Effective interventions for improving routine childhood immunisation in L&MICs

Findings from systematic review of systematic reviews

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International Initiative for Impact Evaluation

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1 Objectives

Systematic review of systematic reviews objectives

Assess effectiveness of interventions to improve routine immunisation of children

Geographic scope: All low- and middle-income countries

Outcomes: All immunisation outcomes, e.g., coverage related or preceding outcomes such behavioural, knowledge and attitude related.

Intervention matrix

1st tier	2nd tier	3rd tier
Caregiver oriented	Information & education	Sustained or one-time sensitisation & education & Public information campaigns
	Incentives & motivation	Incentives for caregivers; Automated voice or SMS messages
Health system oriented	Education & training	Frontline health worker training and education
	Planning & implementation	Frontline health worker involvement in planning & monitoring; Promoting outreach to vaccine-hesitant, hard-to-reach or migrant populations; Home visits
	Incentives & motivation	Incentives for health workers; Pay for performance schemes
	Infrastructure	Building & upgrading health clinics or Cold chain infrastructure improvements
	Health system governance	Strategic planning; Guidelines; Strengthening capacity of existing governance structures
	Technology & mHealth	New HMIS/Dashboard systems; Capacity building for existing systems
Community oriented	Outreach	Outreach involving local or religious leaders
	Communication & dialogue	Collaborating with community; Comprehensive community programmes; Community groups and networks
	Tracking & registering	Community tracking and registering

2 Methods

Methods

Search strategy

- Search designed for 3ie evidence gap map on routine child immunisation – completed on 5 May 2020 (Engelbert, 2022)
- Search updated in October 2021
- Academic database and grey literature

Quality of included reviews

- Adapted version of the Specialist Unit for Review Evidence – SURE – checklist, 2018
- Appraisal based on:
  1. Methods used to identify (search & time frame), include (selection bias thru independent screening) and critically appraise primary studies
  2. Methods used to analyse and report the findings (independent data extraction, heterogeneity, combining findings)
  3. Overall assessment of reliability of review

Data extraction

- Independently, by two researchers
- Type of data extracted at SR level
  - Context
  - Type of intervention
  - Type of review, design, methods used
  - Outcome measures
  - Quality assessment
  - Review results and findings

Methods

Overlap

- Determination of independent reviews: To what extent the primary studies included in the pool of systematic reviews are the same or different – important as overlap indicates the degree to which reviews address the same or different literatures of primary research
- Compilation of citation matrix to calculate corrected covered area (CCA) index (Hennessy & Johnson, 2020; Pieper et al., 2014)

$$CCA = \frac{N - r}{(rxc) - r}$$

N is the total number of primary studies included in the systematic reviews

r is the number of primary studies

c is number of included systematic reviews

- Interpretation of CCA: 0-5% suggests slight overlap, 6-10% moderate overlap, 11-15% high overlap and >15% very high overlap (Pieper et al., 2014)
- Literature recommends further overlap investigations in case of a heterogeneity, hence we also compare sub-clusters of reviews examining similar outcomes.

Methods

Data synthesis: Mixed methods synthesis

Quantitative Synthesis:

1. **Robust variance estimation (RVE) meta-regression**: include all dependent effect sizes in a single model even when the exact form of the dependence is unknown (Pustejovsky & Tipton, 2022) – RVE performs well when study numbers are low, and heterogeneity is high
2. **Random-effects model** when RVE was not possible

Effect estimate conversion was necessary:

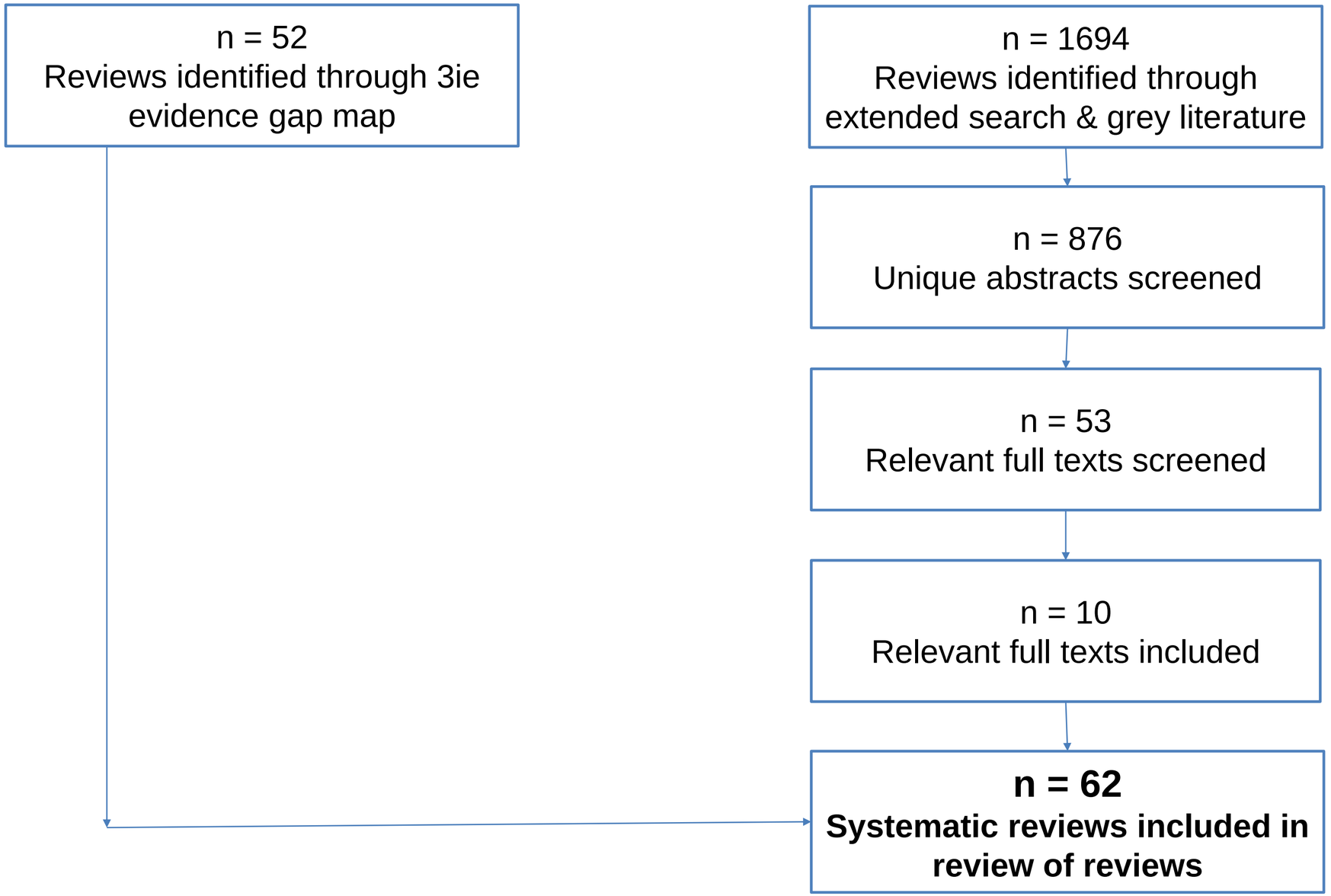
OR to RR: RR = OR / (1 – p + (p x OR)) where p is risk in the control group

Qualitative Synthesis: Narrative synthesis

We focus our synthesis on the high and medium confidence studies.

3 Results

PRISMA flow diagram



Results

62 systematic reviews are included

- 18 high confidence
- 6 medium confidence
- 38 low confidence

Included systematic reviews published between 2004 and 2021

Larger number of meta-analytical approaches among high and medium confidence studies

Geographical scope: SSA and South Asia dominate

High levels of heterogeneity in terms of scope of the reviews, intervention types and outcomes

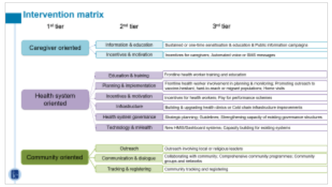
Overlap

- Suggests limited overlap for most outcomes
- Vaccination timeliness: moderate overlap
- Overlap does not pose a major challenge in the context of the evidence base

Outcomes	Times studies appeared in reviews	Number of primary studies	Number of reviews	CCA values	
	N	r	c	Proportion	Percentage
Overall	1428	1079	62	0.0053	0.5
Measles	54	46	13	0.0145	1.4
Full routine immunisation	136	121	20	0.0065	0.7
DPT3	69	53	12	0.0274	2.7
Vaccination timeliness	40	27	8	0.0688	6.9
Vaccination coverage	346	220	42	0.0140	1.4

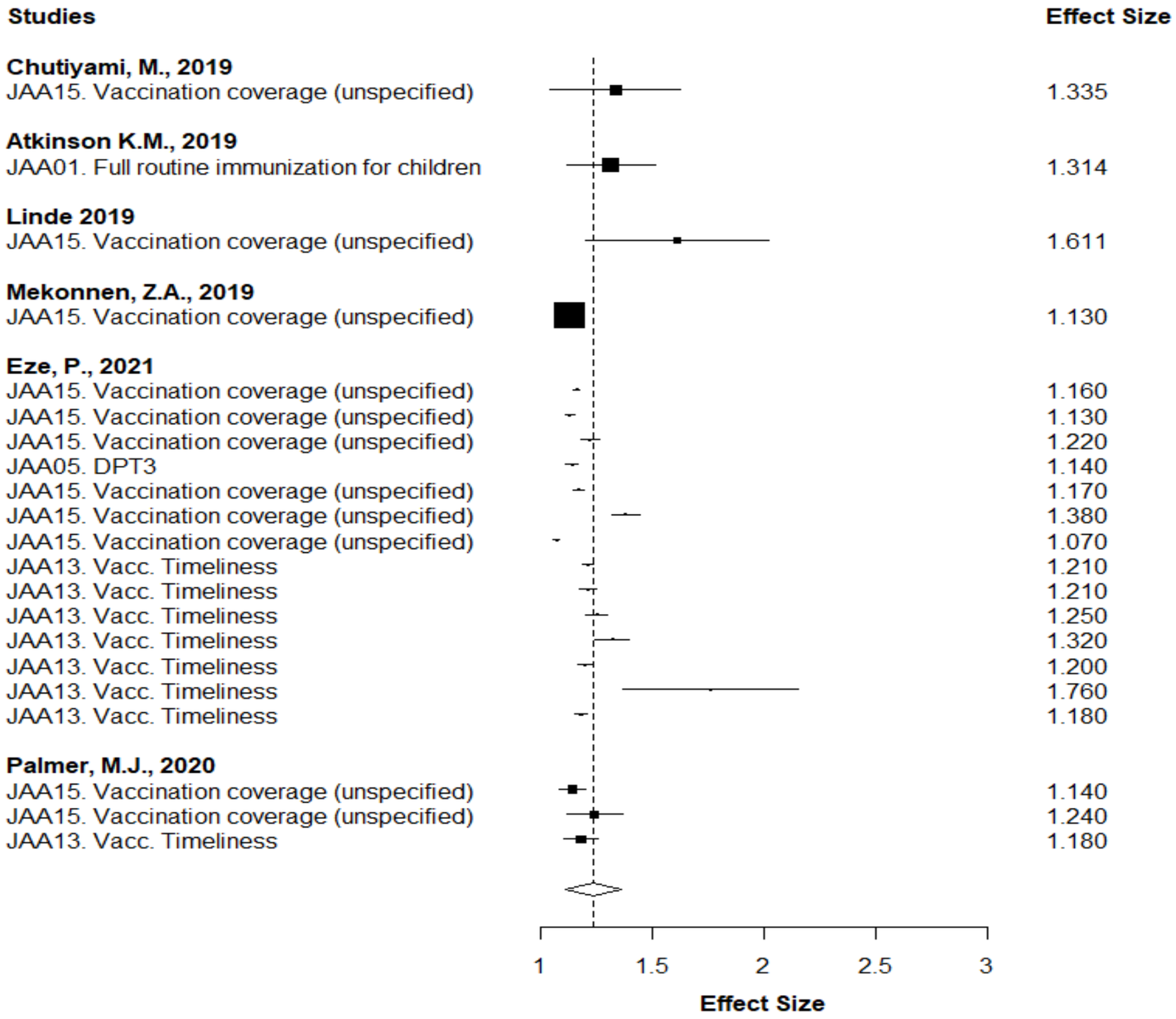
3.A Caregiver oriented interventions

Caregiver-oriented interventions (A)



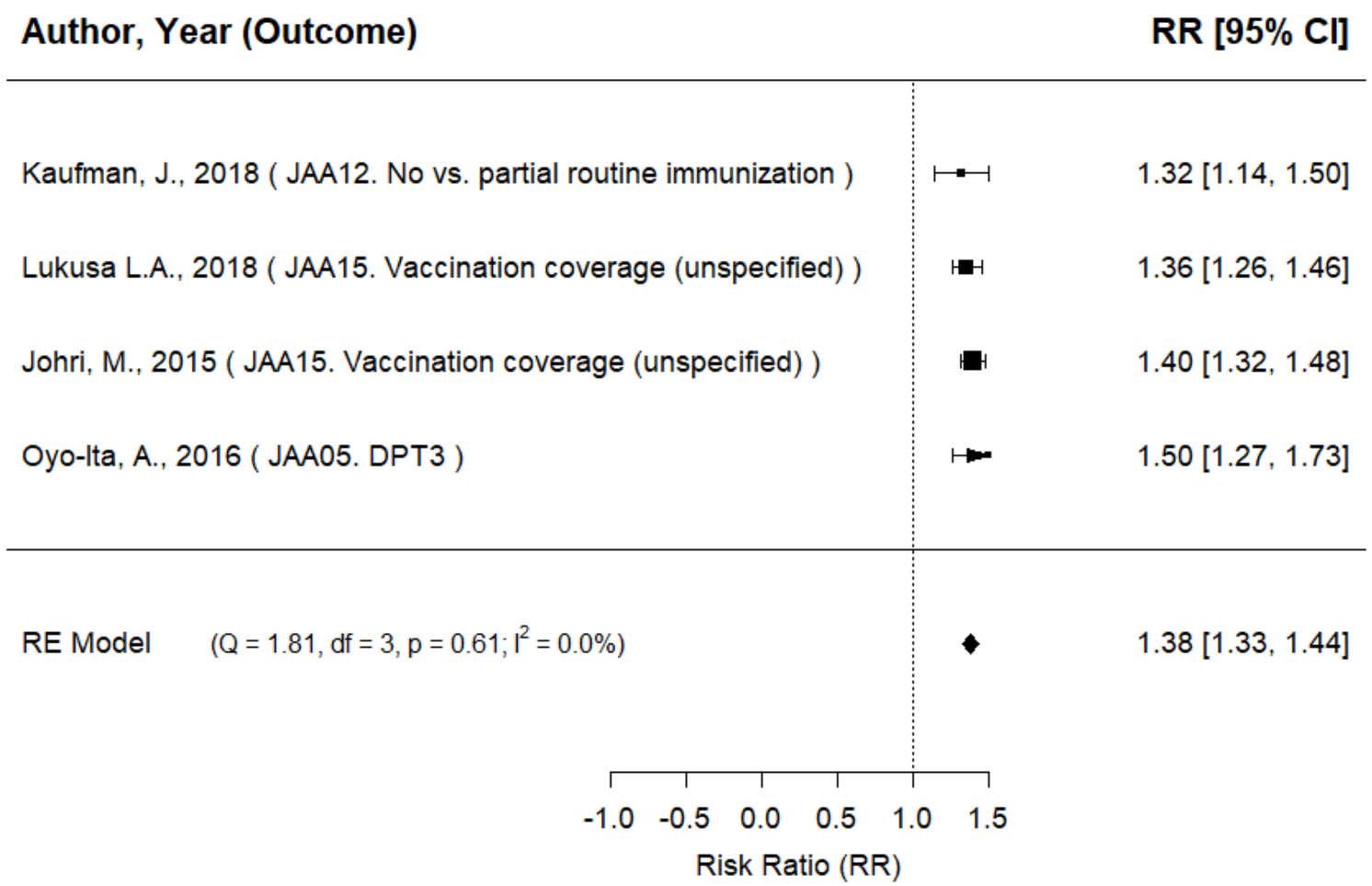
- The evidence base for caregiver-oriented interventions is of reasonable quality and sufficiently large
- Analysis carried out by tiers
  - 1st tier - Positive and statistically significant effects supported by an RVE analysis. Treated children are more likely to be vaccinated than untreated children
  - 2nd tier - Positive and statistically significant effects supported by an RVE analysis. Information and education interventions are statistically significantly more effective than incentives and motivation interventions. However, the degrees of freedom have fallen just below 4.

Caregiver-oriented interventions (A): 3rd tier - SMS or pictorial messages



RVE meta-regression - weighted average RR of 1.24 ([95% CI: 1.11 to 1.36]

Caregiver-oriented interventions (A): 3rd tier - One-time sensitisation and edu campaigns



Random effects model: RR of 1.38 (95% CI: 1.33 to 1.44)

Caregiver-oriented interventions (A) – 3rd tier

Intervention	Findings	
Sustained sensitisation and education campaigns (AA1)	Low confidence evidence, thus no further synthesis	-
Public information campaigns (AA3)	Low confidence evidence, thus no further synthesis	-
Material/monetary incentives for caregivers (AB1)	Two SRs	Mixed results, however inconclusive results dominate across outcomes
Non-material incentives for caregivers (AB2)	No evidence	-
Changes to health system user fees (AB5)	One low confidence review, thus no further synthesis	-

3.B Health system oriented interventions

Health system oriented interventions (B)

- The evidence base is thin painting a mixed picture
- No quantitative synthesis was possible
- Could only use narrative synthesis

Health system oriented interventions (B) – 3rd tier

Intervention	Findings	
Home visits (BB7)	Two SRs	Favourable effect on OPV3, measles and full routine immunisation but the results were based on single primary study for each outcome
Pay-for-performance schemes (BD5)	Two SRs	Mixed effects: For most coverage related outcomes, the effect was inconclusive. While, for some intermediate outcomes, it was positive & statistically significant and inconclusive for other
Health system financing (BF4) (contracting out health services)	Two SRs	Inconclusive results for a range of outcomes; based on one or two primary studies for each outcomes.

Health system oriented interventions (B) – 3rd tier

Intervention	Findings	
Formal health worker training and education (BA1)	Single SR	Limited evidence: Inconclusive effect on outcomes based on single primary study
Outreach to vulnerable populations (HTR, SES, caste, etc.) (BB5)	Single SR	Limited evidence: Low certainty favourable effect on the outcome based on single included study
Health system strategic planning (BF1)	Single SR	Limited evidence: Inconclusive results for most outcomes, with a single study and across heterogenous outcomes
Written or pictorial messages (SMS, stickers, flyers etc.) to health workers (BD4)	Low confidence SR, no further synthesis	-
New HMIS/Dashboard systems (incl. improved data collection) (BG1)	Low confidence study, no further synthesis	-
National/sub-national immunisation days (BC1)	Two low confidence SRs, no further synthesis	-
Material/monetary incentives for health workers (BD1)	Low confidence SR, no further synthesis	-

3.C Community oriented interventions

Community level / multicomponent interventions

- Due to very low study numbers, community-oriented intervention category was recategorized as community-level/multicomponent interventions
- No quantitative synthesis was possible

Community-level/ multicomponent interventions – 3rd tier

Intervention	Findings	
Faith-based outreach/outreach using local leaders (CA1)	Low confidence evidence, thus no further synthesis	-
Collaborating with whole community (DA1)	Single SR	Limited evidence: Inconclusive result based on single study
Collaborating with selected community groups and networks (DA2)	Single SR	Limited evidence: Small and statistically insignificant result based on two studies
Community tracking and registering (DB1)	No evidence	-
Community engagement interventions (single or multi-components)*	Single SR	Positive and statistically significant: Meta-analysis done on range of outcomes and found positive and statistically significant effect on most of the outcomes. The positively found SMD ranged between 0.06 and 0.24

*The intervention components were heterogenous. Only summary of Jain et al. (2022) is provided in this table because it is one of the only included SRs that assessed community engagement interventions which do not fit neatly into the intervention framework used in Engelbert et al. (2022).

3.D Zero dose children

Findings on zero-dose vaccination

- Zero-dose children: Children that did not receive any DPT-containing vaccination
- Intervention effects on DPT1 and BCG vaccine uptake
- Limited and inconclusive evidence for interventions improving DPT1 outcomes
- For BCG vaccine uptake, pay-for-performance schemes (qual review) and community engagement interventions (quant review) are effective

4 Implications on policy and practice

Implications for policy

A. Caregiver oriented interventions:

- **Sensitisation and education campaigns** mostly address the knowledge gaps of caregivers on the importance of vaccinations, of maintaining its schedule and potential misconceptions around vaccinations. These were delivered by either frontline health workers or trained facilitators
- **Written messages to caregivers** address the practical barriers faced by caregivers on when and where to take their child for a vaccine or follow-up doses, delivered through SMS to phones

B. Health systems oriented interventions

- Positive effects for home visits interventions
- Pay-for-performance schemes, a recent SR available (Diaconu et al., 2021) and is of high
- Available review of reviews (Hatt et al., 2015) assess the effects of health systems strengthening interventions on health status and health system outcomes in L&MICs

C. Community oriented interventions

- A recent review (Jain et al., 2022) on single and multicomponent community engagement interventions uses a nuanced framework to classify community-oriented interventions based on the process of engaging communities and find them to be effective using meta-analytical methods

Key evidence synthesis gaps

- Monetary incentives to caregivers
- Health worker capacity, motivation and skills
- Digitised HMIS / dashboards
- Multicomponent interventions
- Cost effectiveness of interventions

Implications for research

1) There is need to better understand **complementarity of interventions**; we do not yet know which intervention combinations work best in terms of improving immunisation outcomes.
2) **Theory development** - to a better understanding of the enablers and barriers of interventions and thus improving the selection and targeting of immunisation interventions
3) To learn what works at what cost, reviews need to engage more with the **cost effectiveness** of immunisation interventions
4) Limited and inconclusive evidence for interventions improving **zero dose outcomes** like DPT1 outcomes. Need to build a bigger evidence base
5) Future research needs to pay more **attention to overall study quality**, at the review level and primary study level.
    - At the review level future research should attempt more of subgroup analyses by levels of confidence in primary studies to instill more trust in the results.
    - At the primary study level, the researchers should use more robust evaluation methods to minimise the potential biases in the measurement of effects.
6) More work is required to develop **user friendly quality assessment tools** for systematic reviews that minimise the scope for subjective judgements

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