 2010).

Mass drug administration for parasite control

Seven studies evaluated mass drug administration interventions for parasite control. There was evidence of spillovers of mass administration of azithromycin for trachoma control in Ethiopia, but evidence from studies conducted in other countries would strengthen the generalisability of these findings. There was also evidence of spillovers in a study of school-based deworming in Kenya.

Health education

Five studies evaluated health education programmes focusing on reducing neonatal mortality, reducing sexually transmitted infections, and improving child nutrition and growth. Evidence of spillovers of health education programmes is not consistent across studies and settings, and the quality of evidence is moderate at best.

Cash transfers

Five studies evaluated cash transfer programmes conditional on healthcare visits or school attendance and unconditional cash transfer programmes, which may improve self-esteem and mental health by increasing personal consumption. Cash transfers were associated with increased preventive health screenings and some increases in health among non-participants, but the quality of evidence from these studies was low. Two of these studies were based on the same conditional cash transfer programme (the Mexican scheme PROGRESA), so these studies' findings are likely to be dependent.

Insecticide-treated bednets

Three studies evaluated programmes that distributed insecticide-treated nets for free, with subsidies, and with education and microloans. These studies' findings suggest that ITN programmes led to positive spillovers from health outcomes for individuals in nearby areas that did not receive free ITNs.

Water and sanitation

Three studies assessed the effect of water source status, water filtration and improved sanitation on health. These studies produced mixed evidence on spillovers.

5. Implications

Evidence for positive spillovers of a specific intervention in multiple populations and settings would support expanded intervention delivery and possibly even public subsidies to support the programme. We found that many of the studies evaluating vaccines documented reduced illness among unvaccinated individuals, indicating spillovers were present. However, for other interventions, the number of studies with high-quality evidence of spillovers was small, and there were few studies in any given intervention category that produced sufficient evidence to result in recommendations for future programming.

In some cases, spillover measurement can easily be incorporated into existing study designs at minimal cost. However, it is often the case that measuring spillovers rigorously requires measuring outcomes among individuals who were neither targeted by a programme nor included in a control group, which may increase the cost of an impact evaluation since such individuals are not typically enrolled. Thus, funders of impact evaluations may consider whether it is appropriate to provide additional funding to assess spillovers of interventions when there is strong theoretical or preliminary evidence to suggest that they might be present.

We recommend that future impact evaluations measuring spillovers include a clear definition of how spillovers are estimated, ideally with a publicly available protocol registered prior to data collection or analysis. We also recommend a number of other elements of study design, such as pre-specifying the scale of spillovers expected and the hypothesised mechanism of spillovers. Pre-specifying spillover measurement minimises the chance of publication bias and promotes the use of more rigorous designs and estimation methods to estimate spillovers. Finally, at the reporting stage, we recommend that when measuring spillovers in future impact evaluations, a checklist, such as the one provided in Appendix 3b, is used to ensure thorough reporting of spillovers, increased standardisation and greater comparability of spillover findings.

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List of abbreviations and acronyms

AIDS	Acquired immune deficiency syndrome
BCG	Bacillus Calmette-Guérin vaccine
CONSORT	Consolidated Standards for Reporting Trials
DTP	Diphtheria, tetanus and pertussis vaccine
HIV	Human immunodeficiency virus
ITN	insecticide-treated net
SUTVA	stable unit treatment value assignment

1. Introduction

The choice of which global health interventions to fund and implement is increasingly based on rigorous evidence of intervention impact. In order for impact evaluations to measure the full population-level impact of interventions, they must estimate both direct effect on recipients and any indirect or spillover effects on non-recipients. We define spillovers as the effects of an intervention on individuals who did not receive the intervention but were connected to intervention recipients through physical or social proximity; for example, an unvaccinated mother of a child who receives a cholera vaccine may be less likely to contract cholera herself. A spillover of an intervention that improves health is positive if it leads to improved health among beneficiaries; a spillover of such an intervention is negative if it harms health. If an intervention leads to positive spillovers, studies that only estimate effects on intervention recipients will underestimate the effectiveness of the intervention. In addition, cost-effectiveness calculations that exclude positive spillovers will underestimate intervention benefits. Conversely, if negative spillovers exist, evaluations only measuring intervention recipients may overestimate the health impact and cost-effectiveness of an intervention.

Scientists have used a wide range of terms to describe spillovers (Sinclair *et al.* 2012) including interference (Cox 1958; Rosenbaum 2007; Hudgens and Halloran 2008; VanderWeele and Tchetgen Tchetgen 2011; Tchetgen Tchetgen and VanderWeele 2012), contamination (Hayes *et al.* 2000; Vermeersch and Kremer 2004), herd immunity (Fine 1993; Fox *et al.* 1995; John and Samuel 2000), stable unit treatment value assignment (SUTVA) violations (Rubin 1990), stability violations (Halloran and Struchiner 1995) and indirect effects (Halloran *et al.* 1991; VanderWeele *et al.* 2012). While there is a rich body of work in the vaccine literature that describes empirical and causal inference methods for estimating spillovers (Longini *et al.* 1988; Halloran and Struchiner 1991, 1995; Hudgens and Halloran 2008; Halloran *et al.* 2010; Tchetgen Tchetgen and VanderWeele 2012; VanderWeele *et al.* 2012) and the economics literature on spillovers is growing (Miguel and Kremer 2004), methods for estimating spillovers have developed independently with little cross-referencing between disciplines.

We conducted a systematic review focused on health-related spillovers of health interventions targeting populations in low- and middle-income countries. Our goal was to summarise the existing evidence for health spillovers and the estimation methods used. To our knowledge, this is the first systematic and interdisciplinary review of health-related spillovers and their estimation methods. The Inter-American Development Bank published a report that provides an overview of spillover effects within programme evaluations and brief guidelines for estimating spillovers for one type of study design (Angelucci and Maro 2010), but this report did not include a comprehensive review of research on spillovers. Others have published on the topic of spillovers, but these reports have also only focused on one study design (Baird *et al.* 2014) or focused only on vaccines and not other interventions (Halloran and Struchiner 1991; Longini *et al.* 1998; Hudgens and Halloran 2008; Halloran *et al.* 2010; Tchetgen Tchetgen and VanderWeele 2012; VanderWeele *et al.* 2012).

We synthesised results of spillover studies identified through a systematic review and defined types of spillovers within a unified framework. Specifically, the objectives of this study were to:

1. Identify all studies with a control group that have detected the presence of or measured spillovers arising from interventions intended to improve human health;
2. Summarise methods used to detect and estimate the magnitude of spillovers, as well as identification strategies and assumptions used to make causal inference;
3. Highlight methodological areas where the field would benefit from further application, development and standardisation; and
4. Provide guidance for the application, development and standardisation of methods to estimate spillovers in impact evaluations.

In this document, we summarise the primary research on spillovers (Section 4) and make recommendations for future research on spillovers (Section 5). We discuss the more technical aspects of spillover estimation, including the causal inference framework, in the technical report (Benjamin-Chung et al., 2015).

We included studies that evaluated interventions in low-, lower middle-, or upper middle-income countries as defined by the World Bank (2012). Studies were eligible if they measured health outcomes and evaluated interventions related to health, agriculture, education, employment generation, empowerment, governance (including voting and corruption), health, microfinance or migration. Eligible studies also clearly articulated a comparison group for the measurement of spillover and direct effects. We included studies that measured intermediate health outcomes, such as use of insecticide-treated nets (ITNs) that are likely to be correlated with terminal health outcomes within a theory of change. We only included studies that estimated spillovers using quantitative methods.

We searched 19 electronic databases for articles published before 2014 and hand-searched titles from 2010–2013 in five journals in relevant fields. We reviewed 34,042 titles, 12,836 abstracts and 775 full texts. At least one team member reviewed each record retrieved for relevance. This process yielded a total of 54 qualifying texts (see details in Appendix B). We classified types of spillovers estimated in each study and compared results for each intervention category.

In this report, we describe the interventions evaluated by studies included in the review, discuss mechanisms of spillover, summarise the evidence of spillovers in the included studies, and discuss implications for research, practice and policy.

2. Mechanisms of spillover

The mechanism by which spillovers may occur depends on the intervention and outcomes measured, as well as features of the population receiving the intervention. The method of measuring and the magnitude of spillover estimates depend upon the hypothesised mechanism. In public health, there is a rich literature describing theories of infectious disease transmission and mechanisms of behaviour change, both of which are relevant to spillovers. Theories of disease transmission are particularly relevant to understanding spillovers of interventions targeting infectious diseases. Spillover effects of infectious disease interventions may occur through several different mechanisms: (1) There may be changes in the quantity of an agent or pathogen individuals are exposed to; for example, individuals in close social or geographic proximity to intervention recipients may be less exposed to a pathogen if the intervention is effective. (2) An intervention may change the quality of the agent individuals are exposed to; for example, intervention recipients may develop resistance to a particular treatment, and then individuals in close social or physical proximity may also develop resistance. (3) An intervention may cause changes in the immunity of individuals in close social or physical proximity to intervention recipients; for example, vaccination of some individuals in a population may alter the immunity of those in close contact to them (Hayes *et al.* 2000).

The public health literature has also drawn on a variety of theories developed by sociologists, anthropologists and psychologists to understand how and why humans adopt certain behaviours in a social context. These theories fall into three domains:

- **Social cognitive theory**, developed by the psychologist Albert Bandura, which states that individuals model their own behaviour on that of others. Behaviour adoption could occur through imitation of other people or of behaviours seen in the media (Bandura 1986);
- **Social network theory**, which describes methods of defining the structure of a particular social network and defines theoretical mechanisms by which networks can affect health: social support, social influence, social engagement, person-to-person contact, and access to resources and material goods (Barnes 1954; Bott 1957; Berkman and Syme 1979; Marsden 2006); and
- The theory of **diffusion of innovations**, which describes the spread of ideas and behaviours as a function of innovation, communication channels, social systems and time (Haider and Kreps 2004; Rogers 2010). More recent studies within social epidemiology have explored how social and behavioural norms develop and exert influence on people in the same social network or environment using empirical data (Berkman and Syme 1979; Oakes and Kaufman 2006; Auchincloss and Diez Roux 2008; Galea *et al.* 2010; O'Malley and Marsden 2008; Smith and Christakis 2008).

Traditionally, economists have explored the concept of spillovers within markets by studying how equilibrium prices affect the demand of consumers and supply by firms. Methods of identifying spillover effects in other contexts were given less attention until recently (Manski 1993) as development economists in particular have explored how interventions may spill over

via learning and imitation, norm shaping, income effects and other mechanisms, which we discuss below (Banerjee 1992; Bikhchandani *et al.* 1992; Ellison and Fudenberg 1995).

In this systematic review, we categorise studies by the possible mechanism(s) of spillover. Here, we briefly describe these mechanisms, which we identified through a search of the literature on spillovers:

- **Geographic proximity** – Living or spending time in close proximity to individuals receiving an intervention results in improved health outcomes. This mechanism is applicable to interventions that aim to reduce infectious diseases, such as vaccination or mass drug administration, since close proximity is nearly always required for infectious disease transmission; for example, living in the same household as someone vaccinated against pertussis may reduce transmission of pertussis to unvaccinated individuals (Préziosi and Halloran 2003);
- **Social proximity** – Knowing individuals receiving an intervention may result in improved health outcomes because recipients share information with non-recipients triggering behaviour change. Thus, this mechanism is most applicable to interventions that aim to change behaviours. For example, individuals socially connected to participants in a peer intervention to reduce drug use may be likely to reduce their own drug use as well (German *et al.* 2012);
- **Learning/imitation** – Non-recipients of an intervention learn from and imitate recipients, and their change in behaviour can lead to improved health outcomes. This mechanism can be viewed as a type of social proximity. For instance, people who live in the same villages as individuals receiving information about child nutrition may imitate behaviours by improving feeding practices for their own children (Singh 2011);
- **Norm shaping** – Provision of an intervention changes norms among both intervention recipients and non-recipients. This is distinct from learning and imitation because it is a passive process, whereas learning and imitation are an active process. This mechanism can also be viewed as a type of social proximity. For example, a conditional cash transfer programme may alter the norm in a population by requiring certain individuals to complete health screenings to receive the cash transfer (Avitabile 2012);
- **Income/substitution effect** – Provision of an intervention to some individuals in a group results in the reallocation of resources from those individuals to others, who may benefit from additional resources. For example, if a programme provides school meals to certain children in a household, more food may be available to other children through substitution (Kazianga *et al.* 2009). This is sometimes also referred to as the 'redistribution effect';
- **General equilibrium effects** – These effects may occur when an intervention received by some individuals in a population influences prices, transactions and lending behaviour of other individuals within markets in the same economy. For example, providing some individuals with cash transfers may affect economic behaviours of non-recipients by motivating them to spend more on healthcare or nutrition, which may in turn improve their health (Ribas *et al.* 2011); and

- **Relative deprivation** – The economic status of one’s peers may adversely affect an individual’s health. For example, providing a conditional cash transfer to some teenage girls may reduce the psychological well-being of other girls who do not receive a transfer (Baird *et al.* 2013a).

Table 1 lists the percentage of included studies assessing each type of spillover mechanism. The most common mechanism was geographic proximity (70 per cent of studies measured spillovers occurring through this mechanism). Among economic studies, social mechanisms were more commonly assessed.

Table 1: Spillover mechanism (n = 54)

Geographic proximity	72%
Social proximity	31%
Learning/imitation	28%
Norm shaping	28%
Income/substitution effect	4%
Public good effect	13%
General equilibrium effects	2%
Relative deprivation	2%

3. Types of spillover

In this section, we briefly describe the major types of spillover effects identified in our systematic review.

3.1 Within-cluster spillover effect

Within-cluster spillover effects compare illness among individuals in areas with an intervention to illness among individuals in areas without the intervention. Ideally, these areas have very similar characteristics (i.e. individuals were or could have been randomly assigned to each area). Spillovers may occur among non-recipients in intervention areas or among non-recipients in non-intervention areas. For example, an intervention might target a subset of women in particular villages, but other women in the same villages who were not targeted by the intervention may be influenced indirectly by the intervention. Women in nearby villages where the intervention was not implemented may be affected as well. Within-cluster spillovers are appropriate to measure when spillovers are expected to be on a small scale. They are relatively convenient to measure since, typically, the non-recipients in intervention areas are well defined and reachable.

Policymakers can use evidence of within-cluster spillover effects to determine whether a group of individuals may benefit from an intervention delivered only to a subset in the group. For example, if it were shown that offering deworming to schoolchildren led to reduced worm infection among pre-school children and adults in the same areas, future efforts may choose to only target schoolchildren. Such targeting may yield great cost savings and allow for cost-effective scale-up of interventions to larger populations.

3.2 Distance-based spillover effect

When spillovers are likely to occur on a larger scale, estimation of distance-based spillovers may be of interest. Evaluators can measure the health of individuals living at specific distances from intervention areas (for example, 500 metres and 1,000 metres) and compare it to the health of individuals living at the same distances from non-intervention areas. If evaluators found that health was improved among individuals 500 metres from intervention areas, compared to the health among individuals 500 metres from non-intervention areas, this may be evidence of distance-based spillovers. Evidence of spillovers over large distances may indicate that large populations benefit from interventions focused on particular areas or subpopulations. Such spillovers are of interest to policymakers since interventions with large distance-based spillovers are likely to be highly cost-effective compared to those without such spillovers.

3.3 Social network spillovers

When an intervention is likely to lead to behaviour changes (for example, increased physical activity) through social networks, evaluators can measure social network spillovers. Intervention recipients and non-recipients name their main social contacts, and then the health of social contacts of intervention recipients is compared to the health of social contacts of non-recipients. If behaviours are expected to spread widely, evaluators can then ask these social contacts to

name their own social contacts and repeat the process. This type of spillover is most relevant for interventions that influence norms and behaviours. Social network spillovers can span large physical distances since individuals communicating by phone or the Internet may influence each other. Evidence of social network spillovers may shed light on populations benefiting from an intervention in areas far from the targeted population. Such evidence may help policymakers and intervention implementers determine how best to communicate and target future interventions.

4. Findings

The studies included in our systematic review evaluate a variety of interventions related to health and human development. In this section, we provide brief descriptions of the interventions and common mechanisms of spillover. We also describe specific programmes evaluated in multiple studies that measured spillovers. The most common interventions studied were vaccines (n = 22 studies) followed by mass drug administration for infectious disease control (n = 7) and health education (n = 5) (Table 2). A wide range of outcomes were also studied including disease outcomes, such as for cholera (n = 8), trachoma (n = 4) and pertussis (n = 3), and health behaviour outcomes, such as screening for illness (n = 1), healthcare visits (n = 1) and voluntary counselling and testing for human immunodeficiency virus (HIV) (n = 1).

Table 2: Intervention types

	Number of papers
Cholera vaccine	8
Community monitoring and provision of health services	1
Conditional cash transfers	5
Deworming	2
Exposure to information about deworming	1
<i>Haemophilus influenzae</i> type b vaccine	2
Human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) treatment	1
Improved water supply	1
Incentives for voluntary counselling and testing for HIV	1
Information about HIV transmission	1
Information on infant nutrition and health	1
Insecticide-treated nets (ITNs)	1
ITNs for free or with microloans and information sessions	1
Latrines	1
Mass azithromycin administration	3
Maternal and child health programme	2
Nutrition education	1
Online sexual health education	1
Peer-network health education	1
Pertussis vaccine	3
Pneumococcal conjugate vaccine	5
Polio vaccine	1
School feeding programme	2
Subsidised deworming	1
Subsidised ITNs	1
Typhoid vaccine	2
Vaccines (BCG, DPT, polio, measles) + incentives	1
Water filtration with sari cloth and nylon cloth	1
Women's empowerment programme	1
Women's groups and health service strengthening	1
Total	54

4.1 Vaccines

Twenty-two studies estimated spillover effects of vaccines for illnesses including cholera (n = 8) (Ali *et al.* 2005, 2008, 2013; Emch *et al.* 2006, 2009; Root *et al.* 2011; Khatib *et al.* 2012; Perez-Heydrich *et al.* 2014), pneumococcal conjugate (n = 5) (Egere *et al.* 2012; Roca *et al.* 2011, 2013; Hammitt *et al.* 2014; Root *et al.* 2014), pertussis (n = 3) (Cooper and Fitch 1983; Préziosi and Halloran 2003; Baptista *et al.* 2006), *Haemophilus influenzae* type b (n = 2) (Forleo-Neto *et al.* 1999; Chen *et al.* 2014), typhoid (n = 2) (Sur *et al.* 2009; Khan *et al.* 2012), polio (n = 1) (Paul *et al.* 1962), and Bacillus Calmette-Guérin (BCG), diphtheria, tetanus and pertussis (DTP), polio and measles (n = 1) (Banerjee *et al.* 2010). Studies evaluated vaccines delivered in Bangladesh, Brazil, Costa Rica, India, Pakistan, the Philippines, St. Lucia, Senegal and Tanzania. Of these studies, four had high-quality evidence overall, 13 had moderate-quality evidence, and five had low- or very low-quality evidence. Five of the studies evaluated cholera vaccines in the same study population that previously participated in a randomised trial of the cholera vaccine in Matlab, Bangladesh (Ali *et al.* 2005, 2008; Emch *et al.* 2006, 2009; Root *et al.* 2011).

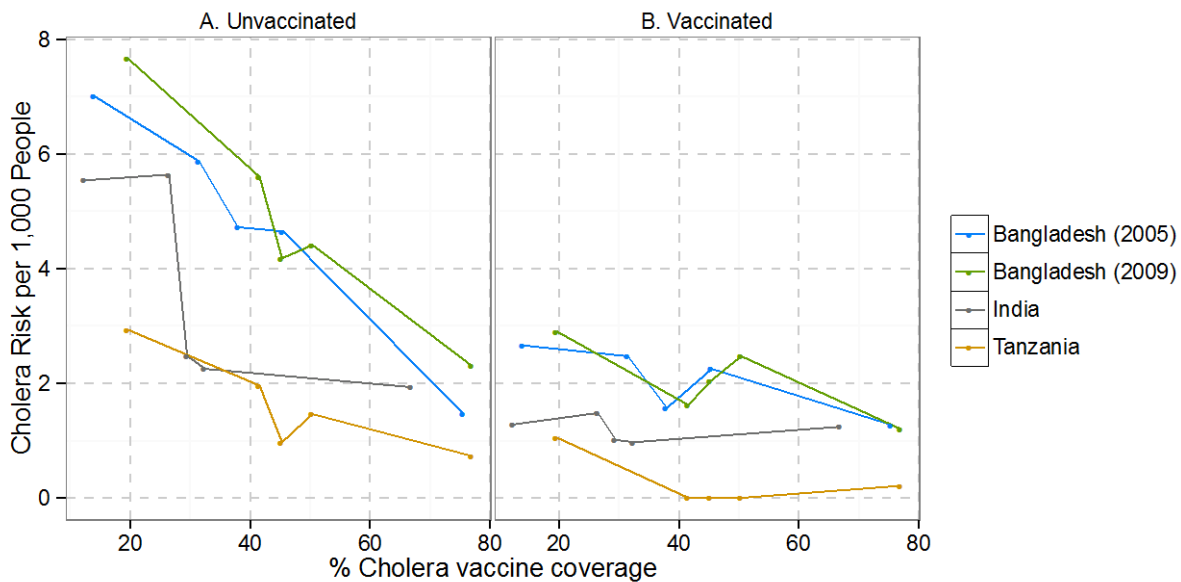
These studies measured diseases targeted by vaccines (for example, evaluations of the cholera vaccine measured cholera) or biological measures related to disease progression (for example, an evaluation of the polio vaccine measured polio antibody conversion). By protecting vaccinated individuals from a specific pathogen, vaccines reduce the number of susceptible individuals in a population, which can result in reduced transmission. Thus, spillovers or herd effects are typically expected for most vaccines, although the magnitude of spillovers varies from vaccine to vaccine. Studies in this review evaluated vaccines that were dispensed either: (1) to small groups or individuals randomly selected to receive the vaccine in a specific population, or (2) through large government-led programmes targeting entire populations. Most of these studies measured spillovers among unvaccinated household members of vaccinated individuals and among unvaccinated people in the same group of households or larger community.

Eleven studies evaluated spillovers of vaccines by comparing illness rates among subpopulations with differing levels of vaccine coverage (Cooper and Fitch 1983; Forleo-Neto *et al.* 1999; Emch *et al.* 2006, 2009; Khatib *et al.* 2012; Ali *et al.* 2005, 2008, 2013; Chen *et al.* 2014; Root *et al.* 2011, 2014). Ten of these studies, which evaluated cholera, pertussis, *Haemophilus influenzae* type b and pneumococcal conjugate vaccines, reported a decrease in illness associated with increased vaccine coverage (Cooper and Fitch 1983; Forleo-Neto *et al.* 1999; Emch *et al.* 2006, 2009; Khatib *et al.* 2012; Ali *et al.* 2005, 2008, 2013; Chen *et al.* 2014; Root *et al.* 2011).

Four studies compared illness within levels of cholera vaccine coverage and risk, allowing for a direct comparison of results. Cholera risk among unvaccinated individuals declined markedly as vaccination coverage increased (Figure 1, Panel A), suggesting strong spillover effects due to herd protection. There was no decrease in risk among vaccinated individuals as vaccination coverage increased (Figure 1, Panel B), which is to be expected since those individuals were protected from illness directly through vaccination, which does not depend on coverage. These

results align with the theory of herd protection. It is important to note that two of the studies presented in Figure 1 utilised the same dataset from Bangladesh, so their findings are likely to be highly dependent. Studies that measured spillovers in a similar way for other vaccines and outcomes revealed a similar pattern (Cooper and Fitch 1983; Forleo-Neto *et al.* 1999; Huq *et al.* 2010).

Figure 1: Cholera risk per 1,000 people among unvaccinated and vaccinated individuals by varying levels of cholera vaccine coverage



Note: The studies conducted in Bangladesh in 2005 and 2009 were conducted using data from the same cholera vaccine trial but used different analysis methods.

Studies estimated other types of spillovers resulting from vaccines by comparing disease rates among unvaccinated individuals in households or neighbourhoods where some individuals were vaccinated to rates among unvaccinated individuals in households where no one was vaccinated (i.e. a within-cluster spillover effect). Effects were larger in studies that measured spillovers on smaller scales (for example, households) as opposed to larger scales (for example, villages). For example, protective efficacy of the typhoid vaccine in clusters of approximately 700 people was 44–45% (Sur *et al.* 2009), whereas the protective efficacy of the pertussis vaccine within households was 61.6 per cent (Baptista *et al.* 2006) and 85 per cent (Préziosi and Halloran 2003). In addition, spillover effects were stronger among studies with a higher vaccine coverage. For example, Egere *et al.* reported a 61 per cent reduction in vaccine-type pneumococcus in villages with complete pneumococcal conjugate vaccine coverage compared to villages in which only young children were vaccinated (Egere *et al.* 2012).

Overall, the majority of studies evaluating spillovers of vaccines in this review found evidence of reduced disease among unvaccinated individuals. Most of these studies were of moderate or high quality. The finding that spillovers were larger in studies assessing spillovers on smaller scales and when vaccine coverage was higher is consistent with what we would expect based on the theory of disease transmission for vaccine-preventable diseases. Since transmission

occurs through physical proximity, we would expect larger spillovers on smaller scales and when coverage is higher. An important caveat is that there is likely to be substantial dependence among these studies' findings – 6 out of the 22 vaccine studies reanalysed data from the same cholera vaccine trial in Matlab, Bangladesh. In addition, three studies evaluated the pneumococcal conjugate vaccine in The Gambia, and two studied the same population, so these studies' findings are likely to be dependent.

4.2 Mass drug administration for parasite control

Mass (i.e. population-wide) drug administration interventions aim to eliminate parasite infection by treating large populations in order to interrupt disease transmission. Spillovers may occur among individuals in populations targeted for mass drug administration who were not eligible for treatment or who did not receive treatment due to incomplete coverage. Seven studies evaluated mass drug administration interventions for parasite control in Ethiopia, Kenya, and Tanzania (Chidambaram *et al.* 2004; Miguel and Kremer 2004; Kremer and Miguel 2007; House *et al.* 2009; Baird *et al.* 2013b; Ozier 2014; Shekhawat *et al.* 2014). One of these studies produced high-quality evidence overall, three had moderate-quality evidence and four had moderate- or low-quality evidence.

Three studies evaluated mass azithromycin administration to control trachoma. Trachoma is spread through interpersonal contact, shared clothing and flies that come into contact with the eyes or nose; thus, physical proximity is also a major driver of transmission. The two studies that reported quantitative spillover estimates of mass azithromycin administration found positive, statistically significant spillovers. In Ethiopia, a mass azithromycin treatment programme reached 75 per cent of children aged 1–10 years, resulting in a 35 per cent decrease in trachoma 12 months after mass treatment among individuals in treatment areas who did not receive treatment (House *et al.* 2009). A similar study in Ethiopia found a 2.9-fold (95% confidence interval 1.1, 7.5) reduction in the odds of trachoma infection among those not receiving azithromycin who lived in areas where mass azithromycin treatment occurred (Chidambaram *et al.* 2004). The studies evaluating control of trachoma through mass drug administration were all conducted in Ethiopia, so these findings may be dependent.

Four studies evaluated mass deworming to control soil-transmitted helminth infections. These infections are transmitted when an infected person passes helminth eggs through their stool and an uninfected person is exposed to the eggs due to faecal contamination of the environment. Thus, transmission is more likely to occur when an individual lives in close proximity to infected individuals. Of these studies, three (Kremer and Miguel 2007; Baird *et al.* 2013b; Ozier 2014) were based on the study of school-based deworming conducted by Miguel and Kremer (Miguel and Kremer 2004). Miguel and Kremer reported spillovers of school-based deworming to untreated students in treated schools as well as spillovers among pupils of schools within 0–3 kilometres (Miguel and Kremer 2004). For the average number of pupils in their study population, they found a 12 per cent reduction in moderate to heavy worm infections for children 0–3 kilometres away from schools receiving the deworming programme and an 11 per cent reduction for children 3–6 kilometres away from such schools; both these findings were statistically significant. The study reported a 12 per cent reduction in moderate to heavy worm

infections among children who attended schools in the programme but did not receive deworming, compared to those in control schools.

Davey *et al.* (2014) and Aiken *et al.* (2015) replicated this study and reanalysed the original data. They clarified some of the design features and reporting of Miguel and Kremer (2004) and presented some alternative results. An error was identified in the coding of a population density variable included in the statistical model used to estimate within-cluster spillovers. Once this error was corrected, the spillover for children 0–3 kilometres away was 9 per cent and the spillover for children 3–6 kilometres away was 6 per cent. Following this change, the spillover for children 0–3 kilometres away was statistically significant but the 3–6 kilometres spillover was not (Davey *et al.* 2014; Hicks *et al.* 2014; Aiken *et al.* 2015). The estimate of within-cluster spillovers was 18 per cent and was statistically significant at the $\alpha = 0.1$ level following this correction.

The other three studies evaluating school-based deworming in the same study population assess spillover effects for other outcomes (self-reported health, body mass index, child growth, deworming uptake) and thus are not directly comparable (Kremer and Miguel 2007; Baird *et al.* 2013b; Ozier 2014).

In summary, there is evidence of spillovers of mass administration with azithromycin for trachoma control in Ethiopia, but evidence from studies conducted in other countries would allow these findings to be applied more generally. There is evidence from one study in Kenya of spillovers of mass deworming administration on helminth infection within schools and to children within 0–3 kilometres of schools in the programme.

4.3 Health education

Five studies evaluated education programmes focusing on reducing neonatal mortality (Azad *et al.* 2010), reducing sexually transmitted infections (Dupas 2006; Chong *et al.* 2013), and improving child nutrition and growth (Singh 2011; Fitzsimons *et al.* 2012). These studies were conducted in Bangladesh, Colombia, India, Kenya and Malawi, and evaluated spillovers that occurred through a variety of mechanisms including physical proximity, social proximity, learning and imitation, and norm shaping. None of these studies produced high-quality evidence, four produced moderate-quality evidence and one produced low-quality evidence. Here, we briefly summarise the findings of the studies with moderate-quality evidence.

Community-based programmes

Two studies evaluated the provision of child health and nutrition information to mothers (Singh 2011; Fitzsimons *et al.* 2012). These studies compared the health and growth of children of non-participants in programme areas who may have been exposed to the programme through conversations with participants to children in areas without the programme. Fitzsimons *et al.* (2012) conducted an evaluation of a programme providing information on infant health and child nutrition to mothers in Malawi to determine whether older children in non-targeted households benefitted from the programme. They did not find any statistically significant spillovers for child growth indicators, diarrhoea, vomiting or other symptoms among these older children. Singh

evaluated a nutrition information programme targeted at mothers and assessed whether spillovers occurred for children of mothers who did not participate in the programme but who lived in programme areas (Singh 2011). There was no evidence of spillovers on child growth indicators.

School-based programmes

Two studies measured spillovers of school-based health education programmes that aimed to increase knowledge of sexually transmitted infections and reduce risky sexual behaviour. One study found that sexual health knowledge was lower among students who had no friends in an online sexual health education programme compared to scores for students with friends participating in the course (Chong *et al.* 2013). There was no evidence of spillover effects among students who did not participate in the course but who attended schools where the course took place.

Spillovers were estimated in a school-based programme that aimed to increase awareness about HIV and acquired immune deficiency syndrome (AIDS) and reduce risky sexual behaviour among students (Dupas 2006). Schools were randomly selected to receive the programme. To assess spillovers, investigators compared health behaviours among students in schools with different proportions of students participating in the programme. Investigators found that the proportion of students participating in the programme was associated with condom use for girls but not for boys. There was no statistically significant finding for boys, and for both boys and girls findings were not statistically significant when evaluating whether the student had sex without a condom.

In summary, evidence of spillovers of health education programmes is not consistent across studies and settings, and the quality of evidence is moderate at best. There was some evidence of spillovers of such programmes within a village and a school, but not within households. Unlike spillovers resulting from physical proximity, spillovers of health education programmes resulting from social mechanisms appear not to be associated with the physical scale on which spillovers are measured.

4.4 Cash transfers

Five studies evaluated cash transfer programmes that were conditional on healthcare visits or school attendance, and unconditional cash transfer programmes, which may improve self-esteem and mental health by increasing personal consumption. These studies evaluated programmes in Colombia, Malawi, Mexico and Paraguay (Contreras and Maitra 2013; Baird *et al.* 2013a; Avitabile 2012; Handa *et al.* 2001; Ribas *et al.* 2011). The purported spillover mechanisms were primarily learning, imitation, norm shaping and social proximity.

Three studies assessed the impact of the cash transfer programmes on preventative health behaviours. There was evidence in two studies of a conditional cash transfer programme in Mexico of increased health screening (for example, nutrition surveillance, cancer screening) among individuals in the same areas who were not eligible for cash transfers because their income level was above the level for programme eligibility (Handa *et al.* 2001; Avitabile 2012). A

possible mechanism for these findings is that increased health screening and improved health behaviours resulting from the conditional cash transfer programme may have altered social norms. Alternatively, non-participants may have learned these health behaviours from participants. A study of a conditional cash transfer programme in Paraguay found that the programme did not lead to increased healthcare visits among people in the same areas who were not eligible based on a quality of life index (Ribas *et al.* 2011).

Two studies assessed cash transfer programmes' effects on health. One study found evidence that ineligible individuals in areas where others received conditional cash transfers experienced less general self-reported illness, but these effects were not sustained after three years among ineligible individuals (Contreras and Maitra 2013). The other study evaluated whether a programme offering conditional and unconditional cash transfers in different areas that targeted adolescent girls reduced psychological distress (Baird *et al.* 2013a). The conditional cash transfers required regular school attendance. While they found 8–14% reductions in psychological distress among participants during the programme, there was evidence that non-participants experienced a 6.4 per cent increase in psychological distress (i.e. a negative spillover). To explain these negative spillovers, the authors hypothesised that adolescent girls' psychological distress is a function not only of their own income but also of their relative income.

In summary, cash transfers were associated with increased preventative health screenings and some increases in health among non-recipients, but the quality of evidence from these studies was low. Two of these studies were based on the same conditional cash transfer programme (the Mexican scheme PROGRESA), so these findings are likely to be dependent. Conditional cash transfer programmes may cause spillovers by altering social norms. Alternatively, non-participants may learn new health behaviours from participants in cash transfer programmes.

4.5 HIV and AIDS counselling and treatment

One study evaluated an HIV and AIDS voluntary counselling and testing programme. The study hypothesised that spillovers may have occurred through social proximity; specifically, it assessed whether the proportion of nearby neighbours who received HIV test results was associated with choosing to learn one's own HIV status (Godlonton and Thornton 2012). The study found positive spillovers: a 10 per cent increase in neighbours who found out their HIV results was associated with a 1.1 per cent increase in the probability that an individual sought out their own HIV test results.

Another study evaluated whether a parent's HIV and AIDS treatment affected their child's nutritional status (Zivin *et al.* 2009). The study hypothesised that improved health and productivity resulting from HIV and AIDS treatment could allow for increased spending on child nutrition via income and substitution effects. In addition, it hypothesised that such spillovers were more likely to occur among parents who were on HIV treatment for more than 100 days compared to those on treatment for less than 100 days due to the time it takes for the treatment to improve parent health and productivity. The study did not find strong evidence of such spillovers when comparing weight-for-height z-scores of children whose parents had been on HIV and AIDS treatment for more than 100 days versus those who were on treatment for less than 100 days.

Because only two studies evaluated interventions related to HIV testing and treatment and both were of moderate quality, we cannot draw conclusions about the evidence of spillovers for this category of interventions.

4.6 Insecticide-treated nets

Three studies evaluated programmes that distributed free (Hawley *et al.* 2003) and subsidised (Bhattacharya *et al.* 2013) ITNs in Kenya and ITNs with education and microloans in India (Tontarawongsa *et al.* 2011). One study had high-quality evidence, one was of moderate quality and one had low-quality evidence.

One study found evidence of notable reductions in malaria and anaemia among individuals who did not receive free ITNs and who lived within 300 metres of villages that received free ITNs (Hawley *et al.* 2003). Reduced malaria infections among individuals using ITNs may have led to reduced transmission of malaria to nearby areas, leading to reductions in malaria and anaemia among nearby individuals. No evidence of spillovers for child mortality was found (Hawley *et al.* 2003). Another study found that the probability of an ITN purchase was associated with the number of people eligible to receive subsidies in nearby areas (Bhattacharya *et al.* 2013). In an assessment of a programme offering ITNs with education and microloans, the proportion of household members that had slept under an ITN the previous night was associated with the number of people participating in the programme, but the programme did not result in spillovers of increased net or ITN acquisition among non-participants (Tontarawongsa *et al.* 2011).

In summary, the few studies that have estimated spillovers of ITN programmes with and without subsidies suggest that they lead to positive spillovers of health outcomes for individuals in nearby areas who do not receive free ITNs. The association between spillovers and distance to treated areas suggests that physical proximity is a major mechanism for spillovers. It is also possible that social proximity results in acquisition of ITNs by individuals living near to programme areas.

4.7 Nutrition

Two studies estimated whether siblings of children that received free meals at school and take home meals in Burkina Faso and Laos experienced spillovers (Kazianga *et al.* 2009; Buttenheim *et al.* 2011). One study produced moderate-quality evidence, and one had low-quality evidence. The mechanism of spillover hypothesised in both studies was substitution: if a fixed amount of resources are available to purchase food for a household, provision of free meals at schools may free up resources to feed siblings more food at home. One study found that the weight-for-age ratio was higher among pre-school aged siblings of children who received take home rations from school but that there were no spillovers for siblings of children who received free meals at school with no take home meals (Kazianga *et al.* 2009). The second study found some evidence of spillovers among younger and older siblings of children participating in a school feeding and take home ration programme, but they did not present disaggregated results for spillovers (Buttenheim *et al.* 2011). In both studies, there was weak evidence of spillovers on siblings of children participating in school feeding programmes.

4.8 Maternal and child health

Two studies evaluated spillovers from a maternal and child health programme in Matlab, Bangladesh, which provided family planning services, basic health education, antenatal care and safe delivery kits (Chaudhuri 2005; Joshi and Schultz 2013). Both studies produced very low-quality evidence. One study estimated spillovers on the body mass index of elderly women and adult men who were not targeted as part of the programme. It was hypothesised that resources provided by the programme may free up household resources to be spent on food for other individuals. It was also hypothesised that health and hygiene information provided to mothers may also benefit other individuals in the household. Spillovers were found for the body mass index of elderly women but not for adult or elderly men.

Another study evaluating the same programme estimated whether individuals living near programme areas experienced improved health. The fertility of women living in comparison sites near to programme areas was compared to the fertility of women in comparison sites further from programme areas. The study found that women in boundary control areas had an average of 0.35 fewer children compared to women in the control areas further from programme areas.

Both of these studies evaluated the same programme and utilised similar datasets, so their results are likely to be dependent. Their results should be interpreted with caution, since both studies had very low-quality evidence.

4.9 Water and sanitation

Three studies assessed the effect of water source status, water filtration and improved sanitation on health in Bangladesh, Ethiopia and Guinea. Two of these studies produced moderate-quality evidence and one produced very low-quality evidence.

One study assessed whether the number of water points in a community affected the proportion of people with diarrhoea (Ziegelhöfer 2012). It was hypothesised that if the number of water points was greater, individuals who did not have access to water points would have less diarrhoea through reduced disease transmission (Ziegelhöfer 2012). No statistically significant evidence of such spillovers was found.

Another study assessed whether communities adopting water filtration through sari or other cloth had a lower incidence of cholera (Huq *et al.* 2010). As expected, communities with higher water filtration adoption had a lower incidence of cholera (Huq *et al.* 2010).

Finally, another study assessed spillovers in a mass azithromycin distribution and latrine construction programme in Ethiopia (Haile *et al.* 2013). A 10 per cent increase in latrine use in study areas was associated with a 2 per cent decrease in trachoma infection (95% confidence interval 0.2, 3.9) (Haile *et al.* 2013). The latter two studies compared health effects at different intervention coverage levels measuring both direct and spillover effects, and indicating that spillover effects may be present.

4.10 Other interventions

Other interventions for which spillovers were measured include a women's empowerment programme (Janssens 2005), a peer-support intervention for drug users (German *et al.* 2012), and community monitoring of health services (Björkman and Svensson 2009). Two studies provided moderate-quality evidence and one study low-quality evidence.

Janssens (2005) evaluated a women's empowerment programme in India and assessed whether non-participants in villages where the programme was conducted experienced any positive spillovers. They found that non-participants in programme villages were approximately 12–27% more likely to vaccinate their children than those in control villages. Spillover effects were nearly as large as the effects among programme participants; for immunisation of children, the spillover effects were 40–54% of the programme effect.

German *et al.* (2012) evaluated a peer-support intervention among drug users in Thailand to assess whether peers who were not participating in the programme experienced decreases in depression. Peers of intervention participants experienced a 9.5 per cent decrease in depression, and those connected to control participants experienced a 9.2 per cent decrease. However, these results were not statistically significant at the $\alpha = 0.05$ level.

Björkman and Svensson (2009) evaluated whether a programme encouraging community monitoring of health services in Uganda resulted in spillovers into the control group; clinics were assigned to treatment or control. They estimated the programme effect, conditional upon an indicator for whether a control clinic was within 10 kilometres of the nearest treatment clinic, and did not find any evidence of spillovers into the control group using this approach.

4.11 Publication bias

Publication bias occurs when investigators and/or journals choose to publish studies with significant, non-null findings and choose not to publish null findings. Such bias results in an incomplete evidence base for decision making about which interventions to fund and implement. We found more evidence of publication bias among spillover effects than among direct effects in the studies in this review.

Opportunistic measurement of spillovers (as opposed to pre-specified measurement) may increase the chance of publication bias. In 33 out of the 54 studies, spillover measurement did not appear to be part of the design of the original study of intervention impact. It is possible that investigators discovered evidence of spillovers while measuring the direct effects of a programme. Investigators may not have noticed an absence of spillovers or may have chosen not to publish findings related to spillover absence. Since efforts to estimate health spillovers outside of the vaccine literature have only recently become more common, it is not surprising that studies that found statistically significant spillovers, either positive or negative, were more likely to be mentioned in publications. Because many of the included studies appeared to measure spillovers opportunistically, the designs used were, in some cases, suboptimal for spillover measurement. Such studies may be more prone to bias than studies with pre-specified spillover measurement.

5. Implications

5.1 Implications for policy

Rigorous impact evaluation is a cornerstone of evidence-based policymaking. Evaluations typically measure an intervention's effect on those who received it. However, many interventions may affect non-recipients by reducing disease transmission or spurring the spread of behaviour change. In order for impact evaluations to accurately measure the population-level impact of interventions, spillovers must be taken into account. If spillovers are present in the same direction as the treatment effect, studies that only estimate effects on intervention recipients will underestimate the effectiveness of the intervention. In addition, cost-effectiveness calculations that exclude such positive spillovers will underestimate an intervention's benefits. Similarly, if negative spillovers are present, studies only estimating effects on intervention recipients will overestimate the intervention's benefits. Thus, from a policy perspective, careful assessment of spillovers in future impact evaluations will allow for more comprehensive and accurate assessments of which programmes yield the greatest health impacts and are most cost-effective.

Because of the low number of studies producing high-quality evidence identified in this review, we do not recommend any policies based on evidence of spillovers for specific interventions. Increased standardisation of spillover measurement and improved design, analysis and reporting of spillovers will produce better evidence that policymakers can draw upon. In some cases, spillover measurement can easily be incorporated into existing study designs at minimal cost. However, it is often the case that rigorously measuring spillovers requires measuring outcomes among individuals who were not targeted by a programme; this could increase the cost of an impact evaluation, since such individuals are not typically enrolled. Funders of impact evaluations might consider whether it is appropriate to provide additional funding for assessment of spillovers for interventions when there is a strong theory or preliminary evidence to suggest that they might be present.

5.2 Implications for programming

Evidence of spillovers from a specific intervention in multiple populations and settings would support expanded intervention delivery and possibly even public subsidies to support the intervention. In this review, there were few studies in any given intervention category that produced high enough quality evidence to draw recommendations for future programming based on spillover evidence. Vaccines were the only intervention assessed for which there were sufficient high-quality studies from a wide range of settings and locations to recommend further implementation because of strong evidence of spillovers. However, the strength of spillovers for many vaccines is well documented, and spillovers are already a major motivator for many governments and other organisations to implement vaccine programmes. For other interventions, evidence from more rigorous evaluations in other study populations and settings would create an evidence base for decisions about future programming.

5.3 Implications for future research

We provide a complete list of recommendations for the design, analysis and reporting of spillovers in future studies in Appendix 3. The majority of included studies did not clearly define the spillover estimation methods. We recommend that, in future studies, investigators provide a clear definition of how they plan to estimate spillovers, ideally in a publicly available protocol registered prior to data collection or analysis (Miguel *et al.* 2014). We also recommend pre-specification of a number of other elements of study design, such as the scale of spillovers expected and the hypothesised mechanism of spillovers. Finally, at the reporting stage, we recommend that investigators use the checklist we developed building on the Consolidated Standards for Reporting Trials (CONSORT) framework (Schulz *et al.* 2010) to ensure thorough reporting of spillovers, increase standardisation and allow for greater comparability of spillover findings.

Appendix A: Studies meeting inclusion criteria

See the full technical report for a summary of the review methodology, specific inclusion criteria, risk of bias assessment, detailed empirical findings, and study limitations.

Author and year	Country	Intervention(s)	Primary outcome(s)*	Primary design	Spillover-related parameters
Ali <i>et al.</i> 2005	Bangladesh	Cholera vaccine	Cholera	Reanalysis of an individually randomised trial	Treatment coverage mean, treatment coverage effect
Ali <i>et al.</i> 2008	Bangladesh	Cholera vaccine	Cholera	Reanalysis of an individually randomised trial	Treatment coverage effect
Ali <i>et al.</i> 2013	India	Cholera vaccine	Cholera	Cluster-randomised trial	Direct effect, within-cluster spillover effect, total effect, treatment coverage mean, treatment coverage effect
Avitabile 2012	Mexico	Conditional cash transfers	Screening for cervical cancer, blood sugar, and blood pressure	Reanalysis of a cluster-randomised trial	Within-cluster spillover effect among ineligible, total effect among eligibles
Azad <i>et al.</i> 2010	Bangladesh	Women's groups and health service strengthening	Neonatal mortality	Cluster-randomised trial	Direct effect, within-cluster spillover effect conditional on exposure to treatment, within-cluster spillover effect
Baird <i>et al.</i> 2013	Kenya	Subsidised deworming	Self-reported health and body mass index	Cross-sectional survey of a population that previously participated in a cluster-randomised trial	Total effect conditional on treatment density, spillover effect conditional on treatment density
Baird <i>et al.</i> 2013	Malawi	Conditional cash transfers	Psychological distress	Double-randomised trial	Within-cluster spillover effect, total effect
Banerjee <i>et al.</i> 2010	India	Vaccines (BCG, DPT, polio, measles) + incentives	Vaccine coverage	Cluster-randomised trial	Total effect, spillover effect conditional on living in an untreated cluster within distance d to treated clusters
Baptista <i>et al.</i> 2006	Brazil	Pertussis vaccine	Pertussis	Case-control study	Vaccine efficacy for susceptibility, vaccine efficacy for infectiousness

Bhattacharya <i>et al.</i> 2013	Kenya	Subsidised insecticide-treated nets (ITNs)	ITN purchase	Reanalysis of an individually randomised trial	Total effect, direct effect, direct effect conditional on treatment density
Björkman and Svensson 2009	Uganda	Community monitoring and provision of health services	Child mortality, health service provision and utilisation, child growth	Cluster-randomised trial	Total effect, total effect conditional on whether treatment and control units were within distance <i>d</i> of each other
Buttenheim <i>et al.</i> 2011	Laos	School feeding programme	Child growth	Cohort study + propensity-score matching + difference-in-differences	Within-cluster spillover effect among ineligible
Chaudhuri, (year not listed)	Bangladesh	Maternal and child health programme	Body mass index	Cross-sectional survey of a population previously in an unmatched cohort study	Total effect among eligibles, within-cluster spillover effect among ineligible
Chen <i>et al.</i> 2014	Bangladesh	<i>Haemophilus influenzae</i> type b vaccine	Pneumonia	Reanalysis of matched case-control study	Treatment coverage effect
Chidambaram <i>et al.</i> 2004	Ethiopia	Mass azithromycin distribution	Trachoma	Unmatched cohort	Within-cluster spillover effect
Chong <i>et al.</i> 2013	Colombia	Online sexual health education	Knowledge about sexually transmitted infections	Double-randomised trial	Total effect, within-cluster spillover effect
Contreras and Maitra 2013	Colombia	Conditional cash transfers	Self-reported illness	Cohort study + propensity-score matching + difference-in-differences	Within-cluster spillover effect among ineligible
Cooper and Fitch 1983	St. Lucia	Pertussis vaccine	Pertussis	Cross-sectional survey	Treatment coverage mean
Dupas 2006	Kenya	Information about HIV transmission	Teen pregnancy	Reanalysis of a cluster-randomised trial	Total effect, total effect conditional on treatment density
Egere <i>et al.</i> 2012	The Gambia	Pneumococcal conjugate vaccine	Pneumococcal nasopharyngeal carriage	Cluster-randomised trial	Within-cluster spillover effect among ineligible
Emch <i>et al.</i> 2006	Bangladesh	Cholera vaccine	Cholera	Reanalysis of an individually randomised trial	Treatment coverage effect
Emch <i>et al.</i> 2009	Bangladesh	Cholera vaccine	Cholera	Reanalysis of an individually randomised trial	Treatment coverage mean, treatment coverage effect

Fitzsimons <i>et al.</i> 2012	Malawi	Information on infant nutrition and health	Child growth and morbidity	Reanalysis of a cluster-randomised trial	Total effect among eligibles, within-cluster spillover effect among ineligibles
Forleo-Neto <i>et al.</i> 1999	Brazil	<i>Haemophilus influenzae</i> type b vaccine	<i>Haemophilus influenzae</i> type b carriage	Cross-sectional survey	Treatment coverage mean
German <i>et al.</i> 2012	Thailand	Peer-network health education	Depression	Individually randomised trial	Direct effect, spillover effect among social network members
Godlonton and Thornton 2012	Malawi	Incentives for voluntary counselling and testing for HIV	Voluntary counselling and testing for HIV	Reanalysis of an individually randomised trial + instrumental variables	Total effect conditional on outcome density
Haile <i>et al.</i> 2013	Ethiopia	Latrines	Trachoma	Reanalysis of a cluster-randomised trial	Treatment coverage effect
Hammit <i>et al.</i> 2014	Kenya	Pneumococcal conjugate vaccine	Pneumococcal nasopharyngeal carriage	Cross-sectional surveys before and after intervention	Spillover before and after treatment
Handa <i>et al.</i> 2001	Mexico	Conditional cash transfers	Child nutrition surveillance	Reanalysis of a cluster-randomised trial	Total effect among eligibles, within-cluster spillover effect among ineligibles
Hawley <i>et al.</i> 2003	Kenya	ITNs	Child mortality, anaemia, clinical malaria	Reanalysis of a cluster-randomised trial	Spillover effect conditional on household distance to nearest treated cluster, spillover effect conditional on household distance to nearest treated cluster
House <i>et al.</i> 2009	Ethiopia	Mass azithromycin distribution	Trachoma	Cluster-randomised trial	Within-cluster spillover effect among ineligibles
Huq <i>et al.</i> 2010	Bangladesh	Water filtration with sari cloth and nylon cloth	Cholera	Cross-sectional survey of a population that previously participated in an individually randomised trial	Treatment coverage mean, direct effect
Janssens <i>et al.</i> 2005	India	Women's empowerment programme	Vaccine coverage	Cohort study + propensity score matching + instrumental variables	Within-cluster spillover effect, direct effect, within-cluster spillover effect in which controls are matched to the untreated

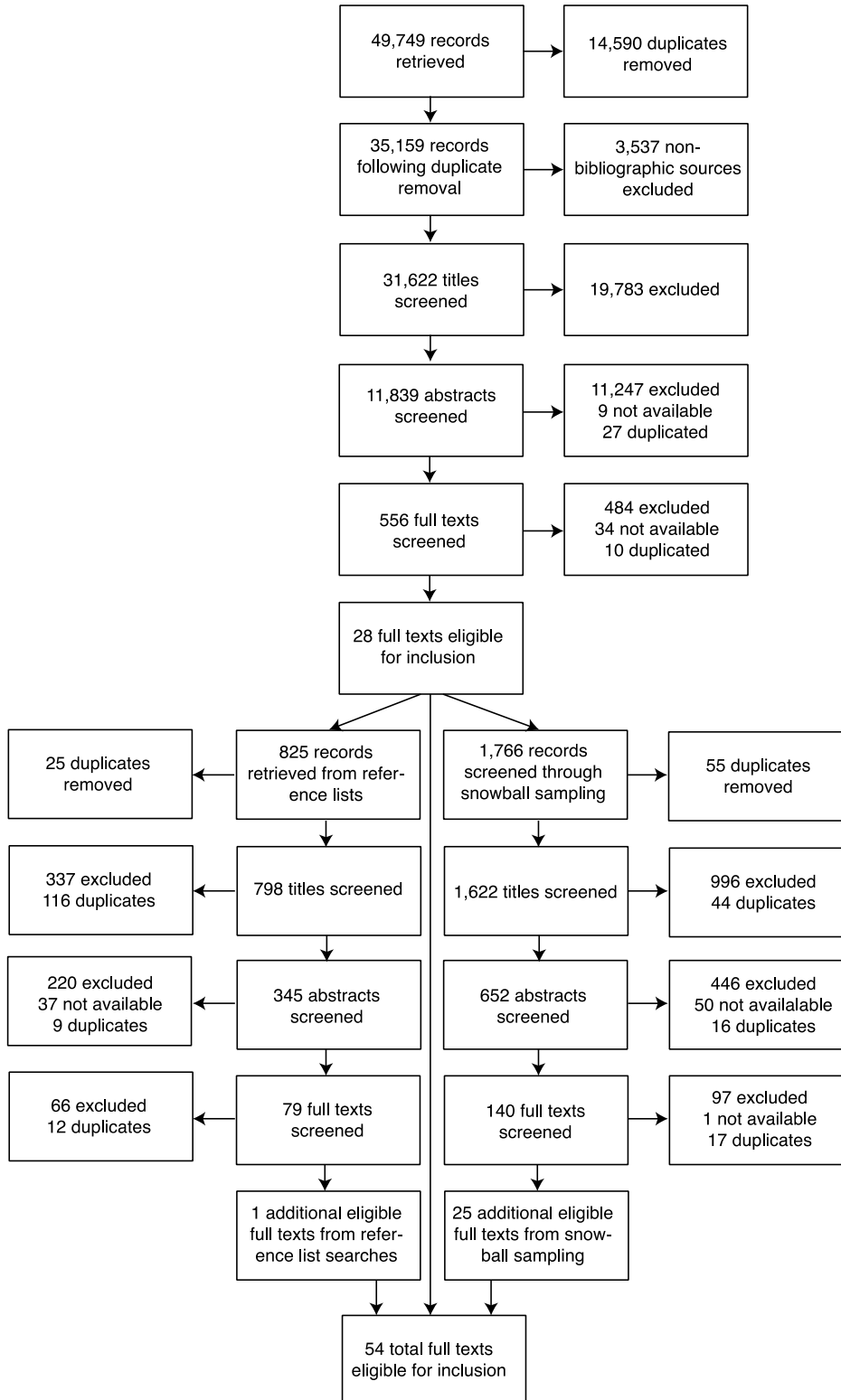
Joshi and Shultz 2013	Bangladesh	Maternal and child health programme	Parity, body mass index activities daily index, childhood vaccination	Cross-sectional survey of a population previously in an unmatched cohort study	Spillover effect into boundary areas of untreated clusters
Kazianga <i>et al.</i> 2014	Burkina Faso	School feeding programme	Child growth	Cluster-randomised trial	Total effect among eligibles, within-cluster spillover effect among ineligibles
Khan <i>et al.</i> 2012	Pakistan	Typhoid vaccine	Typhoid fever	Cluster-randomised trial	Direct effect, within-cluster spillover effect, total effect
Khatib <i>et al.</i> 2012	Tanzania	Cholera vaccine	Cholera	Cohort study without a control group	Direct effect, treatment coverage mean
Kremer and Miguel 2007	Kenya	Exposure to information about deworming	Deworming	Cross-sectional survey of a population that previously participated in a cluster-randomised trial	Total effect conditional on number of social network links
Miguel and Kremer 2004	Kenya	Deworming	Helminth infection	Cluster-randomised trial	Total effect, within-cluster spillover effect, spillover effect conditional on treatment density
Osier 2011	Kenya	Deworming	Child growth and cognitive performance	Cross-sectional survey of a population that previously participated in a cluster-randomised trial	Within-cluster spillover effect
Paul <i>et al.</i> 1962	Costa Rica	Polio vaccine	Polio antibody conversion	Individually randomised trial	Vaccine efficacy**
Perez-Heydrich <i>et al.</i> 2014	Bangladesh	Cholera vaccine	Cholera	Reanalysis of a cluster-randomised trial + inverse probability weighting	Direct effect conditional on treatment density, spillover effect conditional on treatment density, total effect conditional on treatment density
Préziosi and Halloran 2003	Senegal	Pertussis vaccine	Pertussis	Case-control study	Vaccine efficacy for infectiousness, vaccine efficacy for susceptibility, total vaccine efficacy
Ribas <i>et al.</i> 2011	Paraguay	Conditional cash transfers	Healthcare visits	Cohort study + propensity-score matching + difference-in-differences	Direct effect, within-cluster spillover effect among ineligibles

Roca <i>et al.</i> 2011	The Gambia	Pneumococcal conjugate vaccine	Pneumococcal nasopharyngeal carriage	Cluster-randomised trial	Total effect conditional on exposure to treatment
Roca <i>et al.</i> 2013	The Gambia	Pneumococcal conjugate vaccine	Pneumococcal nasopharyngeal carriage	Cluster-randomised trial	Total effect conditional on exposure to treatment
Root <i>et al.</i> 2011	Bangladesh	Cholera vaccine	Cholera	Reanalysis of an individually randomised trial	Treatment coverage effect
Root <i>et al.</i> 2014	Philippines	Pneumococcal conjugate vaccine	Pneumonia	Reanalysis of a cluster-randomised trial	Treatment coverage effect
Shekhawat <i>et al.</i> 2014	Tanzania	Mass azithromycin distribution	Trachoma	Cohort study in a population previously enrolled in a cluster-randomised trial	Within-cluster spillover effect**
Singh 2011	India	Nutrition education	Child growth	Cluster-randomised trial	Total effect, within-cluster spillover effect
Sur <i>et al.</i> 2009	India	Typhoid vaccine	Typhoid fever	Cluster-randomised trial	Total effect, within-cluster spillover effect
Tontarawongsa <i>et al.</i> 2011	India	ITNs for free or with microloans and information sessions	ITN use	Reanalysis of a cluster-randomised trial	Total effect conditional on number of social network links, spillover effect among social network members
Ziegelhöfer 2012	Guinea	Improved water supply	Diarrhoea	Cross-sectional survey + regression discontinuity + instrumental variables	Total effect, spillover effect conditional on treatment density, ratio of village level to household level effect
Zivin <i>et al.</i> 2009	Kenya	HIV and AIDS treatment	Child growth	Cohort study	Within-cluster spillover effect

*If multiple types of primary outcomes are listed, the primary health outcomes are mentioned here.

**This parameter was not explicitly estimated, but it could have been using the data collected in the study.

Appendix B: Records in each stage of the systematic review



Appendix C1: Modifications to Cochrane GRADE tool to incorporate spillover assessment: classification of studies' underlying methodology

Underlying methodology
<p>High quality</p> <ul style="list-style-type: none"> • Double-randomised trials estimating within-cluster spillovers • Cluster-randomised trials estimating within-cluster spillovers among people who were not eligible but were highly comparable to eligible individuals • Individually randomised studies estimating spillover effects among social network members • Studies estimating spillovers conditional on treatment or outcome density in a randomised study in which treatment density is estimated over multiple distances (physical or social) and in which distance cut-offs are defined based on quantiles or other objective criteria • Household-based studies estimating vaccine efficacy parameters that match index cases with household controls
<p>Moderate quality</p> <ul style="list-style-type: none"> • Randomised studies estimating within-cluster spillovers among people who chose not to participate in the intervention (i.e. participants within clusters were not randomised to receive treatment, so selection bias is possible in spillover effects) • Cluster-randomised trials estimating within-cluster spillovers among people who were not eligible and were not highly comparable to eligible individuals • Observational studies estimating within-cluster spillovers • Studies estimating spillovers conditional on treatment or outcome density in a randomised study in which treatment or outcome density is estimated over only one distance level (physical or social) • Studies estimating spillovers conditional on treatment or outcome density in a randomised study in which treatment or outcome density is estimated and distance cut-offs were not based on objective criteria • Ecological studies comparing outcomes over levels of treatment coverage in which the treatment was randomised and a possible dose-response pattern for spillovers was assessed
<p>Low quality</p> <ul style="list-style-type: none"> • Ecological studies comparing outcomes over levels of treatment coverage in which the treatment was not randomised

- Ecological studies comparing outcomes over levels of treatment coverage that did not assess a possible dose–response gradient for spillover effects
- Studies in which instrumental variables were the primary identification strategy but the exclusion restriction suffers from obvious violations or the instrument is not strongly associated with the treatment
- Studies in which systematic differences were likely to be present between the intervention and the control group (for example, a cohort study that did not use matching to make the control group comparable to the intervention group)
- Studies that did not include a rigorous control group

Very low quality

- Studies with any underlying methodology subject to serious additional concerns about risk of bias and the quality of evidence

Appendix C2: Modifications to Cochrane GRADE tool to incorporate spillover assessment: factors that may increase or decrease the quality level of a body of evidence

Factors that may increase (i.e., 'upgrade') the quality level of a body of evidence	Factors that may decrease (i.e., 'downgrade') the quality level of a body of evidence
<ol style="list-style-type: none"> 1. Large magnitude of spillover effect that is plausible relative to the size of the direct or total effect 2. All plausible confounding of the spillover effect would reduce a demonstrated effect or suggest a spurious effect when results show no effect 3. Dose–response gradient for spillover effect 	<ol style="list-style-type: none"> 1. Limitations in the design and implementation specific to spillover effects suggesting high likelihood of bias. These include the GRADE criteria as well as the following criteria specific to spillover effects: <ol style="list-style-type: none"> a. Contamination of the control group may have occurred or did occur b. Magnitude of spillover effect relative to direct/total effect does not seem plausible c. Spillover effects were not explicitly reported in the published manuscript d. Indirect evidence e. Unexplained heterogeneity or inconsistency of results f. Imprecision of results g. High probability of publication bias

Appendix D1: Design and analysis recommendations

- Pre-specify spillover estimation when developing study designs or analysis plans. This includes mentioning spillover estimation methods during protocol registration.
- Pre-specify the specific spillover parameter(s) to be estimated.
- If the spillover parameter incorporates measurement within specific distances or areas, pre-specify these distances or areas and provide a rationale for them. If measures of treatment or outcome density are to be used, pre-specify the definition of areas or the algorithm used to define areas within which density is measured with as much detail as possible. For example, describe the specific distances in which measurement will take place or describe whether measurement will occur within quantiles of the observed distance distribution.
- Define spillover parameters that include contrasts that are likely to be policy relevant. For example, in estimating social network spillovers, estimate the difference in outcomes for a realistic number of social network links compared to no social network links.
- Pre-specify the scale at which spillovers are expected and the hypothesised mechanism(s) of spillover.
- If the study protocol is registered, use the term ‘spillovers’ or ‘indirect effects’ to refer to spillovers in the protocol because these are the most commonly used terms in the literature (Table 10), and they provide a direct link to the theoretical literature on this topic.
- To estimate within-cluster spillovers, utilise a double-randomised design. If it is only possible to utilise a cluster-randomised design, consider using multivariate matching techniques to match untreated individuals in the control clusters to untreated individuals in the treatment clusters. This will ensure internal validity but may decrease external validity in some cases.
- If a clustered study design is used, build in buffer zones between treated and control units in order to prevent contamination and ensure that there is a valid control group to serve as a counterfactual.

Appendix D2: Reporting recommendations for studies estimating spillovers

We have organised the following recommendations within the headings of the CONSORT checklist for reporting of randomised trials (Schulz *et al.* 2010).

Title and abstract

- If spillovers were measured as a primary outcome of a study, mention them in the title and/or abstract. Use the term ‘spillovers’ or ‘indirect effects’ to refer to spillovers.

Introduction

Background and objectives

- Use the term ‘spillovers’ or ‘indirect effects’ to refer to spillovers.

Methods

Design

- Indicate whether spillover estimation was pre-specified.
- Describe whether buffers existed between treatment and control units, whether in physical or social distance.
- If treatment or outcome density was measured within areas, describe the rationale for and method of defining these areas.
- Describe the scale on which spillovers are expected (for example, household, village, and so forth).
- For study designs used to estimate spillovers other than the double-randomised or the cluster-randomised design, provide a clear description of the assumptions required to estimate valid statistical parameters if SUTVA is violated.

Participants

- Provide a clear description of the rationale for treatment eligibility criteria.
- State whether individuals enrolled to measure spillovers were eligible for the treatment or not.

Interventions

- Provide a clear description of how treatment was allocated to groups and individuals.
- State whether the level of treatment allocation was chosen in order to measure spillovers.

- Describe whether untreated individuals in treated areas were randomly assigned to not receive treatment, if they opted out of treatment, if they were ineligible for treatment or if there were other reasons they were not treated.
- Describe the mechanism of spillovers hypothesised and assessed for each treatment.
- Describe whether a buffer zone was created between treatment and control units.

Outcomes

- If outcomes measured to estimate direct or total effects differed from outcomes measured to estimate spillover effects, provide a rationale for the difference.

Sample size

- Describe any calculations conducted to determine the sample size needed to estimate spillover parameters. If none, state that none were conducted.

Statistical methods

- Define the specific spillover parameter(s) estimated for each intervention.
- Describe the design and statistical analysis methods used to identify spillover effects.
- Describe any assumptions underlying statistical methods used to estimate spillovers.
- Describe whether any unplanned analyses were conducted to estimate spillovers. These may include subgroup analyses or analyses with alternative definitions of areas in which treatment coverage or density was estimated.

Results

Participant flow

- Provide the number of clusters allocated to treatment and control.
- Provide the number of individuals eligible to receive treatment in treated clusters.
- Provide the number of individuals allocated to treatment within treatment clusters, allocated to not receive treatment within treated clusters, and allocated to control clusters.
- Provide the number of individuals that received and did not receive treatment within treatment and control clusters.
- For spillovers measured within clusters, provide information about the proportion of individuals receiving treatment within each cluster.
- If measurement occurred in buffer zones between treatment and control clusters, provide the number of individuals who did and did not receive treatment in buffer zones.

Recruitment

- If dates of data collection for spillover measures differed from dates for total or direct effect measures, explain the discrepancy.

Outcomes and estimation

- Clearly label which results estimate each spillover parameter.
- In tables and figures, clearly indicate whether parameters were estimated among individuals *allocated* to treatment vs. those that *received* treatment (i.e. indicate whether an intention-to-treat vs. treatment-on-treated analysis was conducted).
- If multiple spillover mechanisms were hypothesised, label results according to the hypothesised spillover mechanism.
- Present total effects for comparable population subgroups to allow for assessment of the proportion of the total effect attributable to spillovers.
- If direct or total effects are estimated in subgroups, present spillover estimates in these same subgroups to allow for direct comparison.
- Report whether there was any evidence that untreated individuals in the treatment or control group were exposed to treatment (for example, if untreated individuals had heard of the intervention or knew individuals who received it).
- Describe any evidence of contamination of the control group.

Discussion

- Present evidence supporting the proposed mechanism of spillover. Such evidence may or may not have been collected in the study but contributes substantially to the overall understanding and credibility of the results.

Limitations

- Discuss any potential biases that may be present for spillover parameters. Discuss whether these biases may also be present for direct or total effect parameters. This includes contamination of the control group.
- Articulate whether any analyses conducted to estimate spillovers were not pre-specified.

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To estimate the true impact of an intervention, evaluations must measure impact on recipients and non-recipients alike. Estimating spillovers is important to measure the costs and benefits of an intervention accurately. This summary report is based on a systematic review of 54 impact evaluations that estimate spillover in health interventions. The authors tried to identify mechanisms that trigger spillover through geographic or social proximity, learning or imitation, norm-shaping, income and substitution effects, general equilibrium effects and relative deprivation.

For included interventions addressing mass drug administration, health education, cash transfers, insecticide-treated bed nets, and water and sanitation, evidence was too limited or mixed to draw conclusions about health-related spillovers. The exception was in vaccination interventions. The authors found clear evidence of the benefits of vaccination spilling over to non-recipients.

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