Mid-Level Health Providers (MLHPs) for Primary Healthcare: Rapid Policy Brief Supplement

Sandeep Moola, Soumyadeep Bhaumik, Devaki Nambiar



Contributions of authors

Data curation, formal analyses, writing (original draft preparation) - Sandeep Moola Conceptualisation, methodology, validation, writing (review and editing) – Soumyadeep Bhaumik

Conceptualisation, validation, writing (review and editing) - Devaki Nambiar

Competing interests

The authors do not have any relevant competing interests.

Acknowledgements

This gratis rapid evidence synthesis was made possible due to the support from World Health Organisation, Alliance for Health Policy and Systems Research. The funder did not have a role in drafting, revising or approving the content of the policy brief.

The authors would also like to acknowledge and thank the participants of the National Consultation workshop held on 11th April, 2019 for their attendance and feedback on the policy brief report.

Email for correspondence

res@georgeinstitute.org.in

Suggested citation

Moola S, Bhaumik S, Nambiar D. Mid-level health providers (MLHPs) for primary healthcare. The George Institute for Global Health, India, 2019.

Table of Contents

List	t of acronyms	4
Exe	ecutive Summary	5
1.	Background	6
2.	Methods	7
3.	Results	10
4.	Summary of findings tables for each domain of interest	20
ľ	MLHPs for care in pregnancy and child-birth (6)	20
ľ	MLHPs for neonatal and infant health care services (6)	22
ľ	MLHPs for family planning, contraceptive and other reproductive health care services (7)	23
ľ	MLHPs for communicable diseases (8,9)	25
ľ	MLHPs for non-communicable diseases (10,11)	26
ľ	MLHPs for mental health (12)	27
ľ	MLHPs for childhood and adolescent health services	29
ľ	MLHPs for ophthalmic and ENT conditions	29
ľ	MLHPs for elderly and palliative health care	29
ľ	MLHPs for emergency medical services	29
5. I	mplementation considerations in India	30
6. 5	Strengths and Limitations of the policy brief	31
7. k	Key take-aways from the National Consultation	32
8. 1	Next steps	32
9. F	References	33
App	pendix 1: Search Strategies	34
App	pendix 2. GRADE (Grading of Recommendations Assessment, Development and Evaluation)	38
App	pendix 3. List of excluded studies after full text assessment against eligibility criteria	39
App	pendix 4. AMSTAR-2 Appraisal Checklist	41

List of acronyms

- AB Ayushman Bharat
- AMSTAR A MeaSurement Tool to Assess systematic Reviews
- ANM Auxiliary Nurse Midwife
- ART Antiretroviral Therapy
- AYUSH Ayurveda, Yoga and Naturopathy, Unani, Siddha And Homeopathy
- CHO Community Health Officer
- CI Confidence Interval
- CPHC Comprehensive Primary Health Care
- GRADE Grading of Recommendations Assessment, Development and Evaluation
- HRH Human Resource for Health
- LMIC Low- and Middle-Income Country
- MCH Maternal and Child Health
- MD Mean Difference
- MLHP Mid Level Health Provider
- NCD Non-Communicable Disease
- NPHW Non-physician Health Worker
- NSHW Non-specialist Health Worker
- PICO Population, Intervention, Comparison, Outcome
- RCT Randomised Controlled Trial
- RR Relative Risk or Risk Ratio
- SHC Sub Health Centres
- UHC Universal Health Coverage

Executive Summary

According to the World Health Organisation (WHO), a mid-level health provider (MLHP) or mid-level health worker (MLHW) is referred to as a health provider who has completed preservice higher education (at least 2-3 years) and who is trained, authorised and regulated to work autonomously, and whose scope of practice may include (but is not restricted to) diagnosis, management and treatment of illness, disease and impairments (including surgery, where appropriately trained), as well as engage in preventive and promotive care.

There is a growing movement for countries to strengthen and/or initiate the use of MLHPs to increase access to services. This rapid policy brief is a review of systematic reviews that sought to understand the role of MLHPs in relation to the 12 service packages covered under India's Comprehensive Primary Health Care reforms linked to Ayushman Bharat. For the purposes of this policy brief report, MLHPs include midwives, nurses, auxiliary nurses, nurse assistants, non-physician clinicians and surgical technicians.

A majority of the evidence from included systematic reviews is from High Income Countries (HIC) and tertiary care centres. Overall studies have largely assessed mortality outcomes in relation to pregnancy and childbirth and infant care services, finding no significant differences in care provided by MLHPs as compared to doctors. The findings from the included studies showed that there is some evidence regarding the beneficial effects, acceptability and feasibility of using MLHPs for pregnancy and childbirth care, communicable and NCDs in low- and middle-income countries (LMICs) but the certainty of evidence is not high or even moderate for many cases. Quality of care, where data was available, was found to be comparable or greater for care delivered by MLHPs versus doctors. Systematic reviews did not report on whether MLHPs improve access to care. Further, systematic review evidence is lacking for the role of MLHPs in relation to reproductive services beyond abortion care, mental health conditions beyond perinatal depression, childhood and adolescent health, elderly and palliative care, oral health care, ophthalmic and ENT condition, and emergency medical services.

Given their shorter durations of training, and lower salaries, deployment of MLHPs may viewed, in the short term as an option in areas lacking physicians. Further studies are required to look at the cost-effectiveness and equity dimensions of primary health care services provided by MLHPs.

1.Background

Internationally, majority of the countries' health care services, particularly in LMIC are provided by cadres not trained as physicians or surgeons, but capable of performing several diagnostic and clinical functions. They are variously referred to as substitute health workers, auxiliaries, non-physician clinicians, or mid-level health providers (MLHPs), and include cadres such as clinical officers, medical assistants, physician assistants, nurse practitioners, surgical technicians, community health workers etc. Currently, there is no consensus on the official definition of MLHPs. (1)

According to the World Health Organisation (WHO), a MLHP is referred to as "a health provider who is trained, authorised and regulated to work autonomously, receives preservice training at a higher education institution for at least 2-3 years and whose scope of practice includes (but is not restricted to) being able to diagnose, manage and treat illness, disease and impairments (including perform surgery, where appropriately trained), prescribe medicines, as well as engage in preventive and promotive care". (1, p.8) Mid-level health providers are currently being used in high- and low-income countries to assist professionals and/or to render services independently, particularly in rural health centres and district hospitals, making up for the scarcity or absence of health professionals.

Evidence related to MLHPs showed that they improved access to and coverage of health services, and that often well trained and motivated MLHPs provide superior quality and more accessible services than better qualified but less motivated professionals; however, here is a lack of sufficient evidence on cost-effectiveness. (1) There is evidence to show that the shorter duration of training, and lower salaries, make the deployment of MLHPs cheaper than doctors.

An important challenge that India faces is that people continue to use health care services in secondary and tertiary care settings, for conditions which can be managed at the primary care level. The MLHP according to the CPHC guidelines is defined as "a BSc. in Community Health or a Nurse (GNM or B.SC) or an Ayurveda practitioner, trained and certified through IGNOU/other State Public Health/Medical Universities for a set of competencies in delivering public health and primary health care services".(2) The MLHPs could help in promoting and continuing to provide primary health care via the health and wellness centres, under Ayushman Bharat programme. These centres could be led by nurse practitioners, auxiliary nurse midwives or clinical officers, with a short period of training who can aid doctors. India contributes to more than two-thirds of the global burden of NCDs and other diseases, and therefore, the role of the MLHPs becomes even more important. The WHO recommends task shifting as a strategy to optimise health worker roles to improve access and to provide and deliver health care services.

As India advances on the path towards integrating MLHPs in service delivery across 12 packages of care under its Comprehensive Primary Health Care Programme, this process might be enhanced and made more efficient through an understanding of the global evidence and experiences related to the utilisation of this human resource. The programme

is already underway, and to enable relatively rapid decision-making on MLHPs, we carried out a rapid evidence synthesis to determine the effectiveness of MLHPs in improving clinical and quality of care outcomes related to PHC.

A **rapid review** synthesises findings and assess the validity of research evidence using streamlined systematic review methods to generate evidence within a short timeframe.

A **rapid policy brief** presents a summary of the best available evidence in a synthesised and contextualised manner that is tailored to address and meet decision makers' requirements. A rapid policy brief mostly incorporates findings from existing systematic reviews

Rapid review or rapid policy brief methodology is an emergent research methodology with no consensus yet on what represents best practice for these types of rapid evidence syntheses products. For example, limiting the number of electronic databases for searching evidence or excluding studies published in languages other than English could introduce an element of bias. An evidence-based policy brief or a rapid review differs from a full systematic review in that the scope is specific and clearly defined and some of the traditional systematic review method steps are streamlined or skipped in order to synthesize evidence within a short timeframe. An evidence-informed policy brief does not present a comprehensive assessment of knowledge on the topic.

This rapid policy brief represents a comprehensive summary of the available literature, taking into consideration the timeframe available for the conduct of the review. As a rapid evidence synthesis product, this policy brief considered only systematic reviews (SRs), meta-analyses, and umbrella reviews or overviews of systematic reviews identifying relevant international scientific evidence and that provided a LMIC perspective. Assessing relevance to LMICs is difficult at times, and the evidence from high-income countries may not be directly generalisable to LMICs at all times. Therefore, the evidence included in the policy brief has been aligned as much as possible to LMIC context, which may be generalisable to the Indian health care context.

2. Methods

This section describes the methods used in the development of the policy brief report.

Inclusion Criteria (PICOS)

Type of participants

Studies on MLHPs involved in the delivery of health care service were included. For the purposes of this policy brief, MLHPs included midwives, nurses, auxiliary nurses, nurse assistants, non-physician clinicians and surgical technicians.

Type of comparisons:

The following comparisons for MLHPs providing health care services (preventive, promotive or curative) and quality of care were included:

- a. MLHPs versus Doctors
- b. Different types of MLHPs

Types of outcome measures

- a. Healthcare and clinical outcomes such as mortality, morbidity, outcomes associated with care delivery, health status and physiological measures (e.g. blood sugar levels).
- b. Access to care
- c. Quality of care, including patient or client satisfaction with care received

Type of studies

Systematic reviews, overviews of systematic reviews, and meta-analyses.

Setting:

International evidence, with a perspective on LMICs, specifically for India.

Search methods

The search was limited to published and indexed articles involving human subjects, and those available in the English language. The following databases were searched for the relevant studies of interest.

- Cochrane Database of Systematic Reviews
- Medline (PubMed)
- EMBASE
- Health Systems Evidence
- CINAHL

Broad search terms such as 'mid-level health providers' (title or abstract) and 'systematic review' (article type) were utilised. The analysis examined relevant and available synthesised research papers in online search databases, using a list of health and human resources-related keywords. Box 1 provides a comprehensive list of search terms utilised in various search databases. Detailed search strategies are provided in Appendix 1 for each database.

Box 1: Comprehensive list of search terms utilised in various databases

a. Nurse OR nurses OR physician assistant OR mid-level provider OR midwife OR midwives OR nurse practitioner OR nurse practitioners OR non-physician OR non-physicians OR substitute health worker OR substitute health workers OR auxiliary OR auxiliaries OR mid-level cadres OR auxiliary nurse OR auxiliary nurses OR nurse assistant OR nurse assistants OR non-physician clinician OR non-physician clinicians OR surgical technician OR surgical technicians OR clinical officer OR clinical officers OR medical assistant OR medical assistants OR physician assistant OR physician assistants OR alternative cadre OR alternative cadres OR health care assistant OR health care assistants OR allied health personnel OR psychiatric aide OR psychiatric aides OR task shift OR task shifting

b. low and middle income countr* OR LMIC OR developing countr* OR third world c. Systematic review OR Systematic reviews OR umbrella review OR umbrella reviews OR meta-analysis OR meta-analyses

Data collection and analysis

Selection of studies

The titles and abstracts of studies for inclusion were screened, which then enabled retrieval of full texts of eligible studies for full text examination and selection. The primary reviewer independently applied the inclusion criteria to the retrieved publications. Due to this being a rapid policy brief, study selection was streamlined considering the shorter timeframe. For each domain of interest, only one SR was considered and included, the selection of which was based on the comprehensiveness and recency of the published review.

Assessment of risk of bias in included studies

Each SR was independently assessed for methodological quality by the lead author using established standardised criteria (AMSTAR 2 checklist). (3)

Data extraction and management

Data from included reviews was extracted using a standardised template. A primary reviewer independently extracted all relevant outcome data, with random verification of the data by secondary reviewer. The data of interest included:

- a. Review type
- b. Question/focus of review
- c. Countries where studies were conducted
- d. Number of studies in review
- e. Participants (number, age group) and details of setting
- f. Intervention and Outcome measures
- g. Conclusions of review.

Data Synthesis

Relevant outcome data was extracted and tabulated from selected reviews. A narrative summary is presented to address the review questions and document relevant data and findings.

Summary of findings

Summary of findings tables were used to record the results from the SRs, including the outcomes and related effect sizes (relative risks and mean differences). In addition, GRADE study considerations were used to assess the certainty of the evidence and summarise the confidence in the effects of the interventions by outcomes across studies (please see Appendix 2 for the GRADE evidence ratings). The following outcomes were included in the 'Summary of findings' tables: mortality, clinical outcomes (postpartum haemorrhage, virologic response to ART), outcomes associated with care delivery (rate of performing caesarean sections, preterm births, admission to neonatal intensive care, use of intrapartum regional analgesia, initiation and maintenance of ART for HIV/AIDS care), systolic blood

pressure, glycated haemoglobin, low-density lipoprotein, patient satisfaction, and health-related quality of life. Decisions to justify to downgrade or upgrade the certainty of evidence using footnotes were documented.

3. Results

Description of studies

Search Results and Study Selection

Searches of all mentioned databases were conducted in March 2019. The searched identified 5171 studies, and 141 duplicates were removed (Figure 1 – PRISMA flow diagram). The lead author selected potentially relevant studies by scanning the titles and abstracts, and irrelevant studies were discarded. Full text articles were obtained for 30 potentially relevant studies. The studies were reviewed for relevance for each domain of interest, and the inclusion and exclusion criteria were applied for the full texts as well. In cases where there were multiple SRs for the same domain, the SR that was the most recent and provided comprehensive information was selected and included. Any disagreements were resolved by discussion.

Characteristics of included systematic reviews

A snapshot of the available evidence is provided in Table 1. The descriptive characteristics of included SRs are summarised in Table 2. Overall, seven systematic reviews were included in the rapid policy brief report. All systematic reviews, except one (Lassi et al 2013) included majority of the studies conducted in LMICs. The studies related to HIV/AIDS were mostly conducted in sub-Saharan African countries. Most studies compared care provided by midwives or auxiliary nurse midwives or nurses with that provided by doctors working in a team along with midwives or nurses. Most of the studies included in the systematic reviews were RCTs, with some quasi-experimental study designs and observational studies.

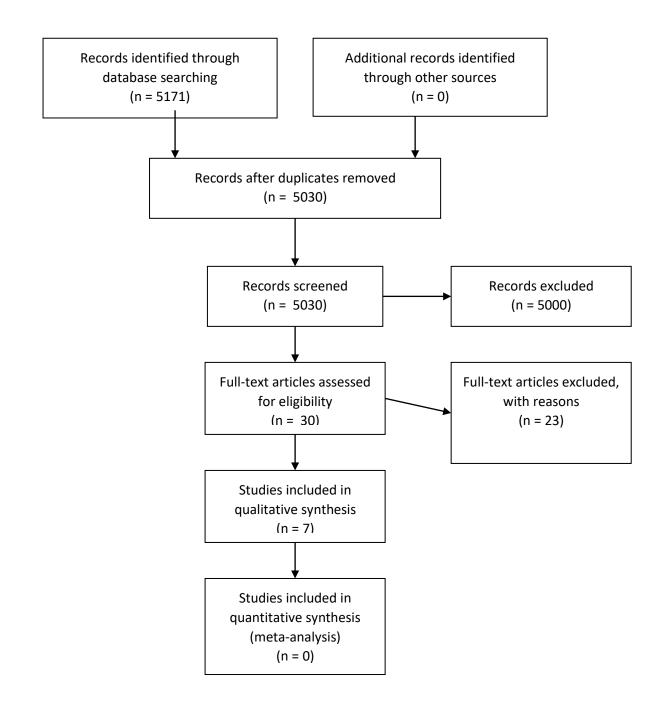


Table 1. A snapshot of the best available evidence

Systematic review (SR)	Healthcare domain	Number of studies included in the systematic review	Countries where studies were conducted
Barnard et al 2015	Family planning, contraceptive and other reproductive health care services	Eight studies; three RCTs and five cohort studies	India, Nepal, South Africa, Sweden, Vietnam and USA
Chowdhary et al 2014	Mental health - perinatal depression	Nine studies; seven RCTs, and two observational studies	Chile, China, Jamaica, India, Pakistan, South Africa and Turkey
Joshi et al 2014	NCDs - management and prevention of most of the NCDs	22 studies; Seven RCTs, and 15 observational studies	Cameroon, China, Ethiopia, Kenya, India, Pakistan, Philippines, South Africa, Tanzania and Zimbabwe
Kredo et al 2014	Communicable diseases – mainly HIV/AIDS	Ten studies; 4/10 RCTs, and six observational studies	Ethiopia, Mozambique, South Africa, Swaziland, Uganda
Lassi et a 2013	Mainly Pregnancy and childbirth, and neonatal and infant health services	Fifty-three studies; 47 RCTs, and six observational studies	Australia, Malawi, Mozambique, Nepal, Netherlands, Philippines, Sweden, Tanzania, Thailand, UK, and USA
Mdege et al 2013	Communicable diseases – ART initiation and maintenance	Six studies; five Cluster- RCTs, and one observational study	Kenya, Rwanda South Africa, and Uganda
Weeks et al 2016	NCDs – prescribing for management of most NCDs	Forty-six studies; 44 RCTs, and two observational studies	Australia, Canada, Colombia, Ireland, Netherlands, South Africa, Thailand, Uganda, UK, and USA

Table 2. Description of Included Studies

Review citation and details	Question/focus of the Review	Review and Demographic characteristics	Interventions & Outcome measure(s)	Brief finding/s and conclusion
Barnard et al	Evaluation of safety and	Eight studies (RCTs and cohort	Any type of abortion procedure	The risk of failure or incomplete
2015	effectiveness of surgical	studies) involving 22,018	provided by either doctors or	abortion was higher among
	abortion procedures, and	participants. The surgical	MLHPs in any setting. Mid-level	women who had a surgical
	medical abortion	abortion studies out in the	providers included nurses,	abortion (RR2.25; 95% CI: 1.38
	procedures administered by	United States, India, South	nurse practitioners, ayurvedic	to 3.68) procedure provided by a
	MLHPs compared to	Africa and Vietnam. The medical	practitioners, physician	MLHP. However, MLHPs can
	doctors.	abortion studies were carried	assistants, midwives, auxiliary	provide medical abortion safely
		out in India, Sweden and Nepal.	nurse midwives and certified	and effectively (RR 0.81; 95% CI:
		The studies included women	nurse midwives. Mid-level	0.48 to 1.36), as doctors.
		with gestational ages up to 14	providers worked	
		weeks for surgical abortion and	independently when carrying	For surgical abortion procedures,
		nine weeks for medical	out the abortion procedure.	there were no significant
		abortion.		differences in the risk of
			Outcomes: Failure/incomplete	complications between MLHPs
			abortion, including continuing	and doctors (RR 0.99; 95% CI:
			pregnancy at follow-up and	0.17 to 5.70). For surgical
			incomplete abortion.	abortion, the proportion of total
			Complications of abortion,	complications among women
			including haematometra,	who had a procedure
			haemorrhage, endocervical	administered by a MLHW was
			injury, anaesthesia-related	1.9%, when compared to
			reactions, uterine perforation,	procedure provided by a
			infection, injury to bowel, any	physician (1.3%).
			complication requiring blood	
			transfusion and any	The findings from this review are
			complication requiring	only applicable to pregnancies
			hospitalisation.	up to nine weeks for medical

Review citation and details	Question/focus of the Review	Review and Demographic characteristics	Interventions & Outcome measure(s)	Brief finding/s and conclusion
Chowdhary et al 2014	Characteristics of the NSHWs, their training and supervision in the treatment of perinatal depression in LMICs.	Nine studies (7/9 were RCTs), with two conducted in South Africa, two in Chile, and one each from China, Jamaica, India, Pakistan and Turkey.	Interventions: Non-specialists health workers who included nurses, midwives and community health workers. Outcomes: perinatal depressive symptoms, physical health of mother and infant, quality of mother—child interaction, infant weight and height, child development and HIV knowledge.	abortion and up to 14 weeks for surgical procedures. Also, the findings from the medical abortion studies cannot be generalised to settings where a misoprostol-only regimen is used to induce abortion and is limited to settings involving the specific regimens used in these studies. The use of NSHWs was effective and feasible to deliver psychological interventions for perinatal depression in LMICs where specialist services are both scarce and expensive, particularly for disadvantaged populations.
Joshi et al 2014	Assessed the effectiveness, cost-effectiveness and barriers to task-shifting for the management and prevention of NCDs in LMICs.	22 studies - Seven were RCTs, and the remaining were beforeafter studies. Six studies were conducted in Cameroon, six in India, two in South Africa and one each in China, Ethiopia, Kenya, Pakistan, Philippines, Tanzania and Zimbabwe. Nine	Seven studies involved task-shifting for the management of hypertension and cardiovascular diseases, five for diabetes, six for mental health, four for neurological conditions, two each for the screening and	Trained NPHWs successfully screened individuals in the community for various NCDs such as asthma, cancer, cardiovascular disease, hypertension, diabetes, depression and epilepsy.

Review citation and details	Question/focus of the Review	Review and Demographic characteristics	Interventions & Outcome measure(s)	Brief finding/s and conclusion	
		studies were based in rural regions, six in urban and seven included both rural and urban regions.	management of respiratory diseases and five for the screening of cancers. Tasks were shifted from physicians to midwives, nurses, or health workers.	Studies which permitted NPHWs to prescribe drugs showed that trained NPHWs can effectively treat patients according to study protocols for conditions such as asthma, hypertension, diabetes, depression and epilepsy.	
Kredo et al 2014	Evaluated the quality of care of initiation and maintenance of HIV/AIDS therapy in HIV care models that task shift care from doctors to non-doctors.	Ten studies were included in this review. Four out of 10 were RCTs, two were prospective cohorts, while four were retrospective cohort Studies. One study, was conducted in urban, peri-urban and rural settings in Ethiopia, two studies were conducted in urban and rural Uganda, one in urban Uganda, one in urban Mozambique, one in rural Swaziland while the remaining four studies were conducted in various urban, peri-urban and rural settings in South Africa.	A model of care that involved the initiation or maintenance of ART by another cadre of health worker other than a doctor. Outcomes: quality of care, time to initiation, virologic and immunologic response, and cost	There was no difference in death at one year when nurses initiated and provided follow-up HIV therapy (RR 0.96; 95% CI 0.82 to 1.12). The model of care included specific training and organisational support for professional nurse practitioners prescribing and following up ART for newly initiated patients. Further, there was evidence that task shifting of ART maintenance care from doctors to nurses showed no difference in death at one year.	
Lassi et a 2013	Assessment of effectiveness of care provided by MLHPs in delivering to the general population health-care services that are associated with the achievement of MDGs on health and	Fifty-three studies, mostly conducted in high-income countries (Australia, USA, Netherlands, Sweden and UK) and conducted at tertiary care facilities. Some studies conducted in LMICs such as	A MLHW who is a health-care provider who is not a medical doctor or physician but who provides clinical care in the community or at a primary care facility or hospital. Included midwives, nurses, auxiliary	There was no significant difference in the antenatal hospitalisation rate was found between care provided by midwives alone and that provided by doctors working with midwives (RR: 0.95; 95% CI:	

Review citation and details	Question/focus of the Review	Review and Demographic characteristics	Interventions & Outcome measure(s)	Brief finding/s and conclusion
	nutrition or with the management of NCDs. Compared the effectiveness of: different kinds of MLPs; MLHPs and doctors or community health workers; and (iii) MLPs working alone or in a team.	Nepal, Thailand, Malawi, Tanzania, Mozambique and Philippines. Most studies compared either care provided by midwives with that provided by doctors working in a team along with midwives or care provided by nurses with that provided by doctors. Studies conducted in Africa compared care delivered by clinical officers, surgical technicians or non-physician clinicians with that delivered by doctors.	nurses, nurse assistants, non-physician clinicians and surgical technicians The main health-care outcomes: morbidity, mortality, outcomes associated with care delivery, health status, quality of life, service utilization and the patient's satisfaction with care.	0.79–1.13). However, the absence of intrapartum analgesia was more likely with care from midwives alone (RR: 1.13; 95% CI: 0.96–1.33). Further, there was no significant difference in rates for the instrumental delivery or caesarean section (RR: 0.94; 95% CI: 0.83–1.06). The postpartum haemorrhage rate (RR 0.53; 95% CI: 0.25–1.14) was not significantly lower with care from midwives alone and there was no significant difference between the groups in the rate of foetal or neonatal death (RR 0.94; 95% CI: 0.56–1.58).
Mdege et al 2013	Evaluated effectiveness, costs and cost-effectiveness of task-shifting models in managing ART.	Six studies which included a total of 19,767 participants: four Cluster-RCT, one RCT and one non-randomised study. Tasks were shifted from health care professionals to lay health workers in four studies; and from doctors to nurses. Studies were conducted in Uganda, Kenya, South Africa, and Rwanda.	Intervention: Any task-shifting model. Outcomes: mortality; occurrence of new AIDS-defining illness; virological outcomes; CD4 cell count; and adherence to ART medicines.	Overall, in the studies that evaluated task-shifting from doctors to nurses, the task-shifting models were not inferior on mortality, virologic outcomes, CD4 cell count, loss to follow-up and adverse events.

Review citation and details	Question/focus of the Review	Review and Demographic characteristics	Interventions & Outcome measure(s)	Brief finding/s and conclusion
Weeks et al 2016	Examined evidence on the clinical, patient-reported and resource use outcomes of non-medical prescribing in primary and secondary care settings compared with medical prescribing (usual care).	Forty-six studies (37,337 participants); non-medical prescribing was undertaken by nurses in 26 studies and pharmacists in 20 studies.	Intervention: Non-medical prescribing to cover prescribing of medicines by a broad range of healthcare providers other than medical doctors, and prescribing in primary or secondary care. Outcome: Clinical surrogate markers for chronic disease (systolic blood pressure, glycated haemoglobin, and lowdensity lipoprotein)	Meta-analysis of surrogate markers of chronic disease (systolic blood pressure, glycated haemoglobin, and lowdensity lipoprotein) reported significant positive intervention group effects for blood pressure at 12 months (MD -5.31 mmHg, 95% Cl) -6.46 to -4.16), lowdensity lipoprotein (MD -0.21, 95% Cl -0.29 to -0.14), and glycated haemoglobin management at 12 months (MD -0.62, 95% Cl 0.85 to -0.38).

Excluded studies

Twenty three SRs were excluded following full text examination. A list of the excluded SRs is provided in Appendix 3. The remaining seven SRs were appraised for methodological quality; however, it was agreed apriori that none of the reviews would be excluded based on critical appraisal.

Methodological quality of included SRs

Systematic reviews included in the report were appraised with the AMSTAR checklist (Appendix 4). The AMSTAR tool consists of a 16-item questionnaire and requires reviewers to respond with 'yes', 'no', or 'partial yes'. Six out of seven systematic reviews were of moderate to high methodological quality and well reported; however, there was no reference to an priori protocol and publication bias was not assessed. One systematic review by Chaudhary et al (2014) was of poor quality, as assessed by the checklist. However, this SR was included as this was the only review identified for the mental health domain.

 Table 3: Critical appraisal results of included systematic reviews assessed using the AMSTAR-2 checklist (see Appendix 4).

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Total
Lassi et al 2013	Υ	N	Υ	PY	N	Υ	N	Υ	Υ	Υ	Υ	Υ	Υ	N	N	Υ	10/16
Barnard et al 2015	Υ	N	Υ	Υ	Ν	Υ	Υ	Υ	Y	N	Υ	Υ	Υ	Υ	Υ	Υ	13/16
Kredo et al 2014	Y	Y	Υ	Υ	Y	Υ	Υ	Υ	Υ	N	Υ	Υ	Υ	Υ	Υ	Υ	15/16
Mdege et al 2013	Υ	PY	Y	Y	Y	Υ	N	Υ	Υ	N	N	N	Υ	Υ	N	Υ	10/16
Joshi et al 2014	Υ	Y	Υ	PY	Y	Υ	N	Υ	PY	Y	N	N	Υ	N	N	Υ	9/16
Weeks et al 2016	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Υ	16/16
Chowdhary et al 2014	Υ	N	Y	PY	N	N	N	Υ	PY	Y	N	N	N	N	N	Υ	5/16

Y- Yes

N-No

PY – Partial Yes

4. Summary of findings tables for each domain of interest

MLHPs for care in pregnancy and child-birth (6)

Population: Patients receiving pregnancy and childbirth services including antenatal care

Settings: Primary health care setting in low- and middle-income country

Intervention: Doctor versus nurse/auxiliary nurse or midwife or auxiliary midwife or clinical officer

	Outcomes	Relative	No of	Certainty of	Plain Language Summary
		effect	participants	the	
		(95% CI)		evidence	
				(GRADE)	
	Midwives alone versus doctors along w	ith midwives			
	Rate of performing caesarean sections	RR 0.94	12144	$\Theta\Theta\bigcirc\bigcirc$	Pregnancy care provided by midwives may slightly reduce the
(s)		(0.81 to	(8 RCTs)	Low ¹	rate of performing caesarean sections (low certainty
(RCTs)		1.06)			evidence).
l) sl					
Trials	Postpartum haemorrhage	RR 0.53	8604	$\Theta\Theta\bigcirc\bigcirc$	Pregnancy care provided by midwives may reduce postpartum
		(0.25 to	(6 RCTs)	Low ^{1,2}	haemorrhage (low certainty evidence)
<u> </u>		1.14)			
Controlled	Preterm births	RR 0.87	9210	$\Theta\Theta\bigcirc\bigcirc$	Pregnancy care provided by midwives may slightly reduce
_		(0.73 to	(5 RCTs)	Low ¹	preterm births slightly (low certainty evidence)
nise		1.04)			
Randomised	Use of intrapartum regional analgesia	RR 0.87	9415	$\Theta\Theta\bigcirc\bigcirc$	Pregnancy care provided by midwives may slightly reduce use
Ran		(0.81 to	(8 RCTs)	Low ¹	of intrapartum regional analgesia (low certainty evidence)
		0.93)			

	Episiotomies	RR 0.85	13205	$\Theta\Theta\bigcirc\bigcirc$	Pregnancy care provided by midwives alone may slightly
		(0.78 to 0.92)	(8 RCTs)	Low ¹	reduce in episiotomies (low certainty evidence)
	Quality of Care (QoC)	RR 1.23 (1.10 to 1.37)	826 (1 RCT)	⊕⊕○○ Low ^{1,3}	Pregnancy care provided by midwives may slightly improve quality of care (low certainty evidence)
	Mortality and Access to care	-	-	1	No studies were found that examined these outcomes
	Auxiliary nurse midwives versus doctors	S			
	Incomplete abortion	RR 0.93 (0.45 to 1.90)	1032 (1 RCT)	⊕⊕○○ Low ^{1,3}	Pregnancy care provided by auxiliary nurse midwives may make little or no difference in likelihood of an incomplete abortion (low certainty evidence)
RCTs	Complications during conduct of manual vacuum aspiration	RR 3.07 (0.16 to 59.1)	2789 (1 RCT)	⊕⊕⊖ Low ^{1,3}	Pregnancy care provided by auxiliary nurse midwives may make little or no difference in complications during manual vacuum aspiration. However, the wide 95% confidence interval includes the possibility of both increased and reduced complications (low certainty evidence)
	Post-operative adverse event	RR 1.36 (0.54 to 3.40)	2761 (1 RCT)	⊕⊕○○ Low ^{1,3}	Pregnancy care provided by auxiliary nurse midwives may increase post-operative adverse events, however the 95% confidence interval includes the possibility of both increased and reduced postoperative adverse events (low certainty evidence)
	Clinical officers versus doctors	1			·
onal	Likelihood of early neonatal death	RR 1.40 (0.51 to 3.87)	(1 observational study)	⊕○○○ Very low⁴	It is uncertain whether pregnancy care provided by clinical officers reduces the likelihood of early neonatal death as the certainty of the evidence has been assessed to be very low
Observational studies	Postoperative maternal health outcomes, such as fever, wound infection, the need for re-operation and maternal death, after emergency obstetric procedures	RR 0.99 (0.95 to 1.03)	(1 observational study)	⊕○○○ Very low ⁴	It is uncertain whether pregnancy care provided by clinical officers reduces effect on postoperative maternal health outcomes as the certainty of the evidence was assessed to be very low

¹Downgraded one level due to serious risk of bias and another two levels due to indirectness (almost all the studies were conducted in tertiary care centres and high income countries)

²Downgraded one level due to serious inconsistency (considerable heterogeneity was found)

³Downgraded one level due imprecision (single study with a small sample size yielding wide confidence intervals spanning line of no effect)

⁴Quality of evidence was downgraded from Low (observational study design) to Very low due to very serious risk of bias.

MLHPs for neonatal and infant health care services (6)

Midwives versus obstetrician or doctor in team with midwives

Population: Patients receiving neonatal and infant health services

Settings Primary health care setting in low and middle income country Intervention: Doctor versus nurse/auxiliary nurse or midwife or auxiliary midwife or clinical officers.

	Outcomes	Relative effect	No of	Certainty of	Plain Language Summary
		(95% CI)	participants	the evidence	
				(GRADE)	
	Foetal or neonatal death	RR 0.94	11562	$\Theta\Theta\bigcirc\bigcirc$	Care provided by midwives alone may result in little to no
		(0.56 to 1.58)	(6 RCTs)	Low ¹	difference in foetal or neonatal deaths (low certainty
RCTs					evidence)
	Clinical outcomes;	-	-	-	No studies were found that examined these outcomes
	Quality of care & Access to care				

¹Downgraded one level due to serious risk of bias and two levels due to indirectness (almost all the studies were conducted in tertiary care centres)

MLHPs for family planning, contraceptive and other reproductive health care services (7)

Nurses, midwives, doctor assistants, and physician assistants versus doctors

Population: Patients requesting abortion procedures

Settings: Primary health care setting in low- and middle-income country

Intervention: Surgical abortion administered by MLHPs/Medical abortion administered by MLHPs Comparison: Surgical abortion administered by doctors/Medical abortion administered by doctors

	Outcomes	Relative effect (95% CI)	No of participants	Certainty of the evidence	Plain Language Summary
	Consider the ortion representation			(GRADE)	
	Surgical abortion procedures				
	Failure/incomplete abortion	RR 2.97	2789 (2 RCTs)	$\Theta\Theta\bigcirc\bigcirc$	Care provided by MLHPs may increase the chance of
		(0.21 to		Low ¹	the abortion being ineffective or incomplete (more
		41.82)			than twice the risk of failure or incomplete abortion
					for surgical abortion procedures provided by MLHPs
					when compared to the procedures provided by
					doctors) (low certainty evidence)
RCTs	Complications	RR 0.99	2789	$\Theta\ThetaOO$	Care provided by MLHPs may make little or no
RC		(0.17 to 5.7)	(2 RCTs)	Low ¹	difference in complications (low certainty evidence)
	Total complications*	RR 3.07	2789	$\Theta\ThetaOO$	Care provided by MLHPs may increase total
		(0.16 to	(2 RCTs)	Low ¹	complications. However, the wide 95% confidence
		59.08)			interval includes the possibility of both increased and
					reduced risk of total complications (low certainty
					evidence)

	Failure/incomplete abortion	RR 2.2	13,715	B OOO	It is uncertain as to whether care provided by MLHPs
studies		(1.34 to 3.6)	(3 observational studies)	Very low ^{1,2}	reduces the risk of failure of incomplete abortion as the certainty of the evidence has been assessed as very low.
Observational studies	Complications	RR 1.38 (0.7 to 2.72)	13,715 (3 observational studies)	⊕○○○ Very low ^{1,2,3}	It is very uncertain whether care provided by MLHPs reduces complications as the certainty of the evidence has been assessed as very low
J	Total complications*	RR 1.36 (0.86 to 2.14)	16,173 (4 observational studies)	Very low ^{1,2,3}	It is very uncertain about the effect of care provided by MLHPs on the risk of total complications.
	Mortality; Quality of Care; and Access to care	-	-	-	No studies were found that examined these outcomes
	Medical abortion procedures				
RCTs	Failure/ incomplete abortion	RR 0.81 (0.48 to 1.36)	1892 (2RCTs)	⊕⊕⊕○ Moderate	Care provided by MLHPs may slightly reduce the risk of failure/ incomplete medical abortion when compared with that provided by doctors (moderate certainty evidence)
Observational studies	Failure/incomplete abortion	RR 1.09 (0.63 to 1.88)	1164 (1 study)	Very low ^{1,2,3}	It is very uncertain about the effect of care provided by MLHPs on failure/incomplete abortion as the quality/certainty of the evidence has been assessed as very low
	Mortality; Quality of Care; and Access to care	-	-	-	No studies were found that examined these outcomes.

^{*}Total complications - incomplete or failed abortion and complications

¹Downgraded one level due to imprecision and additional one level due to indirectness

²Downgraded two levels due to risk of bias and one level for imprecision (wide confidence intervals)

MLHPs for communicable diseases (8,9)

Nurses or Clinical Officers versus Doctors

Population: HIV-infected patients

Settings: Primary health care setting in Low and middle income countries Intervention: Nurse or clinical officer for initiation and maintenance of ART

Comparison: Doctor for initiation and maintenance of ART

	Outcomes	Relative effect	No of	Certainty of	Plain Language Summary
		(95% CI)	participants	the evidence	
				(GRADE)	
	Initiation and Maintenance of ART	RR 0.96	2770	⊕⊕⊕⊕High	Initiation and maintenance of ART by a nurse or
	Mortality	(0.82 to 1.12)	(1 RCT)		a clinical officer slightly reduces mortality (high
10	Follow-up: 12 months				certainty evidence)
RCTs	Maintenance of ART	RR 0.89	4332	$\Theta\Theta\Theta$	Maintenance of ART by a nurse or a clinical
<u> </u>	Death	(0.59 to 1.32)	(2 RCTs)	Moderate ¹	officer makes little or no difference in mortality
	Follow-up: 12 months				when ART had previously been initiated by a
					doctor (moderate quality/certainty evidence)
6	Initiation and Maintenance of ART	RR 1.23	39160	ФФОО	Evidence suggests that there may be an
die	Death	(1.14 to 1.33)	(2	Low ²	increased risk of death when ART is initiated
stu	Follow-up: 12 months		observational		and maintained by a nurse or a clinical officer
nal			studies)		when compared to a doctor's care (low
atio					certainty evidence)
Observational studies	Maintenance of ART	RR 0.19	2772	ФООО	It is uncertain whether nurse-led care reduced
SqC	Death	(0.05 to 0.78)	(1 study)	Very low ³	mortality as the quality/certainty of the
0	Follow-up: 12 months				evidence has been assessed as very low

³Downgraded one level due to serious risk of bias

Quality of care and Access to care	-	-	-	No studies were found that examined these
				outcomes

¹Downgraded by one level for imprecision due to a wide confidence interval

MLHPs for non-communicable diseases (10,11)

Non-medical (non-physician health workers (NPHWs) (nurses, pharmacists, allied health professionals, and physician assistants) prescribing compared to medical (doctors) prescribing for chronic disease management in primary care

Population: Patients with non-communicable diseases

Settings: Secondary care and ambulatory/primary care in low-and middle income countries

Intervention: Prescribing by non-physician (doctor) health worker

Comparison: Prescribing by medical doctor

	Outcomes	Mean Difference (MD) (95% CI)	No of participants	Certainty of the evidence (GRADE)	Plain Language Summary
RCTs	Systolic blood pressure (mmHg) at 12 months	MD -5.31 mmHg lower (-6.46 to - 4.16 lower)	4229 (12 RCTs)	⊕⊕⊕⊕ High	Chronic disease management by non-medical prescribers probably reduces systolic blood pressure (high certainty evidence)
	Glycated haemoglobin (HbA1c, %) at 12 Months	MD -0.62 (-0.85 to -0.38)	775 (6 RCTs)	⊕⊕⊕⊕ High	Chronic disease management by non-medical prescribers reduces the glycated haemoglobin levels (high certainty evidence)

²Rated low because of observational study designs. Not downgraded for risk of bias

³Downgraded by one level for imprecision due to low event numbers

Low-density lipoprotein	MD -0.21 (-0.29	1469	ФФФО	Chronic disease management by non-medical
(mmol/L) at 12 months	to -0.14)	(7 RCTs)	Moderate ¹	prescribers probably reduces low-density
				lipoprotein levels (moderate certainty evidence)
Health-related quality	MD 1.17	2385	$\Theta\Theta\Theta$	Chronic disease management by non-medical
of life measured with	(0.16 to 2.17)	(8 RCTs)	Moderate ²	prescribers probably improves the health-related
SF-12/36 – Physical component				quality of life (moderate certainty evidence)
Health-related quality	MD 0.58	2246	ФФФО	Chronic disease management by non-medical
of life measured with	(-0.40 to 1.55)	(6 RCTs)	Moderate ^{1,2}	prescribers probably reduces health-related quality
SF-12/36 – Mental component				of life (mental component) (moderate certainty evidence)
Mortality	-	-	-	No studies were found that examined this outcome
Access to care	-	-	-	Several studies reported improved access to healthcare at the community level, although the metric to evaluate access was often not described. Data was not reported and the evidence was not assessed according to GRADE criteria.

¹Downgraded one level due to serious inconsistency (considerable heterogeneity was found)

MLHPs for mental health (12)

Non-specialist health workers (NSHWs) (midwives, nurses and community health workers) versus mental health specialists

Population: Women with perinatal depression

Settings: Primary care in low-and middle income countries

Intervention: Non-specialists health workers (midwives, nurses and community health workers)

Comparison: Mental health specialists

²Downgraded one level due to indirectness (prescribing component effect on quality of life difficult to determine)

	Outcomes	Impact	No of	Certainty	Plain Language Summary
			participants	of the	
				evidence	
				(GRADE)	
	Perinatal depression assessed	All nine studies reported	14555	-	Only narrative synthesis was conducted for
	using Edinburgh Postnatal	statistically significant	(9 RCTs)		the systematic review and no pooled
	Depression Scale (EPDS), the	improvements in perinatal			estimate was available. The results
	Center for Epidemiological	depression in the intervention			suggested that NSHWs can feasibly provide
	Studies Depression Scale (CES-	groups compared with control			mental health services leading to
RCTs	D), Beck Depression Inventory	groups. The estimates were			improvement in perinatal depression
<u> </u>	(BDI), the General Health	presented differently for different			scores, particularly in low-resource settings
	Questionnaire (GHQ), Hamilton	measurement scales and at			where specialist services are both scarce
	Depression Rating Scale (HDRS)	different follow up periods.			and expensive. Certainty of evidence by
	Follow up: range 6 weeks to 3				GRADE was not assessed for it due to
	years				paucity of information in the published SR.
	Mortality; Quality of care and	-	-	-	No studies were found that examined
	Access to care				these outcomes

No systematic reviews assessed the role of MLHPs in the provision of following health services.

MLHPs for childhood and adolescent health services

MLHPs for ophthalmic and ENT conditions

MLHPs for elderly and palliative health care

MLHPs for emergency medical services

5. Implementation considerations in India

In a developing country like India, there is little information available on relevant strategies for implementation of universal healthcare policies and provision of equitable health care distribution. Thus, in addition to the review, we scoped out the literature on "mid-level health providers" (MLHPs) and "rural medical practitioners" in India. A study in Chhattisgarh assessing the clinical competence of non-physician clinicians and physicians in delivery of primary health-care services found comparable levels of competency.(11) Another study in India concluded that physicians and nonphysician clinicians performed similarly in terms of patient satisfaction, trust and perceived quality.(12) A 3-year rural health practitioner course developed and implemented to select, train and deploy a Rural Health Practitioners (RMPs, a type of MLHP) in sub centres in Assam resulted in significant improvements in the quantum and the range of services delivered.(13) Successful implementation of this program was possible due to the early inclusion of various stakeholders who had interests in the three-year course, which included the Indian Medical Association (IMA) and the students themselves (with a desire to be given appropriate status as medical doctors).

How could other Indian states go about achieving this in light of CPHC reforms? Relevant literature (8,9,14) cites additional strategies and enablers to be in place, summarised in Table 1.

Table 1. Barriers and enablers for implementation of MLHPs in India

Barrier	Strategies to address each barrier
Health workforce	Optimise the use of MLHPs shifting tasks from doctors and physicians to
shortage	nurses, midwives and pharmacists, particularly in resource poor settings.
	Provide Continuing Medical Education (CME) to keep the MLHPs updated
	on newer skills and knowledge and to retain them to continue serving in
	rural, remote and poorly resourced areas/settings.
	Engage, consult and work with relevant stakeholders to develop a
	national and state-wide strategy and plan for the training of non-
	physician health cadres.
Inequitable	Develop appropriate skill mix of healthcare cadres.
distribution of	A task-sharing model where physicians or doctors will be available for
health workers	complicated cases, for confirming the diagnosis, initiating and monitoring
	treatment.
Lack of incentives	Develop a career progression path for MLHPs to retain them in the public
for health	health system.
workers to	
expand their roles	
Lack of resources	Provide standardised guidelines for screening and treatment.
and training.	Clarify the roles and tasks of different health providers, and provide a
Inadequate or	clear rationale for the distribution of tasks, and training of MLHPs in new
irregular drug	skills.
supply, and	Provide adequate training through educational materials, educational
unavailability of	meetings, and/or outreach visits.
equipment	

There is a dearth of high-quality studies in this domain, particularly from the LMIC perspective. MLHPs may be an effective alternative for pregnancy and childbirth care, communicable diseases and NCDs management, and perinatal depression management. However, for them to function successfully and to an optimal operative level, several changes are required at the health policy and health systems level. These include but not limited to adequate incentives, scaled up training, provision of standardised protocols, adequate equipment and drug supply, integration of MLHPs as part of a multi-disciplinary team with support from physicians, and consultation with regulatory bodies such as medical and nursing councils. Significant improvements in quality of care and healthcare delivery can be achieved with such systems and supports in place.

6. Strengths and Limitations of the policy brief

The strengths of this rapid policy brief include: the use of standard WHO definition for MLHPs that enabled a comparison of studies globally and that which included LMIC perspectives; a robust, transparent and comprehensive search strategy to identify all relevant SRs; methodological quality assessment of included SRs using a standardised checklist; focus on several healthcare domains of interest that aligned with the CPHC packages that also enabled the identification of knowledge gaps; and informed by the relevant stakeholders at the national and state levels.

In terms of limitations of this policy brief, there were very few studies that rigorously linked health outcomes or health status to these cadres. In fact, there is a much larger evidence base on the role of frontline health workers in delivering primary care. In contrast, for MLHPs, there is a lack of sufficient evidence for several domains. Further, MLHPs as defined by the WHO and in most countries, do not include cadres like Ayurvedic, Homoeopathic, Siddha and other practitioners who are part of the MLHP programme in India; and therefore, this brief cannot speak to their performance or appropriateness in delivering primary care. Reviews included in this policy brief were published between 2013 and 2016. Therefore, this brief is not reflective of primary research evidence that may have emerged since the time original systematic reviews were published, given that our inclusion criteria did not include review of primary studies. The lack of evidence contributes to the continued ambiguity regarding the legitimacy and roles of MLHPs, even in countries where they are widely used and health service delivery actually depends on them.

7. Key take-aways from the National Consultation

In April of 2019, a national consultation was held with representatives of 7 state health system resource centres and four Innovation and Learning Centres affiliated with the ongoing CPHC reforms, as well as academic experts specialising in evidence synthesis to discuss the preliminary findings of the policy brief and feedback received on its improvement and role in health decision-making.

Participants overall were appreciative of the policy brief report and acknowledged the complexity of the work undertaken, as it focussed on several domains of healthcare. However, it was suggested that future policy briefs could more narrowly focus on a particular disease or health domain, covering it more comprehensively. The participants suggested that the report could avoid academic language and be written in a 'plain language summary' style with a clear indication of the quality of the evidence. Based on this, substantial revisions to the brief as well as this supporting documentation have been made, including a 'summary of findings tables' according to the GRADE criteria for each domain of interest. More standardised formats and templates are also being developed, in response to feedback, that clearly articulate the question, the methods used, and both the quality and the conclusions drawn from evidence. This was an extremely valuable interaction for the RES team and has helped improve our processes substantially.

8. Next steps

- Further dialogue and engagement with relevant stakeholders. Dissemination and circulation of the policy brief report to the relevant stakeholders.
- Prioritisation of topics from the list of topics requested by the stakeholders at the RES Consultation workshop.
- Conduct of evidence synthesis (if requested) for knowledge gaps identified in the policy brief report or other topics that are prioritised by national and state level stakeholders
- Development of standardised templates and checklists for the conduct and evaluation of rapid evidence synthesis products.

9. References

- 1. World Health Organisation (WHO). Mid-level health providers: a promising resource to achieve the health. 2010. Available from
- https://www.who.int/workforcealliance/knowledge/resources/Final_MLP_web_2.pdf
- 2. National Health Systems Resource Centre (NHSRC). AYUSHMAN BHARAT: Comprehensive Primary Health Care through Health and Wellness Centers. National Health Mission; 2018.
- 3. Shea Beverley J, Reeves Barnaby C, Wells George, Thuku Micere, Hamel Candyce, Moran Julian et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both BMJ 2017; 358: i4008.

Millennium Development Goals. World Health Organisaton; 2010.

- 4. Lassi ZS, Cometto G, Huicho L, Bhutta ZA. Quality of care provided by mid-level health workers: systematic review and meta-analysis. Bulletin of the World Health Organization. 2013;91(11):824-33I.
- 5. Barnard S, Kim C, Park MH, Ngo TD. Doctors or mid-level providers for abortion. The Cochrane database of systematic reviews. 2015;7.
- 6. Kredo T, Adeniyi FB, Bateganya M, Pienaar ED. Task shifting from doctors to non-doctors for initiation and maintenance of antiretroviral therapy. Cochrane Database of Systematic Reviews. 2014; 7.
- 7. Mdege ND, Chindove S, Ali S. The effectiveness and cost implications of task-shifting in the delivery of antiretroviral therapy to HIV-infected patients: a systematic review. Health policy and planning. 2013;28(3):223-36.
- 8. Joshi R, Alim M, Kengne AP, Jan S, Maulik PK, Peiris D, et al. Task shifting for non-communicable disease management in low and middle income countries--a systematic review. PloS one. 2014;9(8):e103754.
- 9. Weeks G, George J, Maclure K, Stewart D. Non-medical prescribing versus medical prescribing for acute and chronic disease management in primary and secondary care. The Cochrane database of systematic reviews. 2016;11.
- 10. Chowdhary N, Sikander S, Atif N, Singh N, Ahmad I, Fuhr DC, et al. The content and delivery of psychological interventions for perinatal depression by non-specialist health workers in low and middle income countries: a systematic review. Best practice & research Clinical obstetrics & gynaecology. 2014;28(1):113-33.
- 11. Rao KD, Sundararaman T, Bhatnagar A, Gupta G, Kokho P, Jain K. Which doctor for primary health care? Quality of care and non-physician clinicians in India. Social science & medicine (1982). 2013;84:30-4.
- 12. Rao KD, Stierman E, Bhatnagar A, Gupta G, Gaffar A. As good as physicians: patient perceptions of physicians and non-physician clinicians in rural primary health centers in India. Global health, science and practice. 2013;1(3):397-406.
- 13. National Health Systems Resource Centre. Rural Health Practitioners in Assam: Mid-Level Care Provider for Comprehensive Service Delivery in Sub Centers. NHSRC; 2014.
- 14. Global Health Workforce Alliance. Mid-level health workers for delivery of essential health services: a global systematic review and country experiences. 2013. Available from https://www.who.int/workforcealliance/knowledge/resources/mlp2013/en/.

Appendix 1: Search Strategies

MEDLINE database search (PubMed platform)

Search	Query	Number of hits
#1	Nurse[tw] OR nurses[tw] OR physician assistant*[tw] OR mid-level provider[tw] OR midwife*[tw] OR midwives[tw] OR nurse practitioner*[tw] OR non-physician*[tw] OR substitute health worker*[tw] OR auxiliar*[tw] OR mid-level cadre*[tw] OR auxiliary nurse*[tw] OR nurse assistant*[tw] OR non-physician clinician*[tw] OR surgical technician*[tw] OR clinical officer*[tw] OR medical assistant*[tw] OR physician assistant*[tw] OR alternative cadre*[tw] OR community health work*[tw] OR community health aide*[tw] OR community care giver*[tw] OR community care coordinator*[tw] OR health care assistant*[tw] OR allied health personnel[tw] OR psychiatric aide*[tw] OR task-shift*[tw]	371191
#2	low and middle income countr*[tw] OR LMIC[tw] OR developing countr*[tw] OR third world[tw]	127367
#3	India[tw] OR Indian[tw]	169649
#4	#2 OR #3	284308
#5	Systematic review*[tw] OR umbrella review*[tw] OR meta-analysis[tw] OR meta-analyses[tw]	256226
#6	#1 AND #5 (Filters: : Humans, English language)	3020
#7	#1 AND #4 AND #5 (Filters: Humans, English language)	142

CINAHL

Search	Query	Number of hits
#1	TX Nurse* OR TX "physician assistant*" OR TX "mid-level provider*" OR TX midwife OR TX midwives OR TX "nurse practitioner*" OR TX "non-physician*" OR TX "substitute health worker*" OR TX auxiliary OR TX auxiliaries OR TX "mid-level cadre*" OR TX "auxiliary nurse*" OR TX "nurse assistant*" OR TX "non-physician clinician*" OR TX "surgical technician*" OR TX "clinical officer*" OR TX "medical assistant*" OR TX "physician assistant*" OR TX "alternative cadre*" OR TX "community health worker*" OR TX "community health aide*" OR TX "community care giver*" OR TX "community care	834517

	coordinator*" OR TX "health care assistant*" OR TX "allied health personnel" OR TX "psychiatric aide" OR TX "psychiatric aides" OR TX "task shift" OR TX "task shifting"	
#2	TX "low and middle income countr*" OR TX "LMIC" OR TX "developing countr*" OR TX "third world"	46048
#3	TX India OR TX Indian	157318
#4	#2 OR #3	193692
#5	TX "Systematic review*" OR TX "umbrella review*" OR TX "meta-analysis" OR TX "meta-analyses"	218349
#6	#1 AND #4 AND #5 (Filters: English Language)	4307

Cochrane Library

Search	Query	Number of hits
#1	Nurse OR nurses OR "physician assistant" OR "mid-level provider" OR midwife OR midwives OR "nurse practitioner" OR "nurse practitioners" OR "non-physician" OR "substitute health worker" OR "substitute health workers" OR auxiliary OR auxiliaries OR "mid-level cadre" OR "mid-level cadres" OR "auxiliary nurse" OR "auxiliary nurses" OR "nurse assistant" OR "nurse assistants" OR "non-physician clinician" OR "non-physician clinicians" OR "surgical technicians" OR "clinical officer" OR "clinical officers" OR "medical assistant" OR "medical assistants" OR "physician assistant" OR "physician assistants" OR "alternative cadre" OR "alternative cadres" OR "community health worker" OR "community health workers" OR "community health aide" OR "community care givers" OR "community care giver" OR "community care givers" OR "health care assistant" OR "health care assistant" OR "health care assistant" OR "psychiatric aide" OR "psychiatric aides" OR "task shift" OR "task shifting"	21794
#2	"low and middle income country" OR "low and middle income countries" OR "LMIC" OR "developing country" OR "developing countries" OR "third world"	4771
#3	India OR Indian	25706
#4	#2 OR #3	29490

#5	"Systematic review" OR "Systematic reviews" OR "umbrella review" OR "umbrella reviews" OR "meta-analysis" OR "meta-analyses"	23064
#6	#1 AND #4 AND #5	591 (499 SRs)

EMBASE

Search	Query	Number of hits
#1	Nurse OR nurses OR "physician assistant" OR "mid-level provider" OR midwife OR midwives OR "nurse practitioner" OR "nurse practitioners" OR "non-physician" OR "substitute health worker" OR "substitute health workers" OR auxiliary OR auxiliaries OR "mid-level cadre" OR "mid-level cadres" OR "auxiliary nurse" OR "auxiliary nurses" OR "nurse assistant" OR "nurse assistants" OR "non-physician clinician" OR "non-physician clinicians" OR "surgical technician" OR "surgical technicians" OR "clinical officer" OR "clinical officers" OR "medical assistant" OR "medical assistants" OR "physician assistant" OR "physician assistants" OR "alternative cadre" OR "alternative cadres" OR "community health worker" OR "community health workers" OR "community health aide" OR "community care givers" OR "community care givers" OR "community care givers" OR "health care assistant" OR "health care assistant" OR "health care assistant" OR "health care assistant" OR "task shift" OR "task shifting"	760804
#2	"low and middle income country" OR "low and middle income countries" OR "LMIC" OR "developing country" OR "developing countries" OR "third world"	143367
#3	India OR Indian	999525
#4	#2 OR #3	1120478
#5	"Systematic review" OR "Systematic reviews" OR "umbrella review" OR "umbrella reviews" OR "meta-analysis" OR "meta-analyses"	403314
#6	#1 AND #4 AND #5	380
#8	#1 AND #4 AND #5 AND [embase]/lim NOT [medline]/lim	164

Health Systems Evidence – Database of syntheses of research evidence

Search	Query	Number of hits
#1	Nurse OR nurses OR physician assistant OR mid-level provider OR midwife OR midwives OR nurse practitioner OR nurse practitioners OR non-physician OR non-physicians OR substitute health worker OR substitute health workers OR auxiliary OR auxiliaries OR mid-level cadre OR mid-level cadres OR auxiliary nurse OR auxiliary nurses OR nurse assistant OR nurse assistants OR non-physician clinicians OR surgical technician OR surgical technicians OR clinical officer OR clinical officers OR medical assistant OR medical assistants OR physician assistant OR physician assistants OR alternative cadres OR community health worker OR community health workers OR community health aide OR community health aides OR community care giver OR community care coordinators OR health care assistant OR health care assistants OR allied health personnel OR psychiatric aide OR psychiatric aides OR task shift OR task shifting AND low and middle income country OR low and middle income countries OR LMIC OR developing country OR developing countries OR third world OR India OR Indian	59

Appendix 2. GRADE (Grading of Recommendations Assessment, Development and Evaluation) Approach

According to the GRADE approach, the quality of the evidence is a judgement about the extent to which we can be confident that the estimates of effect are correct. The quality assessments are provided for each outcome, which are based on the type of study design (randomised trials versus observational studies), the risk of bias, the consistency of the results across studies, the precision of the overall estimate across studies, the indirectness of the available evidence and publication bias. For each outcome, the quality of the evidence is rated as high, moderate, low or very low using the following definitions.

High: Further research is very unlikely to change our confidence in the estimate of effect. ⊕⊕⊕⊕

Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. ⊕⊕⊕○

Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. ⊕⊕○○

Very low: We are very uncertain about the estimate. ⊕⊕○○

¹GRADE Criteria - Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available fromguidelinedevelopment.org/handbook.

Overall, 23 studies were excluded following full text examination.

- 1. Afable A, Karingula NS. Evidence based review of type 2 diabetes prevention and management in low and middle income countries. World Journal of Diabetes. 2016; 7(10):209-29.
- 2. Anand TN, Joseph LM, Geetha AV, Chowdhury J, Prabhakaran D, Jeemon P. Task-sharing interventions for cardiovascular risk reduction and lipid outcomes in low- and middle-income countries: A systematic review and meta-analysis. Journal of Clinical Lipidology. 2018; 12(3):626-42.
- 3. Callaghan M, Ford N, Schneider H. A systematic review of task- shifting for HIV treatment and care in Africa. Human resources for health. 2010; 8:8.
- 4. Ciapponi A, Lewin S, Herrera CA, Opiyo N, Pantoja T, Paulsen E, et al. Delivery arrangements for health systems in low-income countries: an overview of systematic reviews. Cochrane Database of Systematic Reviews. 2017(9).
- 5. Coster S, Watkins M, Norman IJ. What is the impact of professional nursing on patients' outcomes globally? An overview of research evidence. International Journal of Nursing Studies. 2018; 78:76-83.
- 6. Dawson AJ, Buchan J, Duffield C, Homer CS, Wijewardena K. Task shifting and sharing in maternal and reproductive health in low-income countries: a narrative synthesis of current evidence. Health policy and planning. 2014; 29(3):396-408.
- 7. Dolea C, Stormont L, Braichet J. Evaluated strategies to increase attraction and retention of health workers in remote and rural areas. Bulletin of the World Health Organization. 2010; 88(5):379-85.
- 8. Global Health Workforce Alliance. Mid-level health workers for delivery of essential health services: A global systematic review and country experiences. World Health Organisation; 2013.
- 9. Herrera CA, Lewin S, Paulsen E, Ciapponi A, Opiyo N, Pantoja T, et al. Governance arrangements for health systems in low-income countries: an overview of systematic reviews. Cochrane Database of Systematic Reviews. 2017(9).
- 10. Iwu EN, Holzemer WL. Task shifting of HIV management from doctors to nurses in Africa: Clinical outcomes and evidence on nurse self-efficacy and job satisfaction. AIDS Care. 2014; 26(1):42-52.
- 11. Lassi ZS, Musavi NB, Maliqi B, Mansoor N, de Francisco A, Toure K, et al. Systematic review on human resources for health interventions to improve maternal health outcomes: evidence from low- and middle-income countries. Human resources for health. 2016; 14:10.
- 12. Ng'ang'a N, Woods Byrne M. Professional practice models for nurses in low-income countries: an integrative review. BMC Nursing. 2015; 14(1):1-15.
- 13. Nordin N, Hassali MAA, Sarriff A. A global picture of extended pharmacy services, perceptions, and barriers toward its performance: A systematic review. Asian Journal of Pharmaceutical and Clinical Research. 2017; 10(11):417-27.
- 14. Ogedegbe G, Gyamfi J, Plange-Rhule J, Surkis A, Rosenthal DM, Airhihenbuwa C, et al. Task shifting interventions for cardiovascular risk reduction in low-income and middle-income countries: a systematic review of randomised controlled trials. BMJ open. 2014; 4(10):e005983.
- 15. Painuly N, Sharan P. Effectiveness of training of non-mental health care providers in mental health in low- and middle-income countries: a systematic review. Primary Care & Community Psychiatry. 2008; 13(2):83-9.
- 16. Pantoja T, Opiyo N, Lewin S, Paulsen E, Ciapponi A, Wiysonge CS, et al. Implementation strategies for health systems in low-income countries: an overview of systematic reviews. Cochrane Database of Systematic Reviews. 2017(9).
- 17. Polus S, Lewin S, Glenton C, Lerberg PM, Rehfuess E, Gulmezoglu AM. Optimizing the delivery of contraceptives in low- and middle-income countries through task shifting: a systematic

review of effectiveness and safety. Reproductive health. 2015; 12:27.

- 18. Raams TM, Browne JL, Festen-Schrier V, Klipstein-Grobusch K, Rijken MJ. Task shifting in active management of the third stage of labor: a systematic review. BMC pregnancy and childbirth. 2018; 18(1):47.
- 19. Renner RM, Brahmi D, Kapp N. Who can provide effective and safe termination of pregnancy care? A systematic review*. BJOG: an international journal of obstetrics and gynaecology. 2013; 120(1):23-31.
- 20. Sandall J, Soltani H, Gates S, Shennan A, Devane D. Midwife-led continuity models versus other models of care for childbearing women. Cochrane Database of Systematic Reviews. 2016(4).
- 21. Seidman G, Atun R. Does task shifting yield cost savings and improve efficiency for health systems? A systematic review of evidence from low-income and middle-income countries. Human resources for health. 2017; 15(1):29.
- van Ginneken N, Tharyan P, Lewin S, Rao GN, Meera SM, Pian J, et al. Non-specialist health worker interventions for the care of mental, neurological and substance-abuse disorders in low- and middle-income countries. The Cochrane database of systematic reviews. 2013(11):Cd009149.
- 23. Wilson A, Lissauer D, Thangaratinam S, Khan KS, MacArthur C, Coomarasamy A. A comparison of clinical officers with medical doctors on outcomes of caesarean section in the developing world: meta-analysis of controlled studies. BMJ (Clinical research ed). 2011; 342:d2600.

Appendix 4. AMSTAR-2 Appraisal Checklist

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both.³

	D(14)	-1-1		CDICOR
1.		inclusion criteria for the review include th	ie com	ponents of PICO?
For Ye		Optional (recommended) □ Timeframe for follow-up		Yes No
2.		tain an explicit statement that the review of the review and did the report justify an		
The au	rtial Yes: thors state that they had a written ol or guide that included ALL the ng:	For Yes: As for partial yes, plus the protocol should be registered and should also have specified:		Yes
_ _ _	review question(s) a search strategy inclusion/exclusion criteria a risk of bias assessment	 a meta-analysis/synthesis plan, if appropriate, and a plan for investigating causes of heterogeneity justification for any deviations from the protocol 		res Partial Yes No
3.	Did the review authors explain	their selection of the study designs for incl	lusion i	in the review?
For Ye	s, the review should satisfy ONE of Explanation for including only RO OR Explanation for including onl OR Explanation for including bot	CTs y NRSI	0	Yes No
4.	Did the review authors use a con	mprehensive literature search strategy?		
For Par	rtial Yes (all the following):	For Yes, should also have (all the following):		
0	searched at least 2 databases (relevant to research question) provided key word and/or search strategy justified publication restrictions (e.g. language)	searched the reference lists / bibliographies of included studies searched trial/study registries included/consulted content experts in the field where relevant, searched for grey literature conducted search within 24 months of completion of the review		Yes Partial Yes No
5.	Did the review authors perform	study selection in duplicate?		
For Ye	s, either ONE of the following: at least two reviewers independent and achieved consensus on which	tly agreed on selection of eligible studies studies to include sle of eligible studies <u>and</u> achieved good	0	Yes No

6. Did the review authors perform	m data extraction in duplicate?	
included studies	consensus on which data to extract from	□ Yes □ No
	ast 80 percent), with the remainder	
Did the review authors provide	le a list of excluded studies and justify the ex	clusions?
For Partial Yes:	For Yes, must also have:	
□ provided a list of all potentially		□ Yes
relevant studies that were read in full-text form but excluded	the review of each potentially relevant study	□ Partial Yes
from the review	relevant study	□ No
	be the included studies in adequate detail?	
For Partial Yes (ALL the following):	For Yes, should also have ALL the	
	following:	
☐ described populations	☐ described population in detail	□ Yes
☐ described interventions	 described intervention in detail (including doses where 	 □ Partial Yes □ No
☐ described comparators	relevant)	L 140
□ described outcomes	☐ described comparator in detail	
☐ described research designs	(including doses where	
	relevant)	
	☐ described study's setting	
	□ timeframe for follow-up	
Did the review authors use a sindividual studies that were in	atisfactory technique for assessing the risk o	f bias (RoB) in
individual studies that were in		f bias (RoB) in
individual studies that were in RCTs	cluded in the review?	f bias (RoB) in
individual studies that were in	cluded in the review?	f bias (RoB) in
individual studies that were in RCTs For Partial Yes, must have assessed RoB	For Yes, must also have assessed RoB from: allocation sequence that was	□ Yes
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and	□ Yes □ Partial Yes
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result	□ Yes □ Partial Yes □ No
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple	□ Yes □ Partial Yes □ No □ Includes only
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a	□ Yes □ Partial Yes □ No
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple	□ Yes □ Partial Yes □ No □ Includes only
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality)	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a	□ Yes □ Partial Yes □ No □ Includes only
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB:	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain	□ Yes □ Partial Yes □ No □ Includes only NRSI
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and	□ Yes □ Partial Yes □ No □ Includes only NRSI □ Yes □ Partial Yes
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB:	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result	□ Yes □ Partial Yes □ No □ Includes only NRSI □ Yes □ Partial Yes □ No
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result from among multiple	□ Yes □ Partial Yes □ No □ Includes only NRSI □ Yes □ Partial Yes □ No □ Includes only
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result	□ Yes □ Partial Yes □ No □ Includes only NRSI □ Yes □ Partial Yes □ No
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and from selection bias	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result from among multiple measurements or analyses of a	□ Yes □ Partial Yes □ No □ Includes only NRSI □ Yes □ Partial Yes □ No □ Includes only RCTs
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and from selection bias	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result from among multiple measurements or analyses of a specified outcome	□ Yes □ Partial Yes □ No □ Includes only NRSI □ Yes □ Partial Yes □ No □ Includes only RCTs
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and from selection bias 10. Did the review authors report	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result from among multiple measurements or analyses of a specified outcome on the sources of funding for the studies included	☐ Yes ☐ Partial Yes ☐ No ☐ Includes only NRSI ☐ Yes ☐ Partial Yes ☐ No ☐ Includes only RCTs ☐ Includes only RCTs ☐ Yes
individual studies that were in RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) NRSI For Partial Yes, must have assessed RoB: from confounding, and from selection bias 10. Did the review authors report	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, and selection of the reported result from among multiple measurements or analyses of a specified outcome For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, and selection of the reported result from among multiple measurements or analyses of a specified outcome on the sources of funding for the studies included g that the reviewers looked for this information	☐ Yes ☐ Partial Yes ☐ No ☐ Includes only NRSI ☐ Yes ☐ Partial Yes ☐ No ☐ Includes only RCTs ☐ Includes only RCTs ☐ Yes

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?			
RCTs For Yes:			
☐ The authors justified combining the data in a meta-analysis			
 AND they used an appropriate weighted technique to combine 			
study results and adjusted for heterogeneity if present.		No meta-analysis conducted	
AND investigated the causes of any heterogeneity	-	conducted	
For NRSI For Yes:			
		Vac	
☐ The authors justified combining the data in a meta-analysis ☐ AND they used an appropriate weighted technique to combine	0 1		
study results, adjusting for heterogeneity if present		No meta-analysis	
☐ AND they statistically combined effect estimates from NRSI that		conducted	
were adjusted for confounding, rather than combining raw data,			
or justified combining raw data when adjusted effect estimates			
were not available			
AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review			
12. If meta-analysis was performed, did the review authors assess the poten individual studies on the results of the meta-analysis or other evidence states.			
For Yes:	_	Von	
□ included only low risk of bias RCTs □ OP, if the needed estimate was based on PCTs and/or NPSI at unriskle		Yes No	
 OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of 		No meta-analysis	
RoB on summary estimates of effect.	_	conducted	
rob on standard y committee of creek.			
13. Did the review authors account for RoB in individual studies when interesults of the review?	rpretin	g/ discussing the	
For Yes:	_	Yes	
□ included only low risk of bias RCTs □ OR, if RCTs with moderate or high RoB, or NRSI were included the		No	
review provided a discussion of the likely impact of RoB on the results	_	1.0	
14. Did the review authors provide a satisfactory explanation for, and disc	ussion (of any	
heterogeneity observed in the results of the review?			
For Yes:			
☐ There was no significant heterogeneity in the results	_		
 OR if heterogeneity was present the authors performed an investigation of 		Yes	
sources of any heterogeneity in the results and discussed the impact of this on the results of the review	ш	No	
		1	
 If they performed quantitative synthesis did the review authors carry or investigation of publication bias (small study bias) and discuss its likely 			
the review?	шрасі	on the results of	
For Yes:			
□ performed graphical or statistical tests for publication bias and discussed	п	Yes	
the likelihood and magnitude of impact of publication bias	п	No	
		conducted	
16. Did the review authors report any potential sources of conflict of inter- they received for conducting the review?	est, inc	luding any funding	
For Yes:			
☐ The authors reported no competing interests OR		Yes	
☐ The authors described their funding sources and how they managed		No	
potential conflicts of interest			