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Review Title:

Health system readiness for non-communicable diseases at the primary care level: A systematic review

Short Title:

Health system readiness for non-communicable diseases: A systematic review

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Abstract

Objective: To synthesise evidence on the primary healthcare system's readiness for preventing and managing non-communicable diseases (NCDs).

Design: Systematic review.

Data sources: Ovid MEDLINE, EMBASE, CINAHL, PsycINFO and Scopus were searched from 1 January 1984 to 30 July 2021, with hand-searching references and expert advice.

Eligibility criteria: Any English-language health research with evidence of readiness/preparedness of the health system at the primary healthcare level in the context of four major NCDs: diabetes mellitus, cancer, chronic respiratory diseases, and cardiovascular diseases.

Data extraction and synthesis: Two authors independently extracted data and assessed the bias. The full-text selected articles were then assessed using the Mixed Methods Appraisal Tool. Health system readiness was descriptively and thematically synthesized in line with the health system dynamics framework.

Results: Out of 7,843 records, 23 papers were included in this review (15 quantitative, three qualitative and five mixed-method studies). The findings showed that existing literature predominantly examined health system readiness from the supply-side perspective as embedded in the World Health Organization's health system framework. However, at the primary healthcare level, these components are insufficiently prepared for NCDs. Among NCDs, higher levels of readiness were reported for diabetes mellitus and hypertension in comparison to chronic respiratory diseases (asthma, chronic obstructive pulmonary disease), cardiovascular diseases and cancer. There has been a dearth of research on the demand-side perspective, which is an essential component of a health system and must be addressed in future research.

Conclusion: The supply-side components at the primary healthcare level are inadequately ready to address the growing NCD burden. Improving supply-side factors, with a particular focus on chronic respiratory diseases, cardiovascular diseases and cancer, and improving understanding of the demand-

side components of the health system's readiness, may help to prevent and manage NCDs at the primary healthcare level.

Keywords: non-communicable diseases, health system readiness, primary health care, systematic review

Strengths and limitations of this study

- Data synthesis was informed by the health system dynamics framework, which offers a deeper and more comprehensive (both supply-side and demand-side factors) understanding of primary healthcare system readiness for NCDs.
- We conducted an extensive systematic search of literature with hand-searching references and expert advice regarding health system readiness for non-communicable diseases at the primary care level, which increases the validity and trustworthiness of this review's findings.
- Meta-analysis was not possible due to heterogeneity of study designs, methods and techniques, as well as the studies' focus on a variety of health system components.
- A few studies that reported health system readiness at combined primary and secondary healthcare levels were excluded.

Introduction

Globally, non-communicable diseases (NCDs) are the leading causes of deaths and disabilities, accounting for 41 million deaths (71% of all deaths) annually (1), with 77% occurring in low- and middle-income countries (1, 2). The current increased NCD burden may be due to the rise of the ageing population, rapid and/or unplanned urbanisation and lifestyle-related factors (e.g. physical inactivity, unhealthy diets and consumption of tobacco products and alcohol) (3). If current trends continue, the estimated cumulative deaths from NCDs will reach 52 million by 2030 (3), and NCD-related cost was projected to be US$ 47 trillion between 2010 and 2030 (4). NCDs' predicted health outcomes and economic burden will have adverse consequences, such as prolonged illness or disability, greater treatment costs, loss of productivity and substantial opportunity cost, which will eventually affect households' economy and well-being (4, 5). The impact of NCDs may result in increased poverty, higher inequality and low quality of life. Considering the immense influence of NCDs, many commitments and control strategies have been made at the global, national and local levels to prevent and manage them (6-8). The Sustainable Development Goals, for example, by 2030, targeted one-third reduction of premature deaths from the four major NCDs of diabetes mellitus (DM), cancer, chronic respiratory diseases (CRDs) and cardiovascular diseases (CVDs) (8, 9) among people aged 30–69.

Primary healthcare is crucial for promoting essential healthcare services and achieving improved health outcomes, particularly in countries with resource-poor settings (3, 10-12). Growing evidence shows that a well-functioning primary healthcare system has immense potential for improving global health outcomes due to its extensive coverage, cost-effectiveness, well-structured network of healthcare facilities, affordable technologies, socially and culturally acceptable intervention methods and broad community participation (10, 13, 14). NCD prevention and management differ from that of acute conditions, where the primary healthcare approach has a powerful impact. Unlike acute conditions, NCD prevention and management require extended or even life-long healthcare support, early case detection, psychosocial promotion, risk factor identification, self-management, behavioural modifications and regular medical support, such as adherence to medical procedures and treatment (3).

The primary healthcare system is typically the first-line contact for individuals seeking care, making it easier for patients to continue follow-up contacts (15). Therefore, it can be viewed as the most effective and appropriate mechanism for addressing NCDs.

While the literature emphasises the roles and importance of the primary healthcare system in preventing and managing NCDs following a dozen of global commitments and strategies, little is known about the extent to which it is ready to deliver NCD services (16, 17). The concept of 'health system readiness' is often explained in terms of the health system 'components' or 'framework'. Until recently, health system readiness was mostly defined and presented in the context of the World Health Organization's (WHO) health system framework, proposed in 2008, which described six 'key elements' or 'building blocks':, health service delivery, health workforce, health financing, health information system, leadership and governance, medical products, knowledge and technologies (18). However, the WHO's model is viewed as having limited capacity to comprehensively explain how and whether different health system elements within a broader societal context interact and are influenced, as well as how population/individual behaviour and choices and the process impact this mechanism (19, 20). In order to provide an exhaustive understanding of system interactions, van Olmen et al. proposed the 'health system dynamics framework', which included the WHO's six building blocks and concurrent literature. It is comprised of 10 elements that analyse their interactions and functions under a broader societal context (21).

Guided by the 'health system dynamics framework', this systematic review aimed to synthesise the current evidences on primary healthcare system readiness and evaluate its response to NCDs on a global scale. The findings of this review will help policymakers, public health planners and researchers focus on the further actions required to establish a well-prepared health system at the primary healthcare level to address the growing NCD burden.

Methods

Protocol and registration

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline (22) and was registered on the Research Registry (REVIEWREGISTRY1163).

Inclusion criteria

This review included studies that reported on the readiness/preparedness of various health system components at the primary healthcare level in the context of four major NCDs: DM, cancer, CRDs and CVDs. Where studies reported health system preparedness at the primary and secondary care level combined, only information related to the primary healthcare level was included. However, studies in which the primary and secondary care level data could not be separated were excluded.

Exclusion criteria

Studies on other NCDs such as arsenicosis, kidney diseases, mental health disorders, hearing disability, oral disease, birth defects and road injuries were excluded. Papers that focused on NCD interventions/programmes beyond the primary healthcare level were likewise excepted. Editorials, letters, opinion articles, narrative or systematic reviews, study protocols, conference abstracts, posters, reports, and book chapters were also not considered. Additionally, works that were published in a language other than English were excluded.

Data sources and search strategy

The search strategy aimed to find English language studies in five databases (Ovid Medline, Ovid Embase, Ovid PsycInfo, CINAHL and Scopus) published between 1 January 1984 and 30 July 2021 (Figure 1). The WHO's health system model proposed in 1984 was considered appropriate to identify and assess the key components of the primary healthcare system. The studies published in 1984 onward were deemed to be relevant to this review. Therefore, the earliest date of the search was set to ensure

the optimum number of studies published since 1984. The search strategies used a combination of subject headings and free text terms that aimed to cover the areas of (1) non-communicable diseases (e.g., chronic disease or chronic conditions or chronic disorders), AND (2) primary health system (e.g. primary health service or first-level healthcare facility or local health system or local-level health facility) AND (3) readiness or preparedness or capacity.

Searches were adapted as appropriate to the specifications of each of the 5 databases. The final searches are presented in the (Supplementary Appendix file). Hand-searching and reference checking of citations and reference lists were undertaken, and additional records were identified through personal consultations with experts, including researchers, administrators, policy planners, and public health practitioners.

[FIGURE 1 SHOULD BE INSERTED HERE]

Figure 1 PRISMA flowchart for study inclusion.

Data extraction

Three authors were involved in the data extraction process. First, records identified through database and manual searches were imported into the Endnote library (EndNote X9.2, Thomson Reuters 2019). Afterwards, the duplicate records were removed. Next, two authors (AK and NK) independently screened the studies based on their titles and/or abstracts. The full-text selected articles were then assessed using the inclusion and exclusion criteria and the standard quality assessment. When inconsistencies and discrepancies arose, a senior author (BB) was brought in to resolve the disagreements through discussion and consensus. A standardised data extraction sheet was developed and piloted. The extraction sheet contains the following study-specific information: authors, publication year, country, study aims, study design and settings, sample size and participants, data collection method and tool used, NCD/risk factor studied, health system component focus and key findings.

Quality assessment

The Mixed Methods Appraisal Tool (MMAT) was used to assess the methodological quality of the included studies (23). The distribution of MMAT scores varied with the study design and the evaluation of some selected parameters. The score is 25% when quantitative study (QUAN) = 1, qualitative study (QUAL) = 1 or mixed-method study (MM) = 0. It is 50% when QUAN = 2, QUAL = 2 or MM = 1; 75% when QUAN = 3, QUAL = 3 or MM = 2; and it is 100% when QUAN = 4, QUAL = 4 or MM = 3. Thus, each study was given a score ranging from 25% to 100% (Table 1). Two authors (AK and NK) independently assessed the studies' quality, and the senior author (BB) cross-checked them. Discrepancies and disagreements were resolved through discussion.

Table 1 Type of research design and associated quality of included studies (n=23)

Study design	Number of studies (%)	MMAT score (%)			
		25	50	75	100
Quantitative	15 (65)	-	5	7	3
Qualitative	3 (13)	-	1	2	-
Mixed-methods	5 (22)	1	2	2	-

Note. Entries in the table show the number of studies

Data synthesis

Data analysis was guided by the health system dynamics framework (24). The following themes were synthesised using this framework: (i) health service delivery, (ii) healthcare workforce, (iii) health financing, (iv) access to medical products and knowledge/technologies, (v) health information system, (vi) leadership and governance and (vii) community perspective. Under these themes, data from quantitative studies were reported descriptively using frequencies or percentages, while qualitative studies were synthesised by determining themes. In this process, a few steps were followed: (i) familiarising, (ii) identifying themes (health system components), (iii) indexing, (iv) charting and (v) mapping and interpreting. Data from mixed-methods studies were analysed both descriptively and thematically analysed. The heterogeneous study design of the included studies precluded a meaningful meta-analysis in this review.

Ethics statement

This review has been done as part of a PhD project. The project has been approved by the Monash University Human Research Ethics Committee (Project ID: 27112) and Bangladesh Medical Research Council (Ref: BMRC/NREC/2019-2022/270).

Patient and public involvement

There was no patient or public involvement.

Results

General characteristics of the study

Initially, 7,843 studies were retrieved, from which 2,213 duplicates were excluded (Figure 1). Then, 5,630 studies were excluded based on a title and abstract review, with 107 meeting the inclusion criteria for a full-text review. Following the full-text review, 23 studies were ultimately included in this study (Table 2): 15 were quantitative (cross-sectional) (25-39), three were qualitative (40-42) and five were mixed-method studies (43-47). Most of the research was conducted in resource-poor settings (20 studies), mostly in sub-Saharan Africa and South Asian countries. Eighteen studies focused on the health service delivery component at the primary healthcare level, while four studies addressed the leadership and governance (Fig-2a). Eight studies were conducted in the South Asian-East Asia Region (SEAR), and only a single study (n=1) was performed in both the Region of the Americas (AMR) and the European Region (EUR). One study involved multiple nations (Benin, Eritrea, Sudan, Syria, Bhutan, Sri Lanka, Vietnam and Suriname) (Fig-2b). DM was the most studied NCDs, with 12 studies reported on it, while mental illness (MI) was the least researched, with only two studies (Fig-2c) focused on it. Thirteen studies addressed multiple NCDs, six focused on a single NCD and four did not mention any specific NCD (e.g. termed chronic diseases) (Fig-2d).

[FIGURE 2 SHOULD BE INSERTED HERE]

Figure 2 Number of published studies that investigated the primary healthcare system's readiness between January 1984 and July 2021, broken down by NCD type, NCD focus and WHO region.

Note. AFR: African Region, AMR: Region of the Americas, SEAR: South East-Asian Region, EUR: European Region, WPR: Western Pacific Region, CRD: Chronic Respiratory Diseases, CVD: Cardiovascular Diseases, DM: Diabetes Mellitus, HTN: Hypertension, MI: Mental Illness, HSD: Health Service Delivery, HW: Health Workforce, HF: Health Financing, HIS: Health Information System, L&G: Leadership and Governance, MPK&T: Medical Products, Knowledge and Technologies.

252 Table 2 Summary – Characteristics of the studies included in this review

Author (Year)	Country	Study aims	Study design and settings	Sample size and participants	Data collection method and tool used	NCDs/Risk factors studied	Health system components' focus	Key findings/NCD Readiness
Biswas et al. (2018) (38)	Bangladesh	To assess health facilities' readiness to manage CVD and DM	Quantitative; Countrywide	319 healthcare facilities	Survey; Modified WHO SARA questionnaire	CVD, DM	HSD, HW, MPK&T	58% DM, and 24.1% CVD services were available.
Islam et al. (2016) (29)	Bangladesh	To assess the availability and provision of NCD service delivery	Quantitative; One district	50 health facilities	Survey; Modified WHO SARA questionnaire	CRD, CVD, DM	HSD	52% CRD, 73% CVD and DM 52% services were available.
NIPORT++ (2020) (39)	Bangladesh	To assess health facilities' readiness to manage cancer, CRD, CVD, DM and HTN	Quantitative; Countrywide	1524 healthcare facilities	Survey; Modified DHS questionnaire	Cancer, CRD, CVD, DM, HTN	HSD, HW, MPK&T	Availability of services varied from CCs to UHCs: cervical cancer (0.4%-37.5%), CRD (34.1%-93.9%), CVD (1.4%-69.6%), DM (0.9%-84.5%), and, hypertension (3.5%-91.5%).
Nyame et al. (2019) (34)	Ghana	To assess health facilities' capacity to implement the WHO PEN pilot	Quantitative; Three regions	23 health facilities	Survey; Modified WHO PEN questionnaire	NCD focus was not specified	HSD, HW, HF	Health facilities had inadequate capacity to implement WHO-PEN interventions.
Elias et al. (2017) (43)	India	To investigate the local health system's preparedness for DM and HTN	Mixed-methods; One district	1,149 patients, 39 healthcare staff, 30 pharmacists, 14 FGDs±	Survey; Non-validated questionnaire; Interview; IDI and FGD guides	DM, HTN	HSD, MPK&T	Public healthcare facilities had insufficient capacity for HTN and DM service delivery due to inadequate diagnostic capacity and frequent medicine stockouts.
Pakhare et al. (2015) (35)	India	To identify facility-level gaps that affect CVD care and management	Quantitative; 24 districts	85 medical officers	Survey; Modified WHO PEN questionnaire	DM, HTN	HSD, HW, MPK&T	The community health centre had a relatively better CVD management capacity than the primary health centre but lacked sufficient equipment, medicine and human resources.
Panda et al. (2018) (42)	India	To describe the health system's response and preparedness to NCDs	Qualitative; One district	13 key stakeholders	Interviews; IDI guide	Cancer, CVD, DM and Stroke	HSD, HW, HF, L&G	Health facilities were overburdened and lacked trained staff, and resources to manage NCDs.
Van Dijk-de Vries et al. (2016) (46)	Netherlands	To examine patients' readiness to consult psychosocial problems with nurses	Mixed-methods; Primary care setting	217 diabetic patient participants	Survey; Non-validated questionnaire; IDI guide	DM	Patients' readiness	90% of respondents had positive attitudes towards the existing diabetes consultation.
Honey et al. (2016) (28)	New Zealand	To assess older people's readiness to e-health	Quantitative; Urban settings	263 patients in primary healthcare centres	Survey; Non-validated questionnaire	Cancer, CRD, DM, HTN, Mental Illness	HIS	36% of participants sought health information from an online platform.
Adinan et al. (2019) (25)	Tanzania	To assess health facilities' readiness to manage DM and HTN	Quantitative; Rural and urban districts	43 health facilities, 62 healthcare workers	Survey; Modified WHO SARA questionnaire	DM, HTN	HSD, HW, HIS, MPK&T	86% DM, and 79% HTN services were available.
Bintabara et al. (2018) (26)	Tanzania	To assess health facilities' readiness to manage HTN	Quantitative; Countrywide	725 healthcare facilities	Survey; Modified WHO SARA questionnaire	HTN	HSD	28% of the health facilities had outpatient HTN services.

Peck et al. (2014) (36)	Tanzania	To assess NCDs burden and investigate facilities' readiness to manage DM and HTN	Quantitative; Urban and rural settings	335 healthcare workers	Modified WHO SARA questionnaire	DM, HTN	HSD, MPK&T	Most first-line healthcare facilities lacked guidelines, diagnostic equipment, trained staff and effective reporting systems.
Aekplakorn et al. (2005) (40)	Thailand	To assess primary healthcare providers' readiness to manage CVD along with community members perception and knowledge	Qualitative; Rural district	18 CVD patients, 33 community members, 29 health workers/professionals	Semi-structured interview; IDI, KII and FGD guides	CVD	HSD, MPK&T	Community members lacked minimal knowledge of the symptoms and signs of heart attack or stroke. Healthcare workers had limited skills to manage heart disease, while emergency care hospitals were insufficiently equipped to treat CVD patients.
Katende et al. (2015) (30)	Uganda	To assess the readiness of CD-related services	Quantitative; Urban and rural settings	28 health facilities, 222 health workers	Survey; Modified WHO SARA questionnaire	CRD, CVD, DM, Epilepsy, HTN, HIV	HSD, HW, MPK&T	Most primary care facilities had inadequate capacity to manage CDs
Musinguzi et al. (2015) (32)	Uganda	To assess health facilities' capacity to manage hypertension	Quantitative; Two districts	126 public & private health facilities, 271 healthcare workers	Survey; Non-validated questionnaire	HTN	HSD, MPK&T	Nearly 93% health facilities managed HTN services and all of them lacked trained staff, guideline, supplies, and diagnostic equipment.
Volk et al. (2015) (37)	USA	To examine clinicians' readiness to implement lung cancer screening programmes	Quantitative; Medical attendees	350 participants	Survey; Non-validated questionnaire	Cancer	HSD (screening)	50% clinicians planned to refer eligible patients for lung cancer screening.
Duong et al. (2019) (27)	Vietnam	To explore NCD service delivery availability, readiness and utilisation	Quantitative; Rural settings	89 community health centres	Survey; Modified WHO SARA questionnaire	DM, Cancer, CRD, HTN, Mental Illness	HSD, HW	25% of the health facilities had NCD services.
Kien et al. (2018) (41)	Vietnam	To explore responsiveness of commune health stations in urban settings to NCDs	Qualitative; Two districts	19 healthcare staff	Interviews; IDI guide	NCD focus was not specified	HSD, HW, HIS, MPK&T, HF, L&G	Healthcare professionals had limited knowledge about the national NCD strategy and lacked NCD-specific training and skills.
Meiqari et al. (2020) (44)	Vietnam	To describe the delivery and organisation of HTN care in primary healthcare settings	Mixed-methods; Rural and urban setting	90 healthcare staff, 29 hypertensive patients	Survey; Modified WHO SARA questionnaire; Semi-structured interview guide	HTN	HW, MPK&T	District-level health facilities had HTN services; however, capacity of facilities across districts to monitor prescription refills and disease for HTN patients varied.
Thi Thuy Nga et al. (2017) (45)	Vietnam	To describe commune health stations' readiness for NCD prevention and control	Mixed-methods; One district	20 commune health stations	Survey; Modified WHO SARA questionnaire; IDI and FGD guides	Cancer, CRD, DM, HTN	HSD, HW, HIS, MPK&T, HF, L&G	Commune health stations (CHSs) had limited capacity for NCD screening, diagnosis and treatment services.
Van Minh et al. (2014) (47)	Vietnam	To describe the primary care system's readiness for NCDs	Mixed-methods; One district	Health facilities and staff±	Survey; Non-validated questionnaire; Interview; IDI guide	NCD focus was not specified	HSD, HW, HIS, MPK&T, HF, L&G	Primary healthcare facilities had limited NCD management capacity and service integration.
Mutale et al. (2018) (33)	Zambia	To assess the health system's readiness to address NCDs	Quantitative; Three districts	46 primary healthcare facilities	Survey; Modified WHO PEN questionnaire	NCD focus was not specified	HSD	Only the first-level hospitals had a mean readiness index score (=>70%) for managing NCDs.
Mendis et al. (2012) (31)	Multi-country	To evaluate primary care facilities' capacity for the major NCDs	Quantitative; Multi-country*	90 primary healthcare facilities	Survey; Modified WHO PEN questionnaire	Cancer, CRD, CVD, DM	HSD, HW, HIS, MPK&T, HF, RS	Primary care facilities had inadequate financing, basic technologies and medicines, medical information systems and health workforce

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Note. CVDs: Cardiovascular Diseases, DM: Diabetes Mellitus, DHS: Demographic and Health Surveys, FGD: Focus Group Discussion, HTN: Hypertension, IDI: In-depth Interviews, KII: Key Informant Interview, HSD: Health Service Delivery, HW: Health Workforce, HIS: Health Information System, MPK&T: Medical Products, Knowledge and Technologies, HF: Health Financing, CRDs: Chronic Respiratory Diseases, NCD: Non-communicable Disease, WHO: World Health Organization, LMIC: Low- and Middle-Income Countries, L&G: Leadership and Governance, RS: Referral System, WHO SARA: WHO Service Availability and Readiness Assessment, WHO PEN: WHO Package of Essential Non-communicable Disease Interventions

*Multi-country includes Benin, Bhutan, Eritrea, Sri Lanka, Sudan, Suriname, Syria and Vietnam

[±]The number of participants/sample size was not specified.

[++]National Institute of Population Research and Training

Health service delivery

Of the 23 studies, 18 addressed issues related to the health service delivery system's readiness in preventing and managing NCDs at the primary healthcare level. Eleven of the 18 studies were quantitative studies, assessing primary healthcare facilities' readiness in implementing the WHO SARA reference manual (25-27, 29, 30, 36, 38, 45) or WHO PEN interventions (33-35). Three papers adopted the qualitative approach (40-42), while another three used the mixed-method approach (43, 45, 47). Four studies focused on a single NCD: DM, CVD (40) or HTN (26, 32). Five papers studied two NCDs (25, 35, 36, 38, 43), while seven investigated multiple NCDs and risk factors (27, 30, 31, 39, 41, 42, 48). However, two articles did not specify the NCDs that were evaluated (34, 47). Most of the studies found that healthcare facilities had insufficient capacity to deliver NCD prevention, care and treatment at the primary level. Among the NCDs, a higher level of readiness at the primary healthcare level was reported for hypertension prevention and management. The availability of hypertension services at healthcare facilities was reported to be 92.9% in Uganda (32) and 86% in Tanzania (25); however, one study found that hypertension preparedness was only 28% in Tanzania's outpatient care (26). A mixed-methods study in Thailand revealed that commune health stations were significantly prepared to manage HTN (44). The services readiness for CVD (47.8%), and DM (50%), were reported at the upazila health complex (UHC) in 2014 in Bangladesh(29, 38). However, the most recent data reported the availability of services largely varied from community clinic (CC) to 'UHC' for cervical cancer (0.4%-37.5%), CRD (34.1%-93.9%), CVD (1.4%-69.6%), DM (0.9%-84.5%), and, hypertension (3.5%-91.5%) (39). In Vietnam, only 25% of commune health centres were equipped to prevent, diagnose and treat major NCDs, with a noticeably lower utilisation rate of services by the users (27). Capacity for managing DM was predominantly low across all studies; however, one study in Tanzania (25) found that care for diabetes mellitus was available in 79% of healthcare facilities. Moreover, a lower level of readiness for managing CVD was reported across countries (31, 40, 42, 45). Qualitative studies conducted in Thailand (40) and India (43) noted facilities' low-level preparedness to manage HTN, DM and CVD, with healthcare facilities/programmes lacking effective community engagements and limited support

from the national programmes. In Kien et al.'s 2018 study conducted in Vietnam, one of the district-level health staff shared the following:

> [In our district] we implemented the hypertension programme for only four communes and implemented the diabetes programme for four other communes [among 18 communes]. We do not have any NCD programmes for the rest of the communes (41).

In a cross-sectional study conducted in Madhya Pradesh, India, the preparedness level for DM and HTN was reported to be slightly high (35). However, inadequate capacity was found for managing the common NCDs in a qualitative study in Odisha and Kerala, India (42). Lower levels of readiness for major NCDs have also been commonly reported in Zambia (33) and Ghana (34).

Overall, the delivery of NCD services was affected by multiple factors and revealed to be insufficient at the primary healthcare level. Inadequate and ill-equipped healthcare facilities were the most common issues hampering service delivery (25, 27, 31-35, 43). Moreover, notable key barriers include patients' lack of self-management education and knowledge (25), primary-level healthcare professionals' limited NCD management skills and national NCD strategies (25, 41), insufficient NCD service management and implementation capacity of local-level healthcare organisations (26, 47), a weak referral and follow-up system (30, 31), poor adherence to clinical guidelines (25, 30, 32, 36), inadequate screening opportunity (45), lack of information-education-community material (45) and the healthcare facility's rural location.

Healthcare workforce

Twelve of the studies reviewed reported a healthcare workforce issue related to NCD services and care. According to these papers, a common bottleneck for NCD services is insufficient primary-level healthcare professionals. One cross-sectional study in Tanzania reported only 53% and 15% of healthcare facilities had trained health professionals to manage HTN and DM, respectively (25). In Thailand (40) and Vietnam (45, 47), there was an acute lack of trained healthcare staff to manage CVD.

Moreover, a study conducted in Uganda found that only 26% and 16% of primary healthcare staff had an adequate level of knowledge to manage DM and HTN outpatients, respectively (30). This study also revealed that medical doctors had a higher level of knowledge (85% for HTN and 8% for DM) than nurses (8% for HTN and 4% for DM) (30). One study in Vietnam reported that only 9% of primary healthcare facilities in rural and urban locations had five categories of human resources (medical doctor, assistant doctor, nurse, midwife and pharmacist) to deliver HTN services (44). The shortage of trained healthcare staff (at least one staff received in-service training in the last 24 months before the data collection date) was reported at the primary healthcare in Bangladesh (39). The trained staff for cervical cancer (29% trained staff at the UHCs, but no trained staff in CCs and union-level facilities), CRD (4% union-level facilities, 11% CCs, and 29% UHCs), CVD (7% union-level facilities, 15% CCs, and 40%, UHCs), DM (3% union-level facilities, 14% CCs, and 28% UHCs), and hypertension (6% union-level facilities, 10% CCs, and 39% UHCs) were reported (39). According to a multi-country study, physicians at primary healthcare facilities were only available in two of the eight participating nations, while nurses and healthcare assistants were the key professionals for NCD services in the remaining six countries (31). A study in Ghana found that more than half of the healthcare centres lacked at least one medical doctor and nurse trained in NCDs (34). In India, while two medical officers were available on average at community health centres to manage DM, CVD, HTN and cancer, this number was lowest (less than half) in primary healthcare centres (35). In qualitative studies conducted in India (42) and Vietnam (41), insufficient healthcare staff jeopardised NCD services in primary care facilities. An NCD programme officer in Odisha, India and a national-level health worker in Vietnam shared their respective thoughts:

> In a big community health centre like ours, there should be more health workforce, and there should be a special training programme for all the health workers (42).

> For the health workforce at commune health stations, some facilities lack human resources and/or capacity. They must be strengthened in their capacity to provide services for NCD prevention, consultation, early detection and management. The reason for this is that we have not implemented NCD services systematically at primary healthcare facilities (41).

Health financing

Seven studies found that inadequate funding/budget support from the national healthcare programme compromised effective NCD service and care at the primary healthcare level. Furthermore, the absence or limitation of healthcare insurance coverage jeopardised NCD services and care. One study in India reported that less than 3% of households had insurance coverage (43). A study in Ghana revealed that healthcare financing is organised by the government as the 'National Health Insurance Scheme', and only those who paid the premium received its benefits (34). Limited public financial/budgetary support has also been identified as a major barrier to NCD services in primary healthcare in Vietnam (45, 47). A national-level health worker in Vietnam conveyed the following to Kien et al. in 2018:

> The budget for NCD primary health care services is extremely limited; [funding is] mainly through national target programmes on NCDs, but the programmes have been reduced. There are some barriers to health insurance reimbursement for NCDs at the primary health care level (41).

Similarly, in a qualitative study, a medical officer from Odisha, India shared his observation:

> Since there is no existing system, funds do not reach the grassroots level. There is no funding (42).

Access to medical products, knowledge and technologies

Across countries and regions, a lack of supply-side factors, such as medical products and knowledge and technologies to prevent and manage NCDs, has been widely reported. Fifteen studies reported inadequate or interrupted access to supplies and technologies at the primary healthcare level, which are vital for diagnosing and treating NCDs. In Bangladesh, the availability of medicine widely varied at the UHCs based on their types for DM (metformin 38.1%, glibenclamide 7.4%), CRD (salbutamol 91.6%, epinephrine 0.3%), CVD (amiodipine/nifedipine 41.5%, aspirin 2.6%), and HTN

(amlodipine/nifedipine 44.7%, thiazide 1.4%), but no supply in the CCs were reported (39). In India, the essential drugs for the management of HTN (beta-blockers and calcium channel blockers) were available at most of the primary health centres (PHCs) and community health centres; however, other drugs (except metformin) were largely unavailable across facilities that resulted in 90% of NCD patients in India to rely on private providers/facilities for NCD service and care (35). More than 60% of PHC-level facilities faced a shortage of essential DM medicine, with over 30% of PHCs having a medicine stockout of more than six months. Only 38% of PHCs had functional laboratory facilities (43). According to a study conducted in Tanzania, 50% of health centres, 24% of dispensaries and 80% of hospitals had HTN and DM medicines on hand; however, more than one-third of these locations lacked basic laboratory facilities (25). A qualitative study in Vietnam (41) and a qualitative multi-country investigation (Benin, Bhutan, Eritrea, Sri Lanka, Sudan, Suriname, Syria and Vietnam) (31) likewise reported the shortage of medicine and basic diagnostic facilities at primary healthcare facilities. Moreover, basic amenities and equipment for NCDs were in short supply in Ugandan healthcare facilities (hospitals and healthcare centres), with more than half of them lacking the recommended antihypertensive drug and nearly 30% lacking a blood pressure device (32). Likewise, Tanzanian healthcare facilities reported a shortage of the recommended medicine and supplies required for HTN and DM service and care (36). Similarly, a mixed-method study found a scarcity of medical products and equipment for CRD, DM, cancer and HTN in Vietnam (45). However, basic equipment and diagnostic facilities such as stethoscope (93.2% CCs, 96.9% UHCs), blood pressure apparatus (85.6% CCs, 95.4% UHCs), adult scale (90.9% CCs, 82.9% UHCs), blood glucose testing (22.2% CCs, 48.9% UHCs), urine protein (0% CCs, 36.2 % UHCs), and urine glucose (0% CCs, 30.4 % UHCs) were available in Bangladesh (39).

Health information system

Studies that assessed the health information system's readiness were limited. Only five papers addressed the health information system required for optimising NCD care at the primary healthcare level (25, 31, 41, 45, 47). These studies extensively reported on weak health information systems for detecting,

treating and monitoring NCD patients in primary healthcare settings. Furthermore, only 52.9% of primary healthcare facilities in Tanzania were prepared to collect, analyse and use local-level data for HTN and DM services (25). According to a multi-country survey, 85% of healthcare facilities created paper-based (patient register) individual-level information for patients who attended the facilities, but only half of that information was used at the follow-up visit (31). Weak and ineffective health information system management and inadequate NCD information, such as a lack of population-based NCD-related data on risk factors, mortality, disability and referral systems at the primary healthcare level, have been identified as crucial barriers to managing NCDs in Vietnam (41, 45).

Leadership and governance

Four studies investigated issues of leadership and stewardship in the management of NCDs in primary healthcare (41, 42, 45, 47). The research reported a lack of coordination among stakeholders and departments in implementing nationally designed NCD programmes/interventions. A qualitative study in India discovered weak inter-departmental coordination between various government departments (e.g. mental health programme and tobacco control programme), which resulted in poor NCD outcomes at the primary care level (42). The primary care-level NCD managers lacked knowledge of Vietnam's national NCD strategy or policies affecting targeted interventions for cancer, CVDs and diabetes (41). Limited knowledge of NCD management strategy and insufficient leadership capacity were highlighted among front-line healthcare staff (41). Furthermore, a lack of interaction between private and public providers and stakeholders was reported for NCD prevention/management activities in Vietnam (45). A mixed-method study found that Vietnam's nationally targeted NCD management and control programme lacked leadership and governance capacity (47).

Community perspective

Only two studies, conducted in the Netherlands and New Zealand, explored community perspectives on patients' capacity for using healthcare information, self-management and sharing problems when

seeking aid to manage NCDs at the primary healthcare level. A mixed-method study in the Netherlands (46) showed that, during a consultation, people with diabetes had a low-level ability to share psychological issues with healthcare providers at the primary healthcare level. In New Zealand, the readiness of patients with NCDs (cancer, chronic pain, diabetes and mental health problems) was low, with only 36% of them seeking health-related information from digitalised sources (28). This demand-side perspective was not addressed in studies from low- and middle-income countries.

Quality of included studies / Quality assessment

Nearly three-fifth (61%) of the studies were of good quality (MMAT score of 75) (Table 1): one paper (4%) had an MMAT score of 25 (low quality), eight (35%) scored 50 (medium quality), eleven (48%) received 75 (good quality) and three (13%) reached 100 (high quality). No study had an MMAT score of 0 (poor quality).

Discussion

This review appraised available evidence on health system readiness for NCDs at the primary healthcare level. The key findings of this study were that health systems at the primary healthcare level were inadequately prepared for NCD prevention and management, and that readiness was poorly understood. Health system readiness was examined from the providers' perspectives, which is specifically focused on the availability of infrastructures and supply of resources (e.g. medicine, basic amenities, medical products and technologies) as devised in the WHO SARA methodology or WHO PEN interventions. This may have narrowed the 'systems thinking' approach, which is a core philosophical basis that incorporates various elements and their interactions and interconnectedness to function as a system (19). Viewing the health system from this constricted sense categorically failed to include people's (service users') dimensions, which is an essential consideration for a well-functioning and inclusive health system. One plausible reason for predominantly analysing the health system from the supply-side

perspective was the widespread acceptance of the WHO health system framework and its broader applications in individual studies. Over the past years, the 'building block' approach appeared as a dominant health system method globally (49), supporting the existing trend of assessing the health system from the supply-side perspective. Thus, the demand-side perspectives of health system readiness for NCDs warrant extensive investigation. Future research may focus on the demand-side aspects of the health system's readiness, such as community characteristics and associated determinants needed to establish an effective and inclusive health system to respond to the NCD epidemic.

This review demonstrated that almost all countries' primary healthcare systems have suffered from inadequate supply-side responses to medicine, technologies, equipment, amenities, trained healthcare professionals, health information and leadership and stewardship. The ill-equipped health system may result from insufficient financing mobilised through international and domestic channels and a lack of policy priority in responding to NCDs (50-52). Among the NCDs addressed by the studies in this review, DM and HTN received the most attention in the current literature. Hence, other major NCDs such as CVD, CRD and cancer, which are prioritised by the WHO, remain largely under-researched. The focus on DM and HTN may be due to multiple factors, including increasing prevalence and associated determinants/risk factors for other NCDs in low- and middle-income countries, a nationwide vertical programme, individual-level professional capacity and greater resource mobilisation (53-55), all of which have facilitated DM and HTN care, management and research. Moreover, the integrated model for DM and HTN care has widely been considered in the low-and middle-income countries that accelerated the provision of effective and equitable health service delivery at the primary healthcare level, which would have helped to address the rising burden of them with accessible, equitable, and cost-effective interventions (56-58). This review revealed that at the primary healthcare level, health system readiness for major NCDs was primarily concentrated on the diagnosis and treatment aspects. However, readiness for health promotion and preventive interventions, provision of palliative care, screening, identification of risk factors, self-management and health education have remained under-investigated and of less priority (59, 60). As such, primary and secondary prevention of NCDs was

emphasised in the WHO's NCD prevention and control strategy in 2011 (61) and has been highlighted in the current literature to reduce NCD-related morbidities and deaths (62-64). Preventive and health promotional activities on key NCD risk factors, (61, 65) such as tobacco consumption, salt intake, physical inactivity, harmful alcohol use and unhealthy diet, stress that these can be addressed at the primary healthcare level to improve NCD outcome. The potential for a well-prepared health system is realised when promotional and preventive services are adequately provided at the primary healthcare level (66, 67). Lack of a comprehensive prevention and management approach led us to hypothesise that the full potential of the health system's response to NCDs may have been hindered at the primary healthcare level. Majority of the studies in this review had good or high quality. However, a large proportion of the study reflected inexplicit evidence due to the methodology, small sample size, bias, and incomplete information. A few quantitative studies lacked sufficient details about the participants' selection criteria, standard criteria for minimizing bias, and use of non-validated questionnaires with a relatively small sample size that might affect the scope of generalizability of the findings (27, 29, 32, 34, 35). One mixed-method study was rated low quality due to the homogeneous sample and insufficient information about the data analysis (47). The rest of the mixed-method studies included in the review had a more representative sample size and methodological rigors. The majority of the included studies used the WHO's health system framework as an analytical basis to identify the health system components. However, some studies lacked a deeper analysis of the interplay and interconnectedness between different health system components. Despite these limitations, this study provides important information regarding current evidence on the readiness of the primary healthcare system for NCDs. Additionally, most of the selected studies in this review were conducted in resource-poor settings, primarily in sub-Saharan African and South East Asian countries. The smaller number of studies in developed countries may be explained by their adoption of a specialised disease management strategy, which lessens the focus on comprehensive management of NCDs at the primary healthcare level (68). An extensive investigation of community characteristics and associated factors may be necessary for establishing a well-functioning and more responsive health system to respond to NCDs (24).

Strengths and limitations

This review's main strength was an inclusive data synthesis informed by the health system dynamics framework, which offers a deeper and more comprehensive (both supply-side and demand-side factors) understanding of primary healthcare system readiness for NCDs. Conducting An extensive systematic search of literature with hand-searching references and expert advice increased the validity and trustworthiness of this review's findings. On the other hand, one of its limitations was that a few studies that reported health system readiness at combined primary and secondary healthcare levels were excluded. Moreover, the selected studies had heterogeneous study designs, methods and techniques, and focused on a variety of health system components, preventing meta-analysis. Another limitation was that studies containing relevant information published in languages other than English have been excepted, which may have influenced the results of this review.

Conclusion and future direction

This review demonstrated that health systems at the primary healthcare level are insufficiently prepared for NCD prevention and management, especially for CVD, CRD and cancer. The existing health system response was characterised by insufficient 'supply-side' factors (i.e. supply of medicine, equipment and technology), a lack of appropriate NCD management strategies and guidelines, a weak health information system, limited resources, uncoordinated local-level stewardship and leadership and a shortage of human resources. One of the notable findings was that the primary healthcare system's readiness over the years was evaluated from the 'supply-side' perspective; hence, there is a significant knowledge gap in the literature from the 'demand-side' standpoint. This observation may be useful for future research into users' views on NCD management at the primary healthcare level, including NCD management practice, knowledge, attitude, care-seeking behaviour, adherence to treatment, self-management and coping strategies.

Author Contributions

AK, NK and BB created the manuscript. AK and LR led the literature search. AK, NK, RI and BB screened the literature and completed the mapping. AK led the drafting process, while NK, RI and BB provided substantial input. All authors read and approved the final manuscript.

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Data availability statement

No additional data are available.

Competing interest

The authors declare that they have no competing interests.

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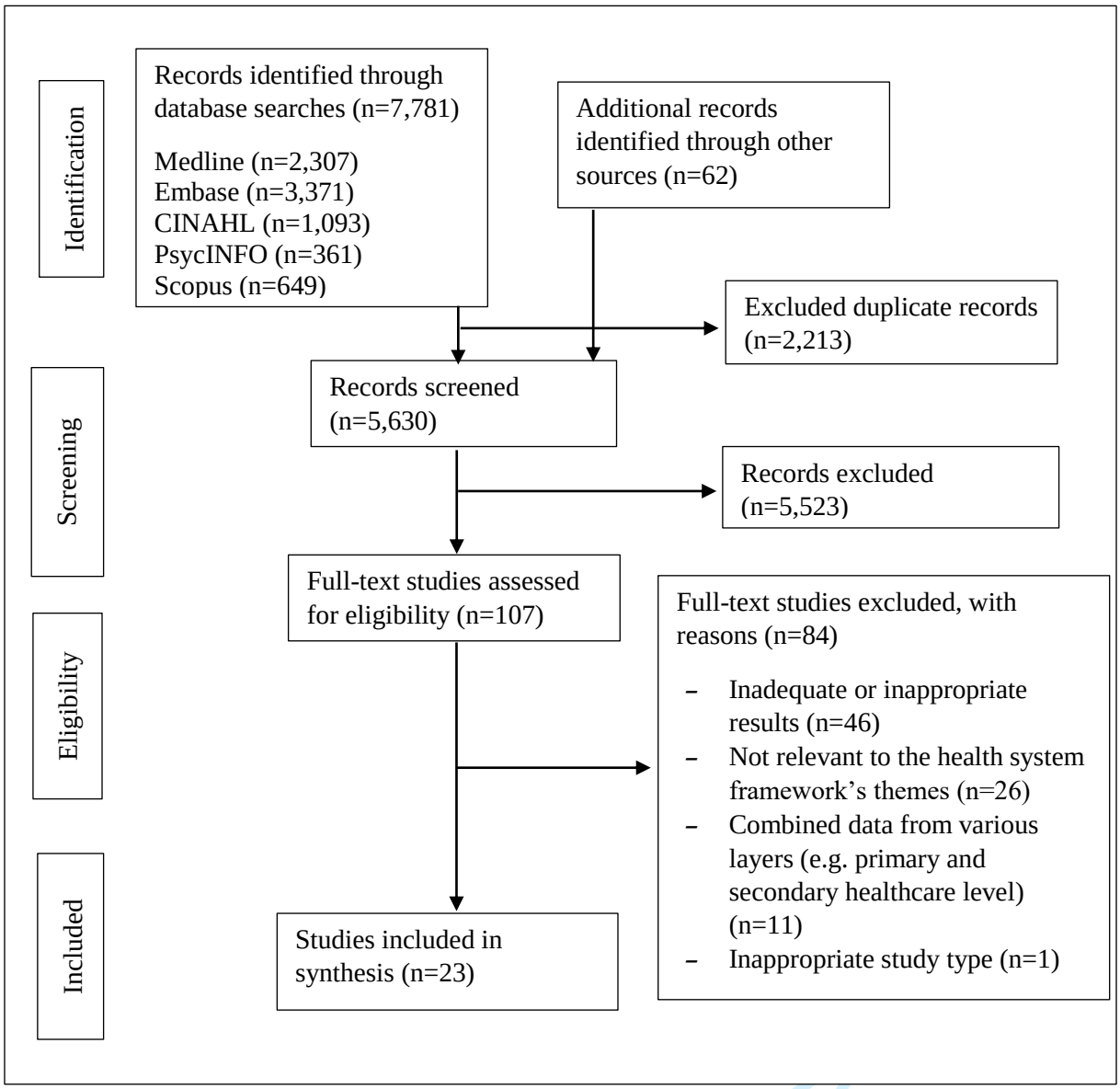
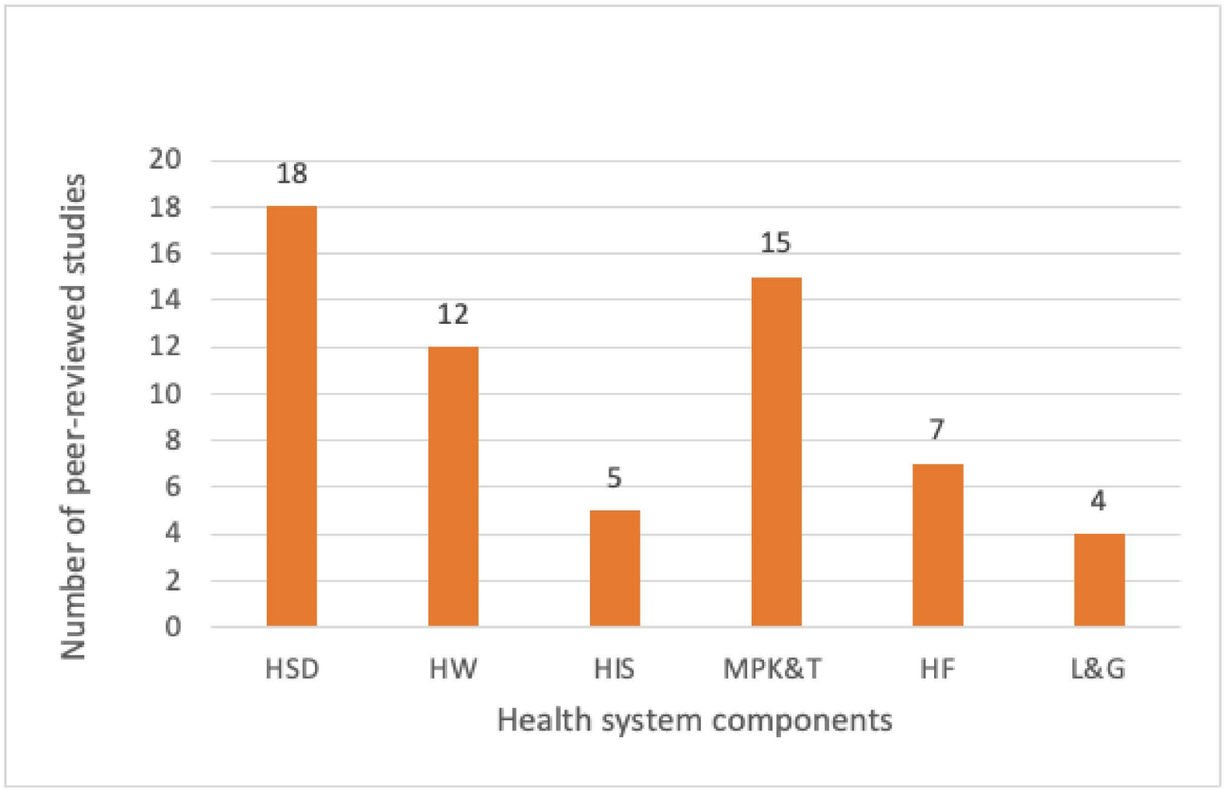
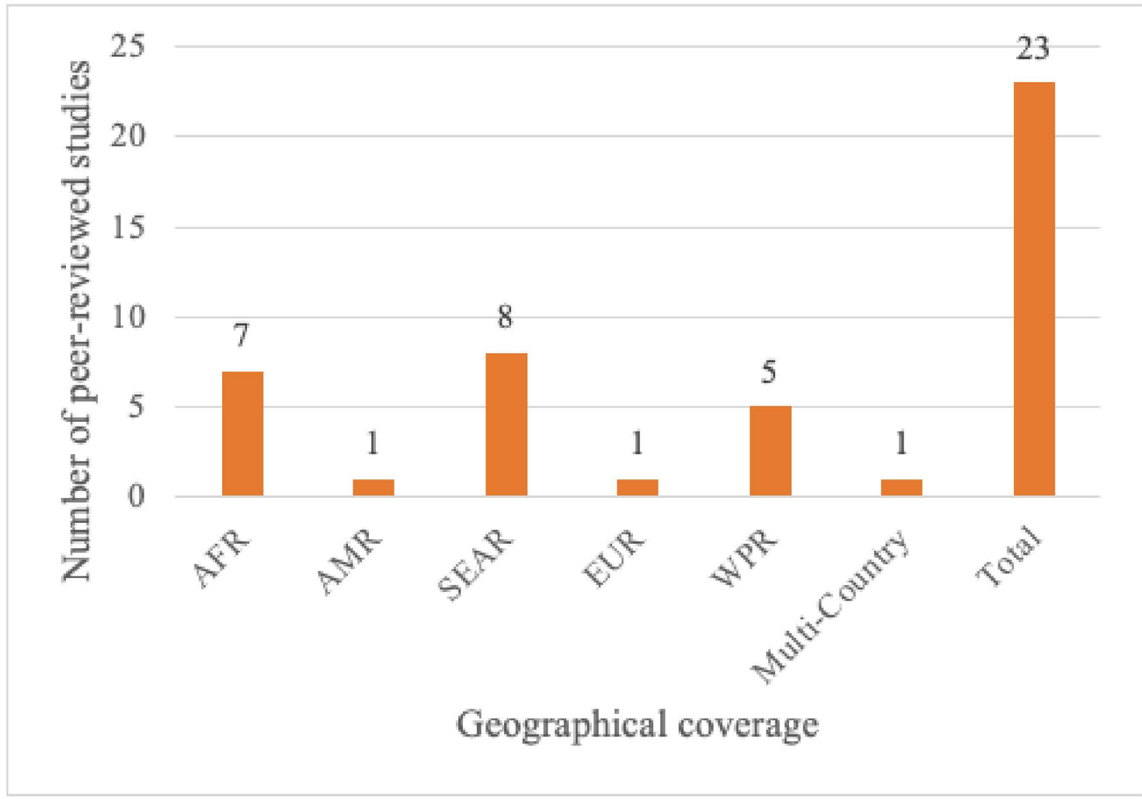


Figure 1 PRISMA flowchart for study inclusion.

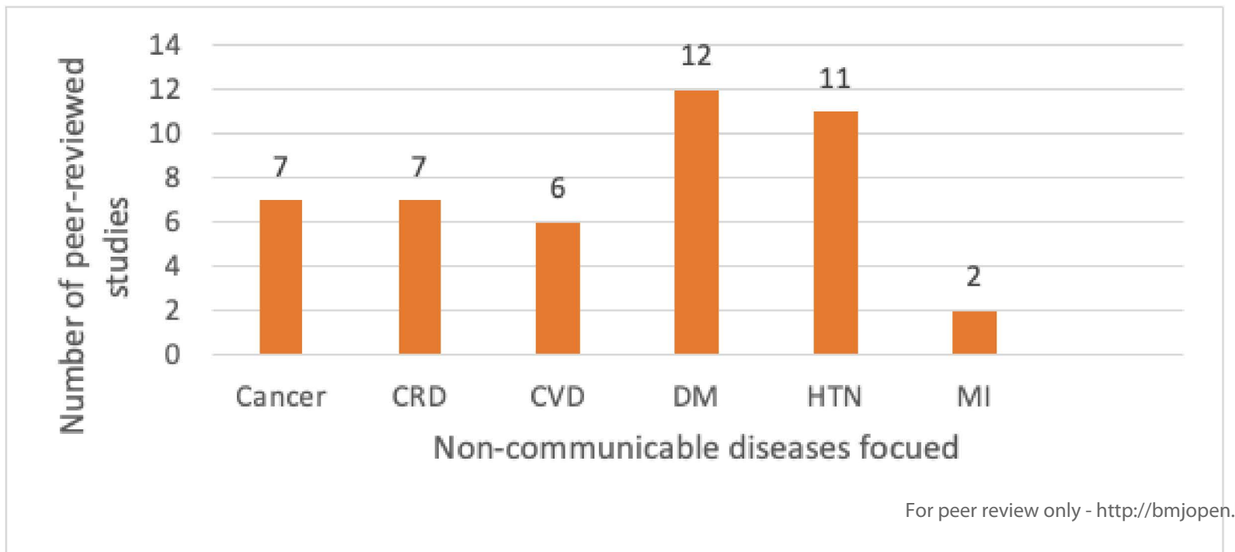
a



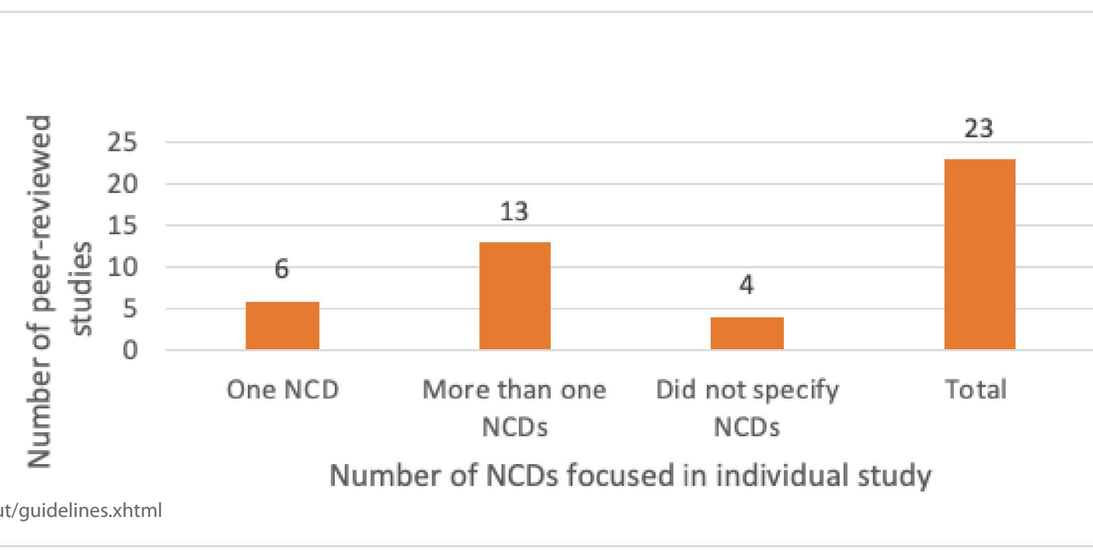
b



c



d



Supplementary appendix

Table S1. Literature search strategy

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)** Search Strategy:**1st of January 1984 to July 30th 2021**

#	Searches
1	chronic disease/ or multiple chronic conditions/ or non communicable disease/
2	(chronic disease* or chronic disorder* or chronic* sick* or chronic health condition* or chronic medical condition* or chronic* ill* or long term condition* or multimorbidit* or mult imorbidit*).mp.
3	(non-communicable disease* or non-infectious disease* or noncommunicable disease* or noninfectious disease*).mp.
4	(cardiovascular disease* or coronary artery disease* or myocardial isch?emia or myocardial infarct* or pulmonary disease* or chronic obstructive pulmonary or chronic obstructive lung or chronic obstructive respiratory or diabetes or coronary heart disease* or neoplasm* or cancer*).mp.
5	(hypertension or hypertriglycerid?emi* or hyper triglycerid?emi* or high triglyceride* or high cholesterol or hypercholesterol?emi* or hyperlipid?emia* or hyperlipidemi*).mp.
6	(diastolic pressure or systolic pressure or blood pressure or cardiometabolic syndrome*).mp.
7	(copd or asthma or renal disease* or kidney disease*).mp.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	Primary Health Care/
10	Delivery of Health Care/
11	(primary health system or primary health service or primary healthcare system or primary health care system or primary healthcare service or primary health care service or primary medical service delivery or primary medical care service or primary care service or primary care system).mp.
12	(first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*).mp.
13	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*)).mp.
14	9 or 10 or 11 or 12
15	8 and 14
16	(readiness or preparedness or capacity or quality improvement or quality of Improvement).mp.
17	15 and 16
18	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj5 (accessibility or availability)).mp.
19	8 and 18
20	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj (need* or demand*)).mp.
21	8 and 20
22	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*) adj3 (need* or demand*)).mp.

23	8 and 22
24	17 or 19 or 21 or 23
25	limit 24 to english language
26	limit 25 to (case reports or comment or editorial or letter or news)
27	25 not 26

Database(s): Embase Classic+Embase

Search Strategy:

#	Searches
1	exp antineoplastic agent/ or cancer therapy/ or bone marrow purging/ or bone marrow rescue/ or exp cancer adjuvant therapy/ or exp cancer chemotherapy/ or cancer gene therapy/ or cancer hormone therapy/ or exp cancer immunotherapy/ or exp cancer radiotherapy/ or multimodality cancer therapy/ or oncolytic virotherapy/ or target cell destruction/ or immunotherapy/ or adoptive immunotherapy/ or exp chimeric antigen receptor immunotherapy/ or radioimmunotherapy/ or exp radiotherapy/ or exp bone marrow transplantation/ or exp hematopoietic stem cell transplantation/ or stem cell transplantation/ or cancer patient/ or cancer survivor/
2	exp neoplasm/dt, rt [Drug Therapy, Radiotherapy]
3	(anti-cancer* or anti-neoplas* or anticancer* or antineoplas* or anticancerogen* or anticarcinogen* or anti-carcinogen* or anti-tumo?r* or antitumor?r* or cancer inhibitor* or tumo?r inhibitor* or anti-leukemi* or antileukemi* or oncotherap* or antimetastatic* or anti-metastatic* or antimetastas#s or anti-metastas#s).mp.
4	((cancer* or tumo?r* or neoplas* or carcinoma* or malignan* or adenocarcinoma* or sarcoma* or lymphoma* or leukemi* or blastoma* or carcinostatic or oncolog* or carcinocidal or oncocidal or oncostatic) adj3 (therap* or drug* or agent* or chemotherap* or electrochemotherap* or treat* or medication* or compound* or immunotherap* or immunological or immunomodul* or immunomodurat*)).mp.
5	((adenoma* or chondrosarcoma* or osteosarcoma* or rhabdomyosarcoma* or astrocytoma* or ependymoma* or glioma* or neuroblastoma* or medulloblastoma* or oligodendroglioma* or pheochromocytoma* or retinoblastoma* or cholangiocarcinoma* or melanoma* or mesothelioma* or pheochromocytoma* or paraganglioma* or craniopharyngioma* or esthesioneuroblastoma* or myeloma*) adj (therap* or treatment* or drug* or agent* or medication* or vaccine*)).mp.
6	((cancer or tumo?r) adj (cure* or healing or remed* or vaccin* or adjuvant therap* or multichemotherap* or polychemotherap* or gene therap* or hormon* therap* or radiation or irradiation or ablation or immun* therap*)).mp.
7	((cancer or carcinoma or adenocarcinoma or sarcoma or lymphoma or leukemia or blastoma or adenoma or chondrosarcoma or osteosarcoma or rhabdomyosarcoma or astrocytoma or ependymoma or glioma or neuroblastoma or medulloblastoma or oligodendroglioma or pheochromocytoma or retinoblastoma or cholangiocarcinoma or melanoma* or mesothelioma or pheochromocytoma or paraganglioma or craniopharyngioma or esthesioneuroblastoma or myeloma or oncolog*) adj (patient* or survivor* or sufferer*)).mp.
8	(alkylating adj (agent* or chemical* or compound* or cytostatic*)).mp.
9	(((angiogenesis or neovascularisation or tumo?r vascularisation) adj inhibitor*) or ((angiostatic or anti-angiogenesis or antiangiogenesis or anti-angiogenic or antiangiogenic or antimutagenic) adj (agent* or drug*))).mp.
10	(abecomotide or abemaciclib or abexinostat or abieslactone or abivertinib or abrotanone or aburatubolactam A or aburatubolactam C or abyssinone V or acalabrutinib or acalisib or aceglatone or acodazole or adaphostin or adarotene or adavosertib or aderbasib or afamitresgene autoleucel or afatinib or afuresertib or Agaricus blazei extract or agatolimod or agerafenib or aglatimagene or besadenovec or albicanyl acetate or aldesleukin or alectinib or alicdamotide or alisertib or adozelesin or alkanesulfonic acid or amsacrine or amsacrine derivative or asulacrine isethionate or busulfan or dimethylbusulfan or mesylic acid or mesylic acid derivative or mesylic acid ethyl ester or mesylic acid methyl ester or mesylmesylic acid 2 chloroethyl ester or methylene dimesylate or treosulfan or ametantrone or anaxirone or aziridine derivative or apaziquone or azimexon or aziridine or aziridinylbenzoquinone or azirine derivative or carboquone or ciamexon or diaziquone or dipin or pumitepa or

	thiotepa or tretamine or tretazicar or triaziquone or uredepa or banoxantrone or bisantrene or bizelesin or brostallicin or carboplatin or carzelesin or chlormethine derivative or acridine mustard or aldophosphamide or alestramustine or ambamustine or amustaline or aniline mustard or bendamustine or benzoquinone mustard or bestrabucil or canfosfamide or chlorambucil or chlormethine or chlornaphazine or cloturin or cortifen or cyclophosphamide or cydrin or dichlorodiethylamine or dopan or estramustine or evofosfamide or galamustine or glufosfamide or gonadorelin or ifosfamide or laromustine or mafosfamide or mafosfamide cyclohexylamine or mafosfamide lysine or mannomustine or melphalan or mepacrine mustard or palifosfamide or peptichemio or perfosfamide or phenesterin or phosphoramide mustard or sarcolysin or sufosfamide or tallimustine or tinostamustine or trofosfamide or uramustine or xylamine or cisplatin or cyclodisone or dacarbazine or dianhydrogalactitol or etoglucid or imidacrine or irofulven or ledoxantrone or losoxantrone or mitoxantrone or nitrosourea derivative or bofumustine or butylnitrosourea or carmustine or chloroethylnitrosourea or chloroethylnitrosourea derivative or cystemustine or ecomustine or elmustine or estradiol 17 or ethylnitrosourea or fotemustine or lomustine or methylnitrosourea or nimustine or nitrosourea or prednimustine or ranimustine or semustine or spirazidine or spiromustine or streptozocin or tauromustine or nortopixantrone or oxanthrazole or pentamethylmelamine or pixantrone or procarbazine or teloxantrone or temozolomide or topixantrone or alobresib or alpelisib or alpha sarcin or altemicidin or alteminostat or altiratinib or altretamine or ambazone or amcasertib or amidox or aminothiadiazole or amonafide or amphethinile or amphidinolide A or amphidinolide B or amphidinolide D or amsilarotene or amuvatinib).mp.
11	(acrizanib or aflibercept or aganirsen or alofanib or anecortave or anginex or angiostatic protein or angiostatin or angiozyme or atiprimod or avadomide or axitinib or beloranib or bermekimab or bevasiranib or brivanib or cabozantinib or canstatin or caplostatin or carlumab or carotuximab or cediranib or cenupatide or cetuximab or cilengitide or combretastatin A1 phosphate or conbercept or conendostatin or crenolanib or crizotinib or dalantercept or depudecin or dovitinib or endostatin or endothelial monocyte activating polypeptide II or fexapotide or foretinib or foslinanib or fruquintinib or fumagillol chloroacetylcarbamate or glesatinib or infigratinib or lapatinib plus pazopanib or lenalidomide or lenvatinib or linifanib or lucitanib or maspin or monoclonal antibody DC101 or monoclonal antibody imc 1c11 or motesanib or muparfostat or dicarboxamide or navicixizumab ornintedanib or ofranergene obadenovec or oglufanide or orantinib or paclitaxel or pazopanib or pegaptanib or pegdinetanib or pegpleranib or pixatimod or pomalidomide or ranibizumab or recombinant endostatin or regorafenib or relzomostat or rinucumab or risuteganib or roneparstat or semaxanib or "siRNA 027" or sonepcizumab or sorafenib or squalamine or sunitinib or tanomastat or tasquinimod or tesevatinib or thalidomide or thrombospondin 1 or thrombospondin 2 or tigapotide or tiomolibdate choline or tirbanibulin or tivozanib or toceranib or trabedersen or trebananib or tumstatin or vandetanib or varisacumab or vascular endothelial growth inhibitor or vascular endothelial cell growth inhibitor or vascular endothelial growth factor antagonist vascular endothelial growth factor inhibitor or VEGF inhibitor or vasculotropin inhibitor or abicipar pegol or bevacizumab or brolucizumab or catequentinib or dilpacimab or faricimab or olinvacimab or pamufetinib or ramucirumab or rivoceranib or sintilimab or vulinacimab vatalanib or volociximab or vorolanib or metastasis inhibitor or carcinostatic alkaloid or acronine or afeletecan or atiratecan or becatecarin or belotecan or camptothecin or topotecan or cephalotaxine or coralyne or cositecan or cyclopamine or datelliptium chloride or deacetylvinblastine or demecolcine or diazepinomicin or diflomotecan or ellipravin or ellipticine or elliptinium or elomotecan or etirinotecan pegol or etoposide or exatecan or exatecan alideximer or fagaronine or firtecan or gimatecan or govitecan).mp.
12	(harringtonine or homoharringtonine or indicine n oxide or indirubin or irinotecan or lorvotuzumab mertansine or lurbinectedin or maytansine or mitopodozide or mureletecan or namitecan or napavin or narciclasine or nitidine or olivacine or patidegib or pazelliptine or pegamotecan or retelliptine or rubitecan or senecionine or sinococuline or solamargine or swainsonine or tenifatecan or teniposide or thalicarpine or trabectedin or trewiasine or trimethylcolchicinic acid or vinblastine or vincristine or vindesine or vinflunine or vinfosiltine or vinleucinol or vinleurosine or vinorelbine tartrate or vintafolide or vintriptol or vinzolidine or withanolide or carcinostatic antibiotic or 21 aminoepothilone B or 3 deazaaristeromycin or actinobolin or 7 aminodactinomycin or actinomycin derivative or adozelesin or alanosine or alvespimycin or ankinomycin or anthracycline antibiotic agent* or 11 deoxydaunorubicin or 2 fluoroidarubicin or 2 pyrrolinodoxorubicin or 4 demethoxy 11 deoxydaunomycinone or 4 demethoxydaunomycinone or 4 demethoxydoxorubicin or 4 iodoesorubicin or 5 iminodaunorubicin or 9 deacetyl 9 methylidarubicin or 9 deoxydoxorubicin or aclacinomycin or aclacinomycin B or aclarubicin or adriamycinone or aklavinone or aldoxorubicin or amrubicin or annamycin or anthracycline or anthracyclinone derivative or barminomycin I or berubicin or camsirubicin or carubicin or cinerubin A or

	cinerubin B or daunomycinone or daunorubicin or monoclonal antibody conjugate or daunorubicinol or decilorubicin or detorubicin or ditrisarubicin B or doxorubicin or doxorubicinol or epirubicin or epirubicinol or epsilon rhodomycinone or esorubicin or galarubicin or gancotamab or idarubicin or idarubicinol or ladirubicin or leurubicin or n benzyldoxorubicin 14 valerate or n trifluoroacetyldoxorubicin or n trifluoroacetyldoxorubicin 14 hydrogen adipate or nemorubicin or obelmycin or oxaunomycin or pirarubicin or pyrromycinone or rhodomycin A or rodorubicin or ruboxyl or sabarubicin or valrubicin or viriplanin A or zoptarelin doxorubicin or zorubicin or anthramycin or arasangivamycin or asperlin or auromomycin or azaserine or bactobolin or bizelesin or blasticidin S or bleomycin or bleomycinic acid or liblomycin or pepleomycin or cactinomycin or cadeguomycin or calicheamicin or gemtuzumab or inotuzumab ozogamicin or calphostin or caplostatin or carzelesin or chartreusin or chlorozotocin or chromomycin or chrysomycin or colabomycin A or congocidine or cordycepin or dactinomycin or dehydrodidemnin B or dehydroxysparsomycin or didemnin or distamycin A derivative or duocarmycin or duocarmazine or duocarmycin SA or dynemicin A or echinomycin or echinosporin or elsamicin A or epothilone or esperamicin or formycin or fostriecin or fredericamycin A or fumagillin or fumagillol).mp.
13	(geldanamycin or gilvocarcin V or glidobactin or granaticin or hadacidin or herbimycin or himastatin or illudin or irofulven or ixabepilone or kapurimycin or kedarcidin or leinamycin or lidamycin or luzopeptin or macbecin I or macromomycin or marcellomycin or menogaril or mithramycin or 7 n acetylmitomycin C or mitomycin or porfiromycin or musettamycin or mycophenolic acid or n bromoacetyldistamycin A or neothramycin or neplanocin A or nogalamycin or olivomycin or oxanosine or ozogamicin or pactamycin or pibenzimol or pibrozelesin or pirazofurin or prodigiosin or puromycin or pyrindamycin A or pyrindamycin B or quinocarcin or rachelmycin or rebeccamycin or resorthiomycin or retaspimycin or reumycin or rodaplutin or romidepsin or rubomycin or rufocromomycin or saframycin or sagopilone or sangivamycin or sapurimycin or sarkomycin or showdomycin or sibiromycin or sparsomycin or spergualin orspicamycin or spongistatin 1 or spongistatin 2 or streptonigrin derivative or tallysomycin or tanespimycin or tetracenomycin C or thiocoraline or thrazarine or tomaymycin or tubercidin or tuftsin or vicenistatin or yunnanmycin or zinostatin or buthionine sulfoximine or folic acid antagonist or folic acid antimetabolite or pteroylglutamic acid antimetabolite or 10 deazaaminopterin or 7 hydroxymethotrexate or aminopterin or arfolitixorin or bromebric acid or dichloromethotrexate or edatrexate or gamma fluoromethotrexate or homofolic acid or lometrexol or metesind or methotrexate or metodiclorofen or nolatrexed or pelitrexol or pemetrexed or piritrexim or plevitrexed or pralatrexate or raltitrexed or talotrexin or triazinate or trimetrexate or oxythiamine or purine antagonist or 4 carbamoylimidazolium 5 olate or 6 methylthioinosine or 6 n benzyladenosine or 8 azaguanine or azaguanosine or azathioprine or cladribine or clofarabine or cloturin or deoxythioguanosine or dezaguanine or fludarabine or guanine 7 oxide or guanine arabinoside or mercaptopurine or nelarabine or pentostatin or selenazofurin or sulfenosine or sulfinosine or sulfonosine or thioguanosine or tiazofurin or tioguanine or pyrimidine antagonist or 3 deazauridine or 3 ethynylcytidine or 5 chlorodeoxycytidine or 5 hydroxymethyldeoxyuridine or 5 aminothymidine or 5 deoxy 5 fluorocytidine or 6 azacytidine or ancitabine or azacitidine or azauracil or azauridine or brequinar or bromodeoxycytidine or capecitabine or carmofur or cloxuridine or cytarabine or cytarazid or decitabine or dihydrofluorouracil or doxifluridine or elacytarabine or emitefur or enocitabine orfazarabine or fiacitabine or floxuridine or flucytosine deoxyriboside or fluorouracil or fluorouridine or fosfluridine tidoxil or fosgemcitabine palabenamide or fosifloxuridine nafalbenamide or galocitabine or gemcitabine or gimeracil plus oteracil potassium plus tegafur or guadecitabine or orzel or ropidoxuridine or sapacitabine or tegafur or tezacitabine or tipiracil plus trifluridine or troxacitabine or uracil arabinoside).mp.
14	(4 hydroxytoremifene or abiraterone or acetylsalicylic acid plus aluminum hydroxide plus ascorbic acid plus prednisone or acetylsalicylic acid plus caffeine plus phenacetin plus prednisolone or acetylsalicylic acid plus calcium carbonate plus methylprednisolone or acetylsalicylic acid plus calcium carbonate plus prednisolone or acetylsalicylic acid plus methylprednisolone or acetylsalicylic acid plus prednisolone or acolbifene or afimoxifene or aluminum hydroxide plus ascorbic acid plus prednisone plus salicylamide or aluminum hydroxide plus calcium ascorbate plus calcium carbonate plus pantothenate calcium plus potassium salicylate plus prednisone or aluminum hydroxide plus magnesium trisilicate plus pantothenate calcium plus prednisolone or aluminum hydroxide plus magnesium trisilicate plus prednisone or amcenestrant or angiopeptin or apalutamide or aromatase inhibitor or estrogen synthetase inhibitor or oestrogen synthetase inhibitor or steroid aromatase inhibitor or abyssinone II or aminoglutethimide or anastrozole or atamestane or exemestane or fadrozole or finrozole or formestane or leflutrozole or letrozole or liarozole or minamestane or plomestane or pyridoglutethimide or testolactone or vorozole or arzoxifene or ascorbic acid plus chlorpheniramine maleate plus prednisone or ascorbic acid plus chlorpheniramine plus prednisone or avorelin or bestrabucil or bicalutamide or buserelin or calcium

	phosphate dibasic plus cyanocobalamin plus ethinylestradiol plus methylphenidate plus methyltestosterone plus nicotinamide plus pyridoxine plus riboflavin plus thiamine or calusterone or carisoprodol plus prednisolone or chloramphenicol plus prednisolone or chlorbutol plus phenylephrine plus prednisolone acetate or chlorotrianisene or chlorpheniramine gluconate plus prednisolone acetate or chlorzoxazone plus paracetamol plus prednisolone or conjugated estrogen or cyproterone or deslorelin or diethylstilbestrol derivative or dienestrol or diethylstilbestrol or fosfestrol or hexestrol or methestrol or dimethylstilbestrol or droloxifene or drostanolone or ectylurea plus ethoxzolamide plus medroxyprogesterone acetate or endoxifen or enzalutamide or ephedrine plus phenobarbital plus prednisone plus theophylline or estradiol undecylate or ethinylestradiol or fluoxymesterone or flutamide or fulvestrant or galeterone or gentamicin plus prednisolone acetate or gestonorone or goserelin or gramicidin plus neomycin plus phenylephrine plus prednisolone acetate or hydroxyflutamide or hydroxyprogesterone or hydroxytamoxifen or hydroxyzine plus prednisolone or idoxifene or leuprorelin or medroxyprogesterone or megestrol or melengestrol or mephenesin plus methylphenobarbital plus prednisone or mepitiostane).mp.
15	(methoxyphenamine plus methylprednisolone or methylprednisolone or methyltestosterone or miproxifene or nafarelin or nandrolone or neomycin plus phenylephrine plus phenylpropanolamine plus prednisolone sodium phosphate or neomycin plus phenylephrine plus prednisolone or neomycin plus phenylephrine plus prednisolone acetate or neomycin plus polymyxin B plus prednisolone acetate or neomycin plus prednisolone or neomycin plus prednisolone acetate or neomycin plus prednisolone sodium phosphate or nilutamide or nortamoxifen or ormeloxifene or orteronel or ospemifene or ozarelix or panomifene or phenylephrine plus prednisolone or pipendoxifene or polyestradiol or prednisolone or prednisone or raloxifene or seviteronel or sivifene or tamoxifen or tesmilifene or testololactone or testosterone propionate or toremifene or trioxifene or triptorelin or zanoterone or zindoxifene or zoptarelin doxorubicin or antineoplastic metal complex or amminebisbutyratodichloro cyclohexylamine platinum or bleomycin cobalt or bleomycin copper or budotitane or capecitabine plus oxaliplatin or carboplatin or carboxyethylgermanium sesquioxide or cisplatin or clivatuzumab tetraxetan or cycloplatam or doxorubicin copper or doxorubicin iron or enloplatin or epratuzumab tetraxetan yttrium y 90 or eptaplatin or imifoplatin or iproplatin or labetuzumab tetraxetan yttrium y 90 or lilotomab satetraxetan lutetium lu 177 or lintuzumab satetraxetan actinium ac 225 or lobaplatin or malopen or miboplatin or miriplatin or nedaplatin or oxaliplatin or oxoplatin or pasireotide tetraxetan gallium ga 68 or picoplatin or platinum ammine cyclohexylamine dichloride or platinum ethylenediamine dichloride or satoreotide tetraxetan or satraplatin or sebriplatin or spirogermanium or spiroplatin or tacatuzumab tetraxetan yttrium y 90 or tetrachloroplatinate potassium or tetrachloroplatinum fast black or tetraplatin or tetulomab tetraxetan lutetium lu 177 or titanocene or triplatin tetranitrate or vipivotide tetraxetan or zeniplatin or antroquinonol or apicidin or apitolisib or aplysianin E or apoptin or apoptosis inducing factor or 2 hydroxymethyl 2 methoxymethyl 3 quinuclidinone or arsenic trioxide or clezutoclax or daratumumab or genistein or isotretinoin or lisavanbulin or moxetumomab pasudotox or otenaproxesul or rimiducid or tapotoclax or apricoxib or arenastatin A or asciminib or aspacytarabine or asparaginase or asunercept or atuveciclib or audencel or avanbulin or avapritinib or avi 4126 or aviscumine or axicabtagene ciloleucel or bafetinib or balamapimod or barasertib or bardoxolone or batabulin or batracylin or beclanorsen or beclin 1 or belapectin or belinostat or belizatinib or belvarafenib or belzupacap sarotalocan or belzutifan or bemcentinib or bempegaldesleukin or benfluron or bersanlimab or berzosertib or beta elemene or beta lapachone or bexarotene or bifikafusp alfa or bimiralisib or binimetinib or birabresib or biricodar or birinapant or bisnafide or bistratene or bomedemstat or borofalan b 10 or bortezomib or bosutinib or briciclib or brigatinib or brilanestrant or bropirimine or bryostatin or bullatacin or bullatacinone or buparlisib or cabazitaxel or calaspargase pegol or camelliin B or camidanlumab).mp.
16	(adagloxad simolenin or adegramotide or algenpantucel L or autogene cevumeran or axalimogene filolisbac or baloramotide or baltaleucel T or belagenpumatucel L or biropepimut S or bizalimogene ralaplasmid or cadalimogene ixalentivec or dasiprotimut T or dorgenmeltucel L or eltrapuldencel T or falimarev or galinpepimut S or imm 101 or inalimarev or lapuleucel T or lovaxin b or maveropepimut S or mavilimogene ralaplasmid or mesmulogene ancovacivec or mitumprotimut T or modified vaccinia virus Ankara 5T4 vaccine or nelatimotide or nelipepimut S or olvimulogene nanivacirepvec or ombipepimut S or onamelatucel L or opolimogene capmilisbac or pemlimogene merolisbac or ranagengliotucel T or rasdegafusp alfa or rindopepimut or rocapuldencel T or rovaleucel or ruxotemitide or seviprotimut L or sipuleucel T or tecemotide or tergenpumatucel L or tertomotide or theratope or tipapkinogene sovacivec or tisagenlecleucel T or vadacabtagene leraleucel or vesigenurtucel L or viagenpumatucel L or vitespen or zastumotide or canertinib or capivasertib or capmatinib or caracemide or carbetimer or carfilzomib or carlecortemcel L or carmethizole or ceclazepide or cedazuridine or cemadotin or cenersen or cenisertib or ceralasertib or cerdulatinib or cergutuzumab amunaleukin or ceritinib or cevipabulin or

	chloroquine or ciforadenant or ciltacabtagene autoleucel or cintirorgon or citarinostat or clervonafusp alfa or clofazimine or cobimetinib or cobomarsen or colloidal gold or combretastatin or conteltinib or contusugene ladenovec or copanlisib or corynebacterium parvum extract or crenigacestat or crisnatol or cryptophycin or curcumin or custirsen or cyclophosphamide plus doxorubicin plus taxane or cysteine ethyl ester methylcarbamate or cytostatic agent or cytotoxic agent or emtansine or mafodotin or mertansine or ravtansine or soravtansine or tafasitamab or dabrafenib or dacinostat or dacomitinib or dactolisib or damistimagene matitucel or danusertib or danvatirsen or daporinad or darinaparsin or darleukin or darolutamide or dasatinib or davamotecan pegadexamer or decernotinib or defactinib or degarelix or dehydroxymethylepoxyquinomicin or delanzomib or delimotecan or delolimogene mupadenorepvec or demethoxycurcumin or demplatin pegraglumer or denileukin diftitox or derazantinib).mp.
17	(azintuxizumab or balstilimab or belantamab or bemarituzumab or benufutamab or bexmarilimab or bintrafusp alfa or bivatuzumab or blinatumomab or blontuvetmab or brentuximab vedotin or brontictuzumab or budigalimab or camrelizumab or cantuzumab or catumaxomab or cemiplimab or cergutuzumab or cetrelimab or cetuximab or cevostamab or cibisatamab or cinrebafusp alfa or cixutumumab orclivatuzumab tetraxetan or cobolimab or codrituzumab or cofetuzumab or coltuximab or conatumumab or cosibelimab or cudarolimab or cusatuzumab or dacetuzumab or dalotuzumab or daratumumab or datopotamab or demcizumab or demupitamab or denintuzumab or denosumab or depatuxizumab or derlotuximab biotin i 131 or detumomab or dilpacimab or dinutuximab or disitamab or dostarlimab or drozitumab or duligotuzumab or durvalumab or dusigitumab or duvortuxizumab or ecromeximab or edrecolomab or efizonerimod alfa or elgemtumab or elotuzumab or emactuzumab or emibetuzumab or enapotamab or enavatuzumab or encelimab or enfortumab or enoblituzumab or enoticumab or ensituximab or envafolimab or epcoritamab or epitumomab or epratuzumab or ertumaxomab or etaracizumab or ezabenlimab or farletuzumab or feladilimab or felzartamab or fianlimab or ficlatuzumab or figitumumab or flanvotumab or flotetuzumab or fresolimumab or futuximab or galiximab or gancotamab or ganitumab or gatipotuzumab or gatralimab or giloralimab or gilvetmab or girentuximab or glembatumumab or glofitamab or hyaluronidase plus rituximab or hyaluronidase plus trastuzumab or ibritumomab tiuxetan or icrucumab or ieramilimab or ifabotuzumab or iladatuzumab or imalumab or imgatuzumab or immunoliposome or immunotoxin or anatumomab mafenatox or cintredekin besudotox or citatuzumab bogatox or moxetumomab pasudotox or nacolomab tafenatox or naptumomab estafenatox or taplitumomab paptox or telimomab aritox or indatuximab or indusatumab or inebilizumab or intetumumab or ipilimumab or iratumumab or isatuximab or istiratumab or ivuxolimab or labetuzumab or lacnotuzumab or lacutamab or ladiratuzumab or laprituximab or lenzilumab or lexatumumab or lifastuzumab or lilotomab or lintuzumab or lirilumab or lodapolimab or loncastuximab or lorukafusp alfa or lorvotuzumab or losatuxizumab or lucatumumab or lumiliximab or lumretuzumab or lupartumab or magrolimab or manelimab or mapatumumab or margetuximab or matuzumab or mavezelimab or mezagitamab or milatuzumab or minretumomab or miptenalimab or mirvetuximab or mirzotamab or mitumomab or modakafusp alfa or modotuximab or mogamulizumab or monalizumab).mp.
18	(deruxtecan or devimistat or dexniguldipine or dexverapamil or dezapelisib or diacetyldianhydrogalactitol or diaspirin crosslinked haemoglobin or didemethoxycurcumin or diglycoaldehyde or dihydroambazone or dilanubicel or dinaciclib or dinaline or discodermolide or disufenton sodium or ditercalinium or docetaxel or dociparstat or dofequidar or dolastatin or domatinostat or dubermatinib or dulanermin or duvelisib or ebifuramin or edelfosine or edicotinib or edotecarin or edotreotide ga 68 or edotreotide lu 177 or edotreotide y 90 or efaprinermin alfa or efatutazone or efgivanermin alfa or efineptakin alfa or eflornithine or eftozanermin alfa or elacestrant or elacridar or elafibranor or elagolix or elesclomol or eleutherobin or elinafide or elisidepsin or eltanexor or empesertib or enasidenib or encequidar or encorafenib or enistimgene setitucel or ensartinib or entasobulin or entinostat or entospletinib or entrectinib or enzastaurin or epertinib or epipodophyllotoxin or erbulozole or erdafitinib or eribulin or erlotinib or erucin or ethazolastone or etidaligide or everolimus or exicorilant or factor AF2 or fadraciclib or falnidamol or fedratinib or felezonexor or fenebrutinib or fenretinide or ferritin antibody i 131 or fetindomide or fibromun or filanesib or filgotinib or fimepinostat or fisogatinib or flavopiridol or flumatinib or fluorocyclopentenylcytosine or forodesine or fosciclopirox or fosquidone or fumitremorgin C or futibatinib or gallium nitrate or galunisertib or gandotinib or gataparsen or gedatolisib or gefitinib or geiparvarin or gendicine or gene expression modulator 231 or ghilanten or gilteritinib or girolline or givinostat or glasdegib or glucopyranosyl lipid A or glycoprotein P inhibitor or golnerminogene pradenovec or golvatinib or goniofufurone or granulocyte macrophage colony stimulating factor vaccine or grifolan or guanazole or gusacitinib or halichondrin B or heat shock protein 27 inhibitor or apatorsen or heat shock protein 90 inhibitor or alvespimycin or celastrol or gambogic acid or gamendazole or ganetespib or geldanamycin or

	luminespib or onalespib or pimitespib or retaspimycin or tanespimycin or hepsulfam or HER dimerization inhibitor or hexamethylenebisacetamide or hydroxymethylpentamethylmelamine or hydroxyurea or hypericin or hypothemycin or iadademstat or ibrutinib or icotinib or idasanutlin or idecabtagene vicleucel or idelalisib or idetrexed or idronoxil or ilixadencel or ilmofosine or ilorasertib or imaradenant or imatinib or imetelstat or imlatoclax or abagovomab or abituzumab or actimab a or adebrelimab or adecatumumab or alacizumab pegol or alemtuzumab or alsevalimab or amatuximab or amivantamab or andecaliximab or anetumab or apolizumab or aprutumab or aprutumab ixadotin or ascrinvacumab or astegolimab or atezolizumab or avdoralimab or avelumab or axatilimab).mp.
19	(monoclonal antibody J591 or mosunetuzumab or murlentamab or nadunolimab or naratuximab or narnatumab or naxitamab or necitumumab or nesvacumab or nimotuzumab or nivolumab or nurulimab or obinutuzumab or ocaratuzumab or odronextamab or ofatumumab or olaratumab or oleclumab or olinvacimab or omburtamab or onartuzumab or ontuxizumab or onvatilimab or oportuzumab monatox or opucolimab or oregovomab or otlertuzumab or pacmilimab or panitumumab or parsatuzumab or pasotuxizumab or patritumab or pembrolizumab or pemtumomab or pepinemab or pertuzumab or petosemtamab or pidilizumab or pimurutamab or pinatuzumab vedotin or plamotamab or polatuzumab vedotin or praluzatamab or pritumumab or prolgolimab or quavonlimab or racotumomab or radretumab or ragifilimab or ramucirumab or rasdegafusp alfa or relatlimab or retifanlimab or revdofilimab or rilotumumab or ripertamab or rituximab or robatumumab or rolinsatamab or rosmantuzumab or rosopatamab or rovalpituzumab or rovalpituzumab tesirine or sabatolimab or sacituzumab or samalizumab or samrotamab or sasanlimab or selicrelumab or serclutamab or seribantumab or serplulimab or sibrotuzumab or siltuximab or simlukafusp alfa or simtuzumab or sintilimab or sirtratumab or sofituzumab or solitomab or sontuzumab or spartalizumab or sugemalimab or tabalumab or tabituximab or tacatuzumab or tetraxetan yttrium y 90 or tacatuzumab y 90 or tafasitamab or talacotuzumab or talquetamab or tamrintamab or tamtuvetmab or tarextumab or tavolimab or tebotelimab or teclistamab or telisotuzumab or tenatumomab or tepoditamab or teprotumumab or tetulomab tetraxetan lutetium lu 177 or ticilimumab or tidutamab or tigatuzumab or tilogotamab or tilvestamab or timigutuzumab or tinurilimab or tiragolumab or tislelizumab or tisotumab or tomuzotuximab or toralizumab or toripalimab or tositumomab or tovetumab or trastuzumab or ublituximab or ulocuplumab or upifitamab or urabrelimab or urelumab or utomilumab or vadastuximab or vandortuzumab vedotin or vantictumab or vanucizumab or varlilumab or veltuzumab or vesencumab or vibecotamab or vibostolimab or vofatamab or vonlerolizumab or vopratelimab or vorsetuzumab or vulinacimab or xentuzumab or zalifrelimab or zalutumumab or zanidatamab or zanolimumab or zolbetuximab or zuberitamab).mp.
20	(inavolisib or inbakicept or incyclinide or indibulin or indisulam or indoximod or ingenol disoxate or ingenol mebutate or inodiftagene vixteplasmid or interferon regulatory factor 2 or intiquinatine or intoplicine or ipafricept or ipatasertib or irosustat or isoswinholide A or ispinesib or itacitinib or itraconazole or ivaltinostat or ivosidenib or ixazomib or kahalalide F or krestin or laetrile or laniquidar or lapachol or lapatinib or lapretolimod or larifan or larotaxel or larotrectinib or laulimalide or lefitolimod or lerociclib or lestaurtinib or letetresgene autoleucel or lexidronam samarium sm 153 or lifileucel or lifirafenib or linperlisib or linrodostat or lisocabtagene maraleucel or litenimod or litronesib or lonafarnib or lonidamine or lorlatinib or ltvax or lurtotecan or maltose tetrapalmitate or masitinib or mavelertinib or mavorixafor or melacine or merbarone or merestinib or methanol extraction residue or metirosine or mevociclib or midostaurin or mifamurtide or milademetan or milataxel or milciclib or miltefosine or mipetresgene autoleucel or mipsagargin or miralimogene ensolisbac or miransertib or mirdametinib or mirostipen or mitazalimab or mitindomide or mitobronitol or mitoflaxone or mitoguazone or mitolactol or mitonafide or mitoquidone or mitotane or mitozolomide or mivavotinib or mivebresib or mivobulin or mobocertinib or mocemestrocel or mocetinostat or molibresib or momelotinib or monastrol or mosedipimod or motixafortide or motolimod or mubritinib or mucocin or murizatoclax or mycalamide or myeloablative agent or nabiximols or nadofaragene firadenovec or namodenoson or nanatinostat or napabucasin or naquotinib or nastorazepide or navitoclax or navoximod or nazartinib or necuparanib or nemiralisib or neratinib or netazepide or nevanimibe or nilotinib or niraparib or nirogacestat or nitracrine or nitrocaphane or noscapine or numidargistat or nutlin or obafistat or obatoclax or oblimersen or oblongifolin C or oblongixanthone A or obovatal or obtusilactone A or oclacitinib or olafertinib or olaparib or olaptesed pegol or olcorolimus or olitresgene autoleucel or olmutinib or olutasidenib or olverembatinib or omidubicel or omipalisib or omtriptolide or onatasertib or oncolytic virus or oncolytic adenovirus or enadenotucirev or lontucirev or tasadenoturev oroncolytic herpes virus or canerpaturev or seprehvir or talimogene laherparepvec or teserpaturev or oncolytic paramyxovirus or oncolytic parvovirus or oncolytic reovirus or pelareorep or pexastimogene devacirepvec or onfekafusp alfa or ontorpacept or onvansertib or opaganib or opigolix or oprozomib or oracin or orelabrutinib or

	ortataxel or orvacabtagene autoleucel or osimertinib or oxamflatin or oxodotreotide lu 177 or paclitaxel ceribate or paclitaxel derivative or paclitaxel poliglumex or paclitaxel tocosol or paclitaxel trevatide or pacritinib or palbociclib or palmerolide A or pamiparib or panaxytriol or panduratin A or panobinostat or panulisib or parsaclisib or pasireotide or paxalisib or pegargiminase or pegcantratinib or pegcrisantaspase or pegilodecakin or pegvorhyaluronidase alfa or pelcitoclax or pelidotin or pelitinib or pemigatinib or penclomedine or peposertib or peretinoin).mp.
21	(perifosine or pevonedistat or pexidartinib or phenethyl isothiocyanate or phomopsin A or phorboxazole or phyllanthocin or phyllanthoside or picibanil or pictilisib or pilaralisib or pimasertib or pinometostat or pipobroman or pivaloyloxymethyl butyrate or plocabulin or plusonermin or podophyllotoxin or polyerga or ponatinib or poziotinib or pracinostat or pralsetinib or prexasertib or prexigebersen or prospidium or ptilocaulin or pyran copolymer or pyrazine diazohydroxide or quarfloxin or quisinostat or quizartinib or rabacfosadine or rabusertib or radiosensitizing agent or radio-sensitizing agent or bromodeoxycytidine or broxuridine or chloroaluminum phthalocyanine or cloxuridine or crocetin ordeclopramide or doranidazole or efaproxiral or etanidazole or etiopurpurin or fimaporfin or gadolinium texaphyrin or gilvocarcin V or hematoporphyrin derivative or isometronidazole or lemuteporfin or lutetium texaphyrin or merocyanine or misonidazole or motexafin or napavin or nimorazole or nocodazole or normisonidazole or padeliporfin or padoporfin or photofrin I or photofrin II or photosan III or phthalocyanine or pimonidazole or porfimer or redaporfin or senazole or talaporfin or temoporfin or tetrachloroplatinum fast black or tetraphenylporphyrin or tetrasulfophthalocyanine or tirapazamine or tretazicar or troquidazole or verteporfin or radium chloride ra 223 or radotinib or ralimetinib or ranpirnase or rapamycin or ravoxertinib or razoxane or rebastinib or recombinant asparaginase or recombinant interleukin 21 or denenicokin or recombinant methionine gamma lyase or recombinant tumor necrosis factor related apoptosis inducing ligand or refametinib or remetinostat or repotrectinib or resminostat or rezivertinib or rhizoxin or rhodamine 6G or ribociclib or ribonucleotide reductase R2 specific phosphorothioate oligonucleotide or ricolinostat or ridaforolimus or rigosertib or rilimogene galvacirepvec or rilimogene glafolivec or ripretinib or riviciclib or rivogenlecleucel or robaveron or roblitinib or rocakinogene sifuplasmid or rociletinib or roniciclib or roridin A or rosabulin or rosomidnar or rucaparib or ruxolitinib or salinosporamide A or salirasib or samotolisib or samuraciclib or sapanisertib or sapitinib or saracatinib or sarcodictyin A or sarcophytol A or sarcophytol B or sardomozide or satoreotide trizoxetan or savolitinib or Sclerotinia sclerotiorum extract or seclidemstat or selectikine or selinexor or selitrectinib or selpercatinib or selumetinib or seocalcitol or sepantronium bromide or serabelisib or serdemetan or serpentine or shikonin derivative or silmitasertib or simotaxel or simurosertib or siremadlin or sitimagene ceradenovec or sitravatinib or sobuzoxane or solcoderm or sonermin or sonidegib or sonolisib or sparfosic acid or spebrutinib or spirobromine or squamocin or ssioriside or stapuldencel T or starch microsphere or sulfatinib or sulforaphane or sulindac sulfone or sulofenur or suramin or swinholide A or swinholide B).mp.
22	(tacedinaline or tafluposide or tagraxofusp or talabostat or talactoferrin or taladegib or talazoparib or talirine or taltobulin or tamibarotene or taminadenant or tandutinib or tanshinone IIA or tanurmotide or tariquidar or tarloxotinib or taselisib or tasidotin or tasisulam or tasonermin or tavokinogene telseplasmid or tazemetostat or tebentafusp or tebrocabtagene autoleucel or tecogalan or tefinostat or tegavivint or teglarinad chloride or telaglenastat or teleukin or telomestatin or telotristat or telratolimod or temarotene or temsirolimus or tenalisib or tengonermin or tepotinib or teprasiran or terameprocol or teroxirone or tesetaxel or tetramethylmelamine or tetravil or thioglucose or tian xian wan or tigilanol tiglate or tilomisole or tilsotolimod or timcodar or timonacic derivative or tipifarnib or tirabrutinib or tivantinib or tomivosertib or topsalysin or tosedostat or tozasertib or trametinib or transferrin aldifitox or trichlormethine or trichosanthin or trichostatin A or triciribine or triciribine phosphate or trilaciclib or trimelamol or tubacin or tubulozole or tucatinib or tucidinostat or tucotuzumab celmoleukin or tumo?r suppressor protein or inhibitor of growth protein 1 or ubiquitin carboxyl terminal hydrolase CYLD or tuvatexib or tylophorine or ulicyclamide or ulipristal or ulithiacyclamide or ulixertinib or umbralisib or upamostat or uproleselan or uprosertib or uzansertib or vaccinia oncolysate or vactosertib or valecobulin or valemetostat or valspodar or varlitinib or vascular targeting agent or anginex or bavituximab or crolibulin or denibulin or lexibulin or n acetylcolchinol phosphate or ofranergene obadenovec or ombrabulin or plinabulin or soblidotin or vadimezan or vecabrutinib or vedotin or velimogene aliplasmid or veliparib or vemurafenib or venetoclax or verdinexor or verrucarin A or verubulin or vesatolimod or virus oncolysate or vismodegib or vistusertib or vocimagene amiretrorepvec or volasertib or vorasidenib or vorinostat or voruciclib or vosaroxin or vosilasarm or voxtalisib or withaferin A or WW domain containing oxidoreductase or xanthone 4 acetic acid or xevinapant or xiaochaihu tang or xiliertinib or zafiride or zandelisib or zanubrutinib or

	zenocutuzumab or zerumbone or zibotentan or zilascorb or zoledronic acid or zoligratinib or zorifertinib or zosuquidar or zotatifin or zotiraciclib).mp.
23	(protein tyrosine kinase inhibitor or tyrosine kinase inhibitor or tyrosine protein kinase inhibitor or anaplastic lymphoma kinase inhibitor or bruton tyrosine kinase inhibitor or adaphostin or alofanib or alpha cyanothiocaffeic acid amide or altiratinib or alvespimycin or amivantamab or amuvatinib or alectinib or brigatinib or ceritinib or crizotinib or ensartinib or entrectinib or lorlatinib or repotrectinib or asciminib or avapritinib or axitinib or bafetinib or belizatinib or bemcentinib or bosutinib or brivanib or brivanib alaninate or acalabrutinib or branebrutinib or dasatinib or elsubrutinib or evobrutinib or ibrutinib or orelabrutinib or poseltinib or remibrutinib or rilzabrutinib or spebrutinib or tolebrutinib or vecabrutinib or zanubrutinib or cabozantinib or capmatinib or catequentinib or cediranib or cerdulatinib or cevidoplenib or conteltinib or crenolanib or damnacanthal or decernotinib or defactinib or derazantinib or dovitinib or dubermatinib or edicotinib or elafibranor or emodin or epidermal growth factor receptor kinase inhibitor or erbstatin or focal adhesion kinase inhibitor or Janus kinase inhibitor or baricitinib or brepocitinib or delgocitinib or fedratinib or fosifidancitinib or gusacitinib or ifidancitinib or ilginatinib or itacitinib or izencitinib or abrocitinib or filgotinib or lorpucitinib or momelotinib or ruxolitinib or tofacitinib or upadacitinib or lavendustin A or lazertinib or linsitinib or lorecivivint or mitogen activated protein kinase kinase inhibitor or peficitinib or pexmetinib or protein kinase Syk inhibitor or fostamatinib or lanraplenib or piceatannol or radicicol or recifercept or ritlecitinib or seralutinib or solcitinib or suppressor of cytokine signaling 1 or telatinib or tilvestamab or tyrphostin).mp.
24	(abscopal effect or bone marrow purging or bone marrow rescue or chemoradiotherap* or chemoradiation or antibody directed enzyme prodrug therap* or chemoembolization or graft versus tumo?r effect or graft versus leuk?emia effect or graft versus lymphoma effect or oncolytic viral therap* or oncolytic virus therap* or target cell destruction or biologic* response modifier therap* or BRM therap* or chimeric antigen receptor immunotherap* or chimeric antigen receptor natural killer cell immunotherap* or chimeric antigen receptor T-cell immunotherap* or CAR immontherap* or CAR T cell therap* or CAR T cell immunotherap* or CAR T therap* or CAR NK cell immunotherap* or CAR NK cell therap* or chimeric antigen receptor T cells or immune checkpoint inhibitor* or immune checkpoint blockade* or radioimmunotherap* or immunoradiotherap* or radiotherap* or bioradiant therap* or hemibody irradiation or irradiation therap* or irradiation treatment* or radiation therap* or radiation treatment* or radio therap* or radiotreatment or beam therap* or blood radiation or brachytherap* or interstitial radiation or radioisotope therap* or radium therap* or electron therap* or gamma irradiation or gamma knife radiosurgery or body radiation or photon beam therap* or proton beam therap* or radioimmunotherap* or stereotactic radiosurgery or teleradiotherap* or bone marrow transplant* or bone marrow cell transfer or bone marrow graft* or bone marrow transfusion* or h?ematopo?etic stem cell* or HSC therap* or HSC transplant* or stem cell transplant* or stem cell based therap* or stem cell therap* or allogeneic stem cell* or autologous stem cell* or peripheral blood stem cell* or allogen?ic HSCT or allogen?ic HSCTs or auto-HSCT or auto-HSCTs or autologous HSCT or autologous HSCTs or tumo?r killing activit* or tumo?r killing effect* or tumo?r killing action* or log cell kill or metastatic* inhibit* or metastas* inhibit*).mp.
25	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
26	blood vessel parameters/ or arterial stiffness/ or arterial wall thickness/ or artery diameter/ or augmentation index/ or blood vessel diameter/ or carotid-femoral pulse wave velocity/ or endothelial dysfunction/ or artery compliance/ or blood vessel compliance/ or vascular remodeling/ or artery blood flow/ or pulse wave/ or blood vessel function/ or blood vessel reactivity/ or vascular resistance/ or vasoconstriction/ or vasodilatation/ or vascular endothelium/ or artery endothelium/ or artery dilatation/ or blood flow velocity/ or blood vessel capacitance/
27	(tunica intima/ or endothelium, vascular/ or tunica media/ or muscle, smooth, vascular/ or Endothelial Cells/) and (cellular senescence/ or telomere shortening/ or Aging/)
28	arteriosclerosis/ or arteriolosclerosis/ or artery intima proliferation/
29	(endothelial function or endothelial vascular function).mp.
30	((vascular* or vasculature or endotheli* or vessel*) adj4 (ag?ing or aged or stiff* or dysfunction* or impair* or deficit* or defect* or change* or alteration* or remode?ling or dilat* or degenerat* or thick* or elasticit* or elastance or distens*)).mp.
31	((vascular* or vasculature or endotheli* or blood vessel*) adj (inflammation or senescen* or cell senescence or damage or dyshomeostasis or measurement* or compliance or calcification or reactivity)).mp.

32	((artery or arteries or arteria* or aorta* or aortic*) adj4 (ag?ing or stiff* or thick* or compliance or distens* or wave reflection or reflection index or elasticit* or elastance or defect* or change* or impair* or diameter* or dilat* or measurement* or dysfunction* or alteration* or remode?ling or calcification)).mp.
33	((Intima* media* or intimamedia* or tunica intima or tunica media) adj3 thick*).mp.
34	(pressure wave transmission or pressure wave reflection or pulse pressure or pulse wave velocity or pulse wave analys#s or pulse wave amplitude or arterial pulsatility or flow mediated dilation or blood flow velocit* or arter* flow velocit*).mp.
35	(aortic blood pressure* or aortic pressure* or aortic pulse pressure* or aortic tension* or central aortic blood pressure* or central aortic pressure*).mp.
36	(central BP or arterial BP or aortic BP or (central SBP or arterial SBP or aortic SBP) or (central PP or arterial PP or aortic PP)).mp.
37	(aortic blood pulse wave* or aortic pulse wave* or aortic tension* or arterial blood pulse wave* or arterial pulse wave* or arterial tension* or central aortic blood pulse wave* or central aortic pulse wave* or carotid to femoral pulse wave* or pulse wave*).mp.
38	(augmentation adj (index* or indice*)).mp.
39	((augmentation or amplification) adj6 (pressure* or pulse* or wave* or aortic or central)).mp.
40	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39
41	25 and 40
42	clinical trial/ or randomized controlled trial/ or randomization/ or single blind procedure/ or double blind procedure/ or crossover procedure/ or placebo/ or prospective study/
43	(randomi?ed controlled or RCT or randomly allocated or allocated randomly or random allocation or (allocated adj2 random) or (single adj1 blind*) or (double adj1 blind*) or ((treble or triple) adj1 blind*) or placebo*).mp.
44	((cross-sectional or prevalence or disease frequency) adj (analys#s or study or studies or survey)).mp.
45	((cohort or incidence) adj (analys#s or study or studies or survey)).mp.
46	((follow-up or followup or longitudinal or prospective or retrospective) adj (study or studies)).mp.
47	42 or 43 or 44 or 45 or 46
48	41 and 47
49	(exp animal/ or exp invertebrate/ or animal.hw. or nonhuman/) not exp human/
50	48 not 49
51	limit 50 to english language
52	limit 51 to (editorial or letter or note)
53	51 not 52
54	53 not (case report* or news or newspaper*).mp,pt.
55	limit 54 to conference abstract
56	54 not 55
57	limit 56 to conference abstracts
58	56 not 57

#	Query
S15	S11 OR S13 Limiters - Publication Year: 1990-2020; English Language; Exclude MEDLINE records
S14	S11 OR S13
S13	S5 AND S12
S12	(((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) N4 (accessibility or availability))) OR (((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) N0 (need* or demand*))) OR (((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*) N2 (need* or demand*)))
S11	S9 AND S10
S10	(readiness or preparedness or capacity or quality improvement or quality of Improvement)
S9	S5 AND S8
S8	S6 OR S7
S7	((primary health system or primary health service or primary healthcare system or primary health care system or primary healthcare service or primary health care service or primary medical service delivery or primary medical care service or primary care service or primary care system)) OR ((first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) OR (((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*)))
S6	(MH "Primary Health Care") OR (MH "Health Care Delivery")
S5	S1 OR S2 OR S3 OR S4
S4	((diastolic pressure or systolic pressure or blood pressure or cardiometabolic syndrome*)) OR ((copd or asthma or renal disease* or kidney disease*))
S3	((cardiovascular disease* or coronary artery disease* or myocardial isch?emia or myocardial infarct* or pulmonary disease* or chronic obstructive pulmonary or chronic obstructive lung or chronic obstructive respiratory or diabetes or coronary heart disease* or neoplasm* or cancer*)) OR ((hypertension or hypertriglycerid?emi* or hyper triglycerid?emi* or high triglyceride* or high cholesterol or hypercholesterol?emi* or hyperlipid?emia* or hyperlipidemi*))
S2	((chronic disease* or chronic disorder* or chronic* sick* or chronic health condition* or chronic medical condition* or chronic* ill* or long term condition* or multimorbidit* or mult imorbidit*)) OR ((non-communicable disease* or non-infectious disease* or noncommunicable disease* or noninfectious disease*))
S1	(MH "Chronic Disease") OR (MH "Noncommunicable Diseases") OR (MH "Chronic Pain")

CINAHL Search

Database(s): APA PsycInfo
Search Strategy:

#	Searches	Results
1	chronic illness/ or chronic fatigue syndrome/ or chronic pain/	27358
2	(chronic disease* or chronic disorder* or chronic* sick* or chronic health condition* or chronic medical condition* or chronic* ill* or long term condition* or multimorbidit* or mult imorbidit*).mp.	48956
3	(non-communicable disease* or non-infectious disease* or noncommunicable disease* or noninfectious disease*).mp.	1052
4	(cardiovascular disease* or coronary artery disease* or myocardial isch?emia or myocardial infarct* or pulmonary disease* or chronic obstructive pulmonary or chronic obstructive lung or chronic obstructive respiratory or diabetes or coronary heart disease* or neoplasm* or cancer*).mp.	121105
5	(hypertension or hypertriglycerid?emi* or hyper triglycerid?emi* or high triglyceride* or high cholesterol or hypercholesterol?emi* or hyperlipid?emia* or hyperlipidemi*).mp.	20201
6	(diastolic pressure or systolic pressure or blood pressure or cardiometabolic syndrome*).mp.	24127
7	(copd or asthma or renal disease* or kidney disease*).mp.	13056
8	1 or 2 or 3 or 4 or 5 or 6 or 7	207978
9	primary health care/	18474
10	health care delivery/	20844
11	(primary health system or primary health service or primary healthcare system or primary health care system or primary healthcare service or primary health care service or primary medical service delivery or primary medical care service or primary care service or primary care system).mp.	511
12	(first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*).mp.	338
13	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*)).mp.	2322
14	9 or 10 or 11 or 12	38723
15	8 and 14	4987
16	(readiness or preparedness or capacity or quality improvement or quality of Improvement).mp.	118317
17	15 and 16	312
18	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj5 (accessibility or availability)).mp.	148
19	8 and 18	19
20	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj (need* or demand*)).mp.	290
21	8 and 20	55
22	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*) adj3 (need* or demand*)).mp.	17
23	8 and 22	2
24	17 or 19 or 21 or 23	387

25	limit 24 to english language	380
26	limit 25 to yr="1990 -Current"	380
27	limit 26 to ("column/opinion" or "comment/reply" or dissertation or editorial or letter)	41
28	26 not 27	339

Scopus

Search Strategy:

((((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND ((TITLE-ABS-KEY (("primary health system" OR "primary health service" OR "primary healthcare system" OR "primary health care system" OR "primary healthcare service" OR "primary health care service" OR "primary medical service delivery" OR "primary medical care service" OR "primary care service" OR "primary care system"))) OR (TITLE-ABS-KEY (("first-level healthcare" OR "first-level health care" OR "first-level health system*" OR "first-level health facilit*" OR "local health system*" OR "local health care" OR "local healthcare" OR "local-level health*"))) OR (TITLE-ABS-KEY ((primary OR "first-level" OR local) W/2 health* W/2 (clinic* OR center* OR centre* OR setting*)))))) AND (TITLE-ABS-KEY ((readiness OR preparedness OR capacity OR "quality improvement" OR "quality of Improvement"))))) OR (((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND (TITLE-ABS-KEY ((("primary care" OR "primary health care" OR "primary healthcare" OR "primary health system*" OR "primary medical service*" OR "primary medical care" OR "first-level healthcare" OR "first-level health care" OR "first-level health system*" OR "first-level health facilit*" OR "local health system*" OR "local health care" OR "local healthcare" OR "local-level

health*") W/4 (accessibility OR availability))))) OR (((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND (TITLE-ABS-KEY ((("primary care" OR "primary health care" OR "primary healthcare" OR "primary health system*" OR "primary medical service*" OR "primary medical care" OR "first-level healthcare" OR "first-level health care" OR "first-level health system*" OR "first-level health facilit*" OR "local health system*" OR "local health care" OR "local healthcare" OR "local-level health*") W/0 (need* OR demand*))))) OR (((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND (TITLE-ABS-KEY (((primary OR "first-level" OR local) W/2 health* W/2 (clinic* OR center* OR centre* OR setting*) W/2 (need* OR demand*))))) AND (LIMIT-TO (LANGUAGE , "English")) AND (EXCLUDE (DOCTYPE , "ch") OR EXCLUDE (DOCTYPE , "no") OR EXCLUDE (DOCTYPE , "bk") OR EXCLUDE (DOCTYPE , "ed")) AND (EXCLUDE (SUBJAREA , "AGRI") OR EXCLUDE (SUBJAREA , "CENG") OR EXCLUDE (SUBJAREA , "ARTS") OR EXCLUDE (SUBJAREA , "BUSI") OR EXCLUDE (SUBJAREA , "EART") OR EXCLUDE (SUBJAREA , "VETE")) View less

Table S2. A list of the excluded studies and reasons for their exclusion

SL	Study	Reason for exclusion
01	Abolhassani N, Santos-Eggimann B, Chiolero A, Santschi V, Henchoz Y. Readiness to accept health information and communication technologies: A population-based survey of community-dwelling older adults. *International Journal of Medical Informatics* 2019; **130**: 103950.	Not relevant to the theme for review
02	Acton KJ, Shields R, Rith-Najarian S, et al. Applying the diabetes quality improvement project indicators in the Indian Health Service primary care setting. *Diabetes Care*; **24**(1): 22-6.	Inadequate or inappropriate results
03	Ahmed S, Chowdhury MA, Khan MA, Huq NL, Naheed A. Access to primary health care for acute vascular events in rural low income settings: a mixed methods study. *BMC Health Services Research*; **17**(1): 47.	Inadequate or inappropriate results
04	Allenby A, Kinsman L, Tham R, Symons J, Jones M, Campbell S. The quality of cardiovascular disease prevention in rural primary care. *Australian Journal of Rural Health*; **24**(2): 92-8.	Inadequate or inappropriate results
05	Armour CL, Reddel HK, Lemay KS, et al. Feasibility and Effectiveness of an Evidence-Based Asthma Service in Australian Community Pharmacies: A Pragmatic Cluster Randomized Trial. *Journal of Asthma* 2013; **50**(3): 302-9.	Not relevant to the theme for review
06	Alzubaidi HT, Chandir S, Hasan S, McNamara K, Cox R, Krass I. Diabetes and cardiovascular disease risk screening model in community pharmacies in a developing primary healthcare system: A feasibility study.	Inadequate or inappropriate results
07	Ahmedov M, Green J, Azimov R, Avezova G, Inakov S, Mamatkulov B. Addressing the challenges of improving primary care quality in Uzbekistan: a qualitative study of chronic heart failure management. *Health Policy & Planning*; **28**(5): 458-66.	Inadequate or inappropriate results
08	Aryal BK, Daud M, Thapa A, Mahotra A, Ale Magar S, Malla CK. Assesssment of Health Facilities for Implementation of Non-communicable Disease Package. *Journal of Nepal Health Research Council*; **16**(2): 149-55.	Combined data on primary and secondary healthcare level
09	Banasiak NC. Implementation of the Asthma Control Test in Primary Care to Improve Patient Outcomes. *Journal of Pediatric Healthcare* 2018; **32**(6): 591-9.	Not relevant to the theme for review
10	Barcelos MRB, Nunes BP, Duro SMS, et al. Utilization of Breast Cancer Screening in Brazil: An External Assessment of Primary Health Care Access and Quality Improvement Program.	Not relevant to the theme for review
11	Bello AK, Ronksley PE, Tangri N, et al. Quality of Chronic Kidney Disease Management in Canadian Primary Care. *JAMA Network Open*; **2**(9): e1910704.	Inadequate or inappropriate results
12	Baeza JI, Fitzgerald L, McGivern G. Change capacity: the route to service improvement in primary care. *Quality in Primary Care*; **16**(6): 401-7.	Inadequate or inappropriate results
13	Bawazir AA, Al-Surimi K, Suwaidan SD, AlShehri AM, AlFarhan AI, Aboulfotouh MA. Capacity and readiness of primary health care centers for implementation of the basic strategy for prevention and control of non-communicable diseases in Saudi Arabia. A case study from the Ministry of National Guard-Health Affairs, Riyadh, Saudi Arabia. *Saudi Medical Journal*; **40**(6): 614-8.	Inappropriate study type (n=1)
14	Boehmer KR, Kyriacou M, Behnken E, Branda M, Montori VM. Patient capacity for self-care in the medical record of patients with	Not relevant to the theme for review

	chronic conditions: a mixed-methods retrospective study. *BMC family practice* 2018; **19**(1): 164.	
15	Bindman AB, Grumbach K, Osmond D, Vranizan K, Stewart AL. Primary care and receipt of preventive services.	Inadequate or inappropriate results
16	Birabwa C, Bwambale MF, Waiswa P, Mayega RW. Quality and barriers of outpatient diabetes care in rural health facilities in Uganda - a mixed methods study. *BMC Health Services Research*; **19**(1): 706.	Combined data on primary and secondary healthcare level
17	Brownson CA, Miller D, Crespo R, et al. A quality improvement tool to assess self-management support in primary care. *Joint Commission Journal on Quality & Patient Safety*; **33**(7): 408-16.	Inadequate or inappropriate results
18	Casalino LP, Wu FM, Ryan AM, et al. Independent practice associations and physician-hospital organizations can improve care management for smaller practices. *Health Affairs*; **32**(8): 1376-82.	Inadequate or inappropriate results
19	Chavannes NH. Integrated chronic obstructive pulmonary disease management in primary care. *Disease Management & Health Outcomes* 2008; **16**(5): 315-8.	Inadequate or inappropriate results
20	Chen M, Patel T, Chang F. The impact of a primary care, pharmacist-driven intervention in patients with chronic non-cancer pain-A pilot study. *Pharmacy* 2020; **8**(8): 113.	Not relevant to the theme for review
21	Chen XRC, Leung SH, Li YC. Chronic Obstructive Pulmonary Disease (COPD) management in the community: how could primary care team contribute? *BMC family practice* 2020; **21**(1): 184.	Not relevant to the theme for review
22	Collins S. Primary care shortages: Strengthening this sector is urgently needed, now and in preparation for healthcare reform. *American Health and Drug Benefits* 2012; **5**(1): 40-7.	Inadequate or inappropriate results
23	Chen LW, Nguyen AT, Jacobson J, Palm D. Assessment of workforce capacity for Local Health Departments in Nebraska: a perspective from public health programmatic areas. *Journal of Public Health Management & Practice*; **18**(6): 595-601.	Not relevant to the theme for review
24	Chen LM, Sakshaug JW, Miller DC, Rosland A-M, Hollingsworth J. The association among medical home readiness, quality, and care of vulnerable patients. *Am J Manag Care* 2015; **21**(8): e480-e6.	Inadequate or inappropriate results
25	Day A, Oldroyd C, Godfrey S, Quinn T. Availability of cardiac equipment in general practice premises in a cardiac network: A survey. *British Journal of Cardiology* 2008; **15**(3): 141-4.	Inadequate or inappropriate results
26	Deckard GJ, Borkowski N, Diaz D, Sanchez C, Boisette SA. Improving timeliness and efficiency in the referral process for safety net providers: Application of the lean six sigma methodology. *Journal of Ambulatory Care Management* 2010; **33**(2): 124-30.	Not relevant to the theme for review
27	Depatie A, Bigbee JL. Rural Older Adult Readiness to Adopt Mobile Health Technology: A Descriptive Study. *Online Journal of Rural Nursing & Health Care* 2015; **15**(1): 150-84.	Inadequate or inappropriate results
28	Due TD, Thorsen T, Waldorff FB, Kousgaard MB. Role enactment of facilitation in primary care - a qualitative study. *BMC Health Services Research*; **17**(1): 593.	Not relevant to the theme for review
29	Fleck S. Unified health services and family focused primary care.	Not relevant to the theme for review
30	Foo KM, Sundram M, Legido-Quigley H. Facilitators and barriers of managing patients with multiple chronic conditions in the community: a qualitative study. *BMC public health* 2020; **20**(1): 273.	Inadequate or inappropriate results
31	Fortin M, Chouinard M-C, Diallo BB, Bouhali T. Integration of chronic disease prevention and management services into primary care (PR1MaC): findings from an embedded qualitative study. *BMC Family Practice* 2019; **20**(1): 1-8.	Inadequate or inappropriate results

32	Fox CH, Brooks A, Zayas LE, McClellan W, Murray B. Primary care physicians' knowledge and practice patterns in the treatment of chronic kidney disease: an Upstate New York Practice-based Research Network (UNYNET) study. *Journal of the American Board of Family Medicine: JABFM*; **19**(1): 54-61.	Not relevant to the theme for review
33	Fuchs S, Jaffe DM, Christoffel KK. Pediatric emergencies in office practices: prevalence and office preparedness. *Pediatrics*; **83**(6): 931-9.	Not relevant to the theme for review
34	Furno M. The primary role: How the availability of primary care physicians affects diabetes care management.	Inadequate or inappropriate results
35	Galaviz KI, Narayan KMV, Manders OC, et al. The Public Health Leadership and Implementation Academy for Noncommunicable Diseases. *Preventing Chronic Disease*; **16**: E49.	Inadequate or inappropriate results
36	Ghimire U, Shrestha N, Adhikari B, Mehata S, Pokharel Y, Mishra SR. Health system's readiness to provide cardiovascular, diabetes and chronic respiratory disease related services in Nepal: analysis using 2015 health facility survey. *BMC Public Health* 2020; **20**(1): 1163.	Combined data on primary and secondary healthcare level
37	Gerbert B, Maurer T, Berger T, et al. Primary care physicians as gatekeepers in managed care. Primary care physicians' and dermatologists' skills at secondary prevention of skin cancer. *Archives of Dermatology*; **132**(9): 1030-8.	Inadequate or inappropriate results
38	Gordon NP, Hornbrook MC. Older adults' readiness to engage with eHealth patient education and self-care resources: a cross-sectional survey. *BMC health services research* 2018; **18**(1): 220.	Not relevant to the theme for review
39	Goytia EJ, Rapkin B, Weiss ES, Golub D, Guzman V, O'Connor M. Readiness and capacity of librarians in public libraries to implement a breast cancer outreach and screening campaign in medically underserved communities. *Cancer control : journal of the Moffitt Cancer Center* 2005; **12 Suppl 2**: 13-20.	Not relevant to the theme for review
40	Gujral UP, Johnson L, Nielsen J, et al. Preparedness cycle to address transitions in diabetes care during the COVID-19 pandemic and future outbreaks. *BMJ Open Diabetes Research & Care* 2020; **8**(1): 07.	Not relevant to the theme for review
41	Haileamlak A. Preparedness to Respond to the Ever-increasing Cancer Cases. *Ethiopian Journal of Health Sciences*; **25**(4): 293-4.	Not relevant to the theme for review
42	Hanusaik N, O'Loughlin JL, Kishchuk N, Paradis G, Cameron R. Organizational capacity for chronic disease prevention: a survey of Canadian public health organizations. *European Journal of Public Health*; **20**(2): 195-201.	Combined data on primary and secondary healthcare level
43	Henderson KH, DeWalt DA, Halladay J, et al. Organizational Leadership and Adaptive Reserve in Blood Pressure Control: The Heart Health NOW Study. *Annals of Family Medicine*; **16**(Suppl 1): S29-S34.	Inadequate or inappropriate results
44	Heslop L, Power R, Cranwell K. Building workforce capacity for complex care coordination: a function analysis of workflow activity. *Human Resources for Health [Electronic Resource]*; **12**: 52.	Not relevant to the theme for review
45	Geboers et al.	Inadequate or inappropriate results
46	Inrig SJ, Higashi RT, Tiro JA, Argenbright KE, Lee SJ. Assessing local capacity to expand rural breast cancer screening and patient navigation: An iterative mixed-method tool. *Evaluation and program planning* 2017; **61**: 113-24.	Inadequate or inappropriate results
47	Jayanna K, Swaroop N, Kar A, et al. Designing a comprehensive Non-Communicable Diseases (NCD) programme for hypertension	Inadequate or inappropriate results

	and diabetes at primary health care level: evidence and experience from urban Karnataka, South India. *BMC Public Health* 2019; **19**(1): 409.	
48	Jigjidsuren A, Byambaa T, Altangerel E, et al. Free and universal access to primary healthcare in Mongolia: the service availability and readiness assessment. *BMC Health Services Research*; **19**(1): 129.	Inadequate or inappropriate results
49	Jin Y, Zhu W, Yuan B, Meng Q. Impact of health workforce availability on health care seeking behavior of patients with diabetes mellitus in China.	Combined data on primary and secondary healthcare level
50	Joffres C, Heath S, Farquharson J, et al. Defining and operationalizing capacity for heart health promotion in Nova Scotia, Canada. *Health Promotion International* 2004; **19**(1): 39-49.	Not relevant to the theme for review
51	Jones D, West R, Lester C. Evaluation of changes in primary health care availability and provision from the patient perspective.	Inadequate or inappropriate results
52	Jones R, Ostrem A. Optimising pharmacological maintenance treatment for COPD in primary care. *Primary Care Respiratory Journal* 2011; **20**(1): 33-45.	Inadequate or inappropriate results
53	Kayser L, Rossen S, Karnoe A, et al. Development of the Multidimensional Readiness and Enablement Index for Health Technology (READHY) Tool to Measure Individuals' Health Technology Readiness: Initial Testing in a Cancer Rehabilitation Setting. *Journal of medical Internet research* 2019; **21**(2): e10377.	Inadequate or inappropriate results
54	Khunti K, Baker R, Rumsey M, Lakhani M. Approaches to the organization of multi-practice audits in primary health care in the UK. *International Journal for Quality in Health Care*; **11**(3): 221-6.	Inadequate or inappropriate results
55	Kaufman ND, Rajataramya B, Tanomsingh S, Ronis DL, Potempa K. Nurse preparedness for the non-communicable disease escalation in Thailand: a cross-sectional survey of nurses. *Nursing & Health Sciences* 2012; **14**(1): 32-7.	Inadequate or inappropriate results
56	Laatikainen T, Inglin L, Collins D, et al. Implementing Package of Essential Non-communicable Disease Interventions in the Republic of Moldova-a feasibility study. *Eur J Public Health* 2020.	Inadequate or inappropriate results
57	Landon BE, Hicks LS, O'Malley AJ, et al. Improving the management of chronic disease at community health centers. *New England Journal of Medicine* 2007; **356**(9): 921-34.	Inadequate or inappropriate results
58	Langer S, Chew-Graham CA, Drinkwater J, et al. A motivational intervention for patients with COPD in primary care: qualitative evaluation of a new practitioner role. *BMC Family Practice*; **15**: 164.	Inadequate or inappropriate results
59	Liu J, Yin H, Zheng T, et al. Primary health institutions preference by hypertensive patients: Effect of distance, trust and quality of management in the rural Heilongjiang province of China.	Inadequate or inappropriate results
60	Maarse JA, Ruwaard D, Spreeuwenberg C. The governance of quality management in dutch health care: new developments and strategic challenges. *Quality Management in Health Care*; **22**(3): 236-47.	Not relevant to the theme for review
61	Madueno A, Martin A, Peculo JA, Anton E, Paravisini A, Leon A. Usefulness of inspiratory capacity measurement in COPD patients in the primary care setting. *International Journal of General Medicine* 2009; **2**: 219-25.	Combined data on primary and secondary healthcare level
62	Main DS, Cohen SJ, DiClemente CC. Measuring physician readiness to change cancer screening: Preliminary results. *American Journal of Preventive Medicine* 1995; **11**(1): 54-8.	Inadequate or inappropriate results
63	Monaghan M, Hilliard M, Sweenie R, Riekert K. Transition readiness in adolescents and emerging adults with diabetes: the role	Inadequate or inappropriate results

	of patient-provider communication. *Current Diabetes Reports*; **13**(6): 900-8.	
64	Moynihan M, Saewyc E, Whitehouse S, Paone M, McPherson G. Assessing readiness for transition from paediatric to adult health care: Revision and psychometric evaluation of the Am I ON TRAC for Adult Care questionnaire. *Journal of Advanced Nursing*; **71**(6): 1324-35.	Inadequate or inappropriate results
65	Neher M, Landen Ludvigsson M, Enblom A. Preparedness to Implement Physical Activity and Rehabilitation Guidelines in Routine Primary Care Cancer Rehabilitation: Focus Group Interviews Exploring Rehabilitation Professionals' Perceptions. *Journal of cancer education : the official journal of the American Association for Cancer Education* 2020.	Inadequate or inappropriate results
66	Nilsson GH, Skånér Y, Krakau I, Hassler E, Sundquist K. Primary prevention of first-ever stroke in primary health care: A clinical practice study based on medical register data in sweden.	Inadequate or inappropriate results
67	Nuno-Solinis R. Are Healthcare Organizations Ready for Change? Comment on "Development and Content Validation of a Transcultural Instrument to Assess Organizational Readiness for Knowledge Translation in Healthcare Organizations: The OR4KT". *International Journal of Health Policy & Management*; **7**(12): 1158-60.	Inadequate or inappropriate results
68	Nyarko KM, Ameme DK, Ocansey D, Commeh E, Markwei MT, Ohene SA. Capacity assessment of selected health care facilities for the pilot implementation of Package for Essential Non-communicable Diseases (PEN) intervention in Ghana. *The Pan African medical journal*; **25**(Suppl 1): 16.	Combined data on primary and secondary healthcare level
69	Ogbimi RI. Leadership in Nigerian health system for cancer prevention and control. *African Journal of Medicine & Medical Sciences*; **38 Suppl 2**: 49-53.	Inadequate or inappropriate results
70	Ostroff JS, Copeland A, Borderud SP, Li Y, Shelley DR, Henschke CI. Readiness of lung cancer screening sites to deliver smoking cessation treatment: Current practices, organizational priority, and perceived barriers. *Nicotine & Tobacco Research* 2016; **18**(5): 1067-75.	Not relevant to the theme for review
71	Oyewole EY, Ojewale LY, Abimbola OO. Primary Health Care Nurses' Competencies and Resources Availability for Diabetes Mellitus Care at Local Government Areas of Ibadan. *International Journal of Caring Sciences* 2020; **13**(1): 368-80.	Not relevant to the theme for review
72	Parchman ML, Anderson ML, Coleman K, et al. Assessing quality improvement capacity in primary care practices. *BMC Family Practice*; **20**(1): 103.	Not relevant to the theme for review
73	Pilkerton CS, Singh SS, Bias TK, Frisbee SJ. Healthcare resource availability and cardiovascular health in the USA. *BMJ Open* 2017; **7**(12): e016758.	Not relevant to the theme for review
74	Radin A, Cote C. Primary care of the patient with chronic obstructive pulmonary disease-part 1: frontline prevention and early diagnosis. *American Journal of Medicine*; **121**(7 Suppl): S3-12.	Inadequate or inappropriate results
75	Rathish D, Premarathna I, Jayathilake T, et al. Availability of essential medicines in selected public, primary and secondary health care institutions of a rural Sri Lankan district: A spot survey.	Combined data on primary and secondary healthcare level
76	Rogers HE, Akiteng AR, Mutungi G, Ettinger AS, Schwartz JI. Capacity of Ugandan public sector health facilities to prevent and	Combined data on primary and secondary healthcare level

	control non-communicable diseases: an assessment based upon WHO-PEN standards. *BMC Health Services Research*; **18**(1): 606.	
77	Roper KL, Thomas AR, Hieronymus L, Brock A, Keck J. Patient and Clinician Perceptions of Prediabetes: A Mixed-Methods Primary Care Study. *Diabetes Educ* 2019; **45**(3): 302-14.	Inadequate or inappropriate results
78	Schwartz R, Smith C, Speers MA, et al. Capacity building and resource needs of state health agencies to implement community-based cardiovascular disease programs. *Journal of Public Health Policy* 1993; **14**(4): 480-94.	Inadequate or inappropriate results
79	Shaw RJ, Kaufman MA, Bosworth HB, et al. Organizational factors associated with readiness to implement and translate a primary care based telemedicine behavioral program to improve blood pressure control: the HTN-IMPROVE study. *Implementation Science*; **8**: 106.	Inadequate or inappropriate results
80	Sorensen A, Le LW, Swami N, et al. Readiness for delivering early palliative care: A survey of primary care and specialised physicians. *Palliative Medicine* 2020; **34**(1): 114-25.	Combined data on primary and secondary healthcare level
81	Soylu TG, Cuellar AE, Goldberg DG, Kuzel AJ. Readiness and Implementation of Quality Improvement Strategies Among Small- and Medium-Sized Primary Care Practices: an Observational Study. *Journal of General Internal Medicine* 2020.	Not relevant to the theme for review
82	Tanjasiri SP, Tran JH. Community capacity for cancer control collaboration: weaving an Islander Network for Cancer Awareness, Research and Training for Pacific Islanders in Southern California. *Cancer Detection & Prevention*; **32 Suppl 1**: S37-40.	Inadequate or inappropriate results
83	Tompkins JW, Mequanint S, Barre DE, et al. National Survey of Indigenous primary healthcare capacity and delivery models in Canada: the TransFORmation of IndiGEnous PrimAry HEAlthcare delivery (FORGE AHEAD) community profile survey. *BMC Health Services Research*; **18**(1): 828.	Combined data on primary and secondary healthcare level
84	Weeks DL, Polello JM, Hansen DT, Keeney BJ, Conrad DA. Measuring primary care organizational capacity for diabetes care coordination: the Diabetes Care Coordination Readiness Assessment. *Journal of General Internal Medicine*; **29**(1): 98-103.	Not relevant to the theme for review

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Lines 2-3, Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Lines 25-48, Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Lines 90-117, Page 4-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Lines 121-122, Page 45
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Lines 132-137, Page 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Lines 146-161, Page 7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary materials
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 192-208, Page 8-9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Lines 181-190, Page 8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Lines 209-218, Page 9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Lines 209-218, Page 9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 192-202, Page 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Result was thematically presented in descriptive manner. Therefore, no effect measure was presented.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Lines 192-202, Page 8

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Lines 192-202, Page 8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Lines 192-202, Page 8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	No meta-analysis performed
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	No meta-analysis performed
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	No sensitivity
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Lines 192-202, Page 8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable in this review
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Lines 229-246, Page 10
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary materials
Study characteristics	17	Cite each included study and present its characteristics.	Lines 229-246, Page 10
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Lines 192-202, Page 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Result was presented thematically. Therefore, no table/confidence interval was presented.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not exactly relevant in this review as reported was described under themes
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not exactly relevant in this review as

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
			reported was described under themes
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Lines 473-481, Page 24
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not exactly relevant in this review as reported was described under themes
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not exactly relevant in this review as reported was described under themes
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not exactly relevant in this review as reported was described under themes
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Lines 420-468, Page 22-24
	23b	Discuss any limitations of the evidence included in the review.	Lines 473-481, Page 24
	23c	Discuss any limitations of the review processes used.	Lines 473-481, Page 24
	23d	Discuss implications of the results for practice, policy, and future research.	Lines 473-481, Page 24
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Lines 128-130, Page 6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Protocol was not prepared
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	No amendment done
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Lines 511, Page

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
			25
Competing interests	26	Declare any competing interests of review authors.	Lines 505, Page 25
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Lines 507, Page 25

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

29-Nov-2021

Dear Mr. Kabir:

I write you in regards to manuscript # bmjopen-2021-057421.R1 entitled "Health system readiness for non-communicable diseases at the primary care level: A systematic review" which you submitted to BMJ Open.

In view of the criticisms of the re-reviewer(s) found at the bottom of this letter, your manuscript has been declined for publication in BMJ Open.

Thank you for considering BMJ Open for the publication of your research and I am sorry to be sending disappointing news. I hope the outcome of this specific submission will not discourage you from the submission of future manuscripts.

Sincerely,

Neil Bennet
Senior Assistant Editor
BMJ Open

*** ***
Respected Editor,
We want to thank you for considering the revision submission to address the reviewers 'comments and queries. We believe these comments and queries have helped to enhance the quality of our paper significantly.

We have carefully revised our manuscript as per the valuable comments provided by all the reviewers. Hoping that the paper now holds up to the requirements of the journal.

Please let us know if it needs any further changes.

Thank you again.
Kind regards,
Ashraful Kabir
On behalf of the authors

Reviewer: 3
Dr. David Hailey, University of Wollongong
Comments to the Author:
A number of corrections have been made to the manuscript and some additional detail provided. However, further checking for errors and omissions is recommended.

Response: Thank you for your recommendation. We have rechecked the manuscript and errors and omissions were thoroughly addressed.

Responses regarding Table 2 were noted. Grouping the studies by country rather than by the names of first authors might be considered.

Response: The comment has been addressed. We have added a column as country in the revised manuscript: **Table 2, Page: 12-15**

The manuscript still states that most of the studies were of acceptable quality (p20, line 409), though 'most' was only 57%. This is followed, in the Discussion, by "Most of the studies included in this

review had a reasonably acceptable quality" (p22, line 458). The details that follow are helpful but a more considered summary statement is required.

Response: The first comment above has been addressed as follows (please **see lines: 432-435, page: 22**) in the revised manuscript:

Nearly three-fifth (61%) of the studies were of good or high quality (MMAT score of 75) (Table 1): one paper (4%) had an MMAT score of 25 (low quality), eight (35%) scored 50 (medium quality), eleven (48%) received 75 (good quality) and three (13%) reached 100 (high quality). No study had an MMAT score of 0 (poor quality).

The second comment above has been addressed as follows (**lines: 485-493, Page:** 24) in the revised manuscript):

The sentence 'Most of the studies included in this review had a reasonably acceptable quality" has been replaced with (**please see line: 485-486, page: 24**) 'Majority of the studies in this review had good or high quality'.

Furthermore, the following texts have been added (**please see lines: 488-493, page: 24**)

'A few quantitative studies lacked sufficient details about the participants' selection criteria, standard criteria for minimizing bias, and use of non-validated questionnaires with a relatively small sample size that might affect the scope of generalizability of the findings (27, 29, 32, 34, 35). One mixed-method study was rated low quality due to the homogeneous sample and insufficient information about the data analysis (47). The rest of the mixed-method studies included in the review had a more representative sample size and methodological rigors.'

The information regarding increasing prevalence of DM and HTN is worthwhile but does not address the point made which referred to "The focus on DM and HTN may be due to multiple factors, including increasing prevalence and associated determinants/risk factors for other NCDs……" (lines 441-443 in R1)

Response: We have provided additional text to explain the possible reason for higher level readiness/availability of services for DM and HTN compare to the other NCDs (cancer, CRD, CVD) in the discussion section: **Lines: 468-477, Page: 23**

'Moreover, the integrated model for DM and HTN care has widely been considered in the low-and middle-income countries that accelerated the provision of effective and equitable health service delivery at the primary healthcare level, which would have helped to address the rising burden of them with accessible, equitable, and cost-effective interventions (56-58)'

Reviewer: 4
Dr. Rajat Das Gupta, BRAC University James P Grant School of Public Health
Comments to the Author:

Thank you for addressing the comments. I have few comments:
1. I am not convinced about the logic of restricting the earliest date of search to January 1990. The authors wrote: ". The studies published in 1985 onward were deemed to be relevant to this review. Therefore, the earliest date of the search was set to ensure the optimum number of studies published since 1990." Then the authors should set the search date starting from January 1985. That would ensure them that they are not missing any studies.

Response: Thank you for raising this concern regarding the starting date of search. The search has been updated from January 1984 to December 1990, which resulted in 17 additional studies and of

them no study satisfied the inclusion criteria. The revised manuscript has been updated with this search results.

2. Also excluding SPA reports is a big fallacy of this manuscript. If this is a systematic review aiming to synthesise the current evidences on primary healthcare system readiness and evaluate its response to NCDs on a global scale, even by amending the study protocol. Without this the systematic review will be incomplete and the evidence will not be robust. DHS does these surveys to generate evidence and these surveys follow rigorous methods. The authors should again consider this.

Response: We acknowledge that SPA report presents important information regarding the preparedness of the primary healthcare system regarding the NCDs. We have considered this report as relevant. However, we understand that SPA reports health system preparedness at the primary as well as secondary healthcare levels on the various health system components. Thus, it was not always possible to retrieve solely the primary healthcare-specific data from these reports. The following texts were included in the revised manuscript.

Lines: 324-330

'The shortage of trained healthcare staff (at least one staff received in-service training in the last 24 months before the data collection date) was reported at the primary healthcare in Bangladesh (39). The trained staff for cervical cancer (29% trained staff at the UHCs, but no trained staff in CCs and union-level facilities), CRD (4% union-level facilities, 11% CCs, and 29% UHCs), CVD (7% union-level facilities, 15% CCs, and 40%, UHCs), DM (3% union-level facilities, 14% CCs, and 28% UHCs), and hypertension (6% union-level facilities, 10% CCs, and 39% UHCs) were reported (39).'

Lines: 368-371, Pages: 18-19

'In Bangladesh, the availability of medicine widely varied at the UHCs based on their types for DM (metformin 38.1%, glibenclamide 7.4%), CRD (salbutamol 91.6%, epinephrine 0.3%), CVD (amiodipine/nifedipine 41.5%, aspirin 2.6%), and HTN (amlodipine/nifedipine 44.7%, thiazide 1.4%), but no supply in the CCs were reported (39).

Lines: 388-392, Page: 20

'However, basic equipment and diagnostic facilities such as stethoscope (93.2% CCs, 96.9% UHCs), blood pressure apparatus (85.6% CCs, 95.4% UHC), adult scale (90.9% CC, 82.9% UHCs), blood glucose testing (22.2% CCs, 48.9% UHCs), urine protein (0% CCs, 36.2 % UHCs), and urine glucose (0% CCs, 30.4 % UHCs) were available in Bangladesh (39).

*** ***

COI statements:

Reviewer: 3
Competing interests of Reviewer: None to declare

Reviewer: 4
Competing interests of Reviewer: None declared

** **

BMJ Open

Health system readiness for non-communicable diseases at the primary care level: a systematic review

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Review Title:

Health system readiness for non-communicable diseases at the primary care level: a systematic review

Short Title:

Health system readiness for non-communicable diseases: a systematic review

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Abstract

Objective: To synthesise evidence on the primary healthcare system's readiness for preventing and managing non-communicable diseases (NCDs).

Design: Systematic review.

Data sources: Ovid MEDLINE, EMBASE, CINAHL, PsycINFO and Scopus were searched from 1 January 1984 to 30 July 2021, with hand-searching references and expert advice.

Eligibility criteria: Any English-language health research with evidence of readiness/preparedness of the health system at the primary healthcare level in the context of four major NCDs: diabetes mellitus, cancer, chronic respiratory diseases, and cardiovascular diseases.

Data extraction and synthesis: Two authors independently extracted data and assessed the bias. The full-text selected articles were then assessed using the Mixed Methods Appraisal Tool. Health system readiness was descriptively and thematically synthesized in line with the health system dynamics framework.

Results: Out of 7,843 records, 23 papers were included in this review (15 quantitative, three qualitative and five mixed-method studies). The findings showed that existing literature predominantly examined health system readiness from the supply-side perspective as embedded in the World Health Organization's health system framework. However, at the primary healthcare level, these components are insufficiently prepared for NCDs. Among NCDs, higher levels of readiness were reported for diabetes mellitus and hypertension in comparison to chronic respiratory diseases (asthma, chronic obstructive pulmonary disease), cardiovascular diseases and cancer. There has been a dearth of research on the demand-side perspective, which is an essential component of a health system and must be addressed in future research.

Conclusion: The supply-side components at the primary healthcare level are inadequately ready to address the growing NCD burden. Improving supply-side factors, with a particular focus on chronic respiratory diseases, cardiovascular diseases and cancer, and improving understanding of the demand-

side components of the health system's readiness, may help to prevent and manage NCDs at the primary healthcare level.

Keywords: non-communicable diseases, health system readiness, primary health care, systematic review

Strengths and limitations of this study

- Data synthesis was informed by the health system dynamics framework, which offers a deeper and more comprehensive (both supply-side and demand-side factors) understanding of primary healthcare system readiness for NCDs.
- We conducted an extensive systematic search of literature with hand-searching references and expert advice regarding health system readiness for non-communicable diseases at the primary care level, which increases the validity and trustworthiness of this review's findings.
- Meta-analysis was not possible due to heterogeneity of study designs, methods and techniques, as well as the studies' focus on a variety of health system components.
- A few studies that reported health system readiness at combined primary and secondary healthcare levels were excluded.

Introduction

Globally, non-communicable diseases (NCDs) are the leading causes of deaths and disabilities, accounting for 41 million deaths (71% of all deaths) annually (1), with 77% occurring in low- and middle-income countries (1, 2). The current increased NCD burden may be due to the rise of the ageing population, rapid and/or unplanned urbanisation and lifestyle-related factors (e.g. physical inactivity, unhealthy diets and consumption of tobacco products and alcohol) (3). If current trends continue, the estimated cumulative deaths from NCDs will reach 52 million by 2030 (3), and NCD-related cost was projected to be US$ 47 trillion between 2010 and 2030 (4). NCDs' predicted health outcomes and economic burden will have adverse consequences, such as prolonged illness or disability, greater treatment costs, loss of productivity and substantial opportunity cost, which will eventually affect households' economy and well-being (4, 5). The impact of NCDs may result in increased poverty, higher inequality and low quality of life. Considering the immense influence of NCDs, many commitments and control strategies have been made at the global, national and local levels to prevent and manage them (6-8). The Sustainable Development Goals, for example, by 2030, targeted one-third reduction of premature deaths from the four major NCDs of diabetes mellitus (DM), cancer, chronic respiratory diseases (CRDs) and cardiovascular diseases (CVDs) (8, 9) among people aged 30–69.

Primary healthcare is crucial for promoting essential healthcare services and achieving improved health outcomes, particularly in countries with resource-poor settings (3, 10-12). Growing evidence shows that a well-functioning primary healthcare system has immense potential for improving global health outcomes due to its extensive coverage, cost-effectiveness, well-structured network of healthcare facilities, affordable technologies, socially and culturally acceptable intervention methods and broad community participation (10, 13, 14). NCD prevention and management differ from that of acute conditions, where the primary healthcare approach has a powerful impact. Unlike acute conditions, NCD prevention and management require extended or even life-long healthcare support, early case detection, psychosocial promotion, risk factor identification, self-management, behavioural modifications and regular medical support, such as adherence to medical procedures and treatment (3).

The primary healthcare system is typically the first-line contact for individuals seeking care, making it easier for patients to continue follow-up contacts (15). Therefore, it can be viewed as the most effective and appropriate mechanism for addressing NCDs.

While the literature emphasises the roles and importance of the primary healthcare system in preventing and managing NCDs following a dozen of global commitments and strategies, little is known about the extent to which it is ready to deliver NCD services (16, 17). The concept of 'health system readiness' is often explained in terms of the health system 'components' or 'framework'. Until recently, health system readiness was mostly defined and presented in the context of the World Health Organization's (WHO) health system framework, proposed in 2008, which described six 'key elements' or 'building blocks':, health service delivery, health workforce, health financing, health information system, leadership and governance, medical products, knowledge and technologies (18). However, the WHO's model is viewed as having limited capacity to comprehensively explain how and whether different health system elements within a broader societal context interact and are influenced, as well as how population/individual behaviour and choices and the process impact this mechanism (19, 20). In order to provide an exhaustive understanding of system interactions, van Olmen et al. proposed the 'health system dynamics framework', which included the WHO's six building blocks and concurrent literature. It is comprised of 10 elements that analyse their interactions and functions under a broader societal context (21).

Guided by the 'health system dynamics framework', this systematic review aimed to synthesise the current evidences on primary healthcare system readiness and evaluate its response to NCDs on a global scale. The findings of this review will help policymakers, public health planners and researchers focus on the further actions required to establish a well-prepared health system at the primary healthcare level to address the growing NCD burden.

Methods

Protocol and registration

This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline (22) and was registered on the Research Registry (REVIEWREGISTRY1163).

Inclusion criteria

This review included studies that reported on the readiness/preparedness of various health system components at the primary healthcare level in the context of four major NCDs: DM, cancer, CRDs and CVDs. Where studies reported health system preparedness at the primary and secondary care level combined, only information related to the primary healthcare level was included. However, studies in which the primary and secondary care level data could not be separated were excluded.

Exclusion criteria

Studies on other NCDs such as arsenicosis, kidney diseases, mental health disorders, hearing disability, oral disease, birth defects and road injuries were excluded. Papers that focused on NCD interventions/programmes beyond the primary healthcare level were likewise excepted. Editorials, letters, opinion articles, narrative or systematic reviews, study protocols, conference abstracts, posters, reports, and book chapters were also not considered. Additionally, works that were published in a language other than English were excluded.

Data sources and search strategy

The search strategy aimed to find English language studies in five databases (Ovid Medline, Ovid Embase, Ovid PsycInfo, CINAHL and Scopus) published between 1 January 1984 and 30 July 2021 (Figure 1). The WHO's health system model proposed in 1984 was considered appropriate to identify and assess the key components of the primary healthcare system. The studies published in 1984 onward were deemed to be relevant to this review. Therefore, the earliest date of the search was set to ensure

the optimum number of studies published since 1984. The search strategies used a combination of subject headings and free text terms that aimed to cover the areas of (1) non-communicable diseases (e.g., chronic disease or chronic conditions or chronic disorders), AND (2) primary health system (e.g. primary health service or first-level healthcare facility or local health system or local-level health facility) AND (3) readiness or preparedness or capacity.

Searches were adapted as appropriate to the specifications of each of the 5 databases. The final searches are presented in the (Supplementary Appendix file). Hand-searching and reference checking of citations and reference lists were undertaken, and additional records were identified through personal consultations with experts, including researchers, administrators, policy planners, and public health practitioners.

[FIGURE 1 SHOULD BE INSERTED HERE]

Figure 1 PRISMA flowchart for study inclusion.

Data extraction

Three authors were involved in the data extraction process. First, records identified through database and manual searches were imported into the Endnote library (EndNote X9.2, Thomson Reuters 2019). Afterwards, the duplicate records were removed. Next, two authors (AK and NK) independently screened the studies based on their titles and/or abstracts. The full-text selected articles were then assessed using the inclusion and exclusion criteria and the standard quality assessment. When inconsistencies and discrepancies arose, a senior author (BB) was brought in to resolve the disagreements through discussion and consensus. A standardised data extraction sheet was developed and piloted. The extraction sheet contains the following study-specific information: authors, publication year, country, study aims, study design and settings, sample size and participants, data collection method and tool used, NCD/risk factor studied, health system component focus and key findings.

Quality assessment

The Mixed Methods Appraisal Tool (MMAT) was used to assess the methodological quality of the included studies (23). The distribution of MMAT scores varied with the study design and the evaluation of some selected parameters. The score is 25% when quantitative study (QUAN) = 1, qualitative study (QUAL) = 1 or mixed-method study (MM) = 0. It is 50% when QUAN = 2, QUAL = 2 or MM = 1; 75% when QUAN = 3, QUAL = 3 or MM = 2; and it is 100% when QUAN = 4, QUAL = 4 or MM = 3. Thus, each study was given a score ranging from 25% to 100% (Table 1). Two authors (AK and NK) independently assessed the studies' quality, and the senior author (BB) cross-checked them. Discrepancies and disagreements were resolved through discussion.

Table 1 Type of research design and associated quality of included studies (n=23)

Study design	Number of studies (%)	MMAT score (%)			
		25	50	75	100
Quantitative	15 (65)	-	5	7	3
Qualitative	3 (13)	-	1	2	-
Mixed-methods	5 (22)	1	2	2	-

Note. Entries in the table show the number of studies

Data synthesis

Data analysis was guided by the health system dynamics framework (24). The following themes were synthesised using this framework: (i) health service delivery, (ii) healthcare workforce, (iii) health financing, (iv) access to medical products and knowledge/technologies, (v) health information system, (vi) leadership and governance and (vii) community perspective. Under these themes, data from quantitative studies were reported descriptively using frequencies or percentages, while qualitative studies were synthesised by determining themes. In this process, a few steps were followed: (i) familiarising, (ii) identifying themes (health system components), (iii) indexing, (iv) charting and (v) mapping and interpreting. Data from mixed-methods studies were analysed both descriptively and thematically analysed. The heterogeneous study design of the included studies precluded a meaningful meta-analysis in this review.

Ethics statement

This review has been done as part of a PhD project. The project has been approved by the Monash University Human Research Ethics Committee (Project ID: 27112) and Bangladesh Medical Research Council (Ref: BMRC/NREC/2019-2022/270).

Patient and public involvement

There was no patient or public involvement.

Results

General characteristics of the study

Initially, 7,843 studies were retrieved, from which 2,213 duplicates were excluded (Figure 1). Then, 5,630 studies were excluded based on a title and abstract review, with 107 meeting the inclusion criteria for a full-text review. Following the full-text review, 23 studies were ultimately included in this study (Table 2): 15 were quantitative (cross-sectional) (25-39), three were qualitative (40-42) and five were mixed-method studies (43-47). Most of the research was conducted in resource-poor settings (20 studies), mostly in sub-Saharan Africa and South Asian countries. Eighteen studies focused on the health service delivery component at the primary healthcare level, while four studies addressed the leadership and governance (Fig-2a). Eight studies were conducted in the South Asian-East Asia Region (SEAR), and only a single study (n=1) was performed in both the Region of the Americas (AMR) and the European Region (EUR). One study involved multiple nations (Benin, Eritrea, Sudan, Syria, Bhutan, Sri Lanka, Vietnam and Suriname) (Fig-2b). DM was the most studied NCDs, with 12 studies reported on it, while mental illness (MI) was the least researched, with only two studies (Fig-2c) focused on it. Thirteen studies addressed multiple NCDs, six focused on a single NCD and four did not mention any specific NCD (e.g. termed chronic diseases) (Fig-2d).

[FIGURE 2 SHOULD BE INSERTED HERE]

Figure 2 Number of published studies that investigated the primary healthcare system's readiness between January 1984 and July 2021, broken down by NCD type, NCD focus and WHO region.

Note. AFR: African Region, AMR: Region of the Americas, SEAR: South East-Asian Region, EUR: European Region, WPR: Western Pacific Region, CRD: Chronic Respiratory Diseases, CVD: Cardiovascular Diseases, DM: Diabetes Mellitus, HTN: Hypertension, MI: Mental Illness, HSD: Health Service Delivery, HW: Health Workforce, HF: Health Financing, HIS: Health Information System, L&G: Leadership and Governance, MPK&T: Medical Products, Knowledge and Technologies.

251 Table 2 Summary – Characteristics of the studies included in this review

Author (Year)	Country	Study aims	Study design and settings	Sample size and participants	Data collection method and tool used	NCDs/Risk factors studied	Health system components' focus	Key findings/NCD Readiness
Biswas et al. (2018) (38)	Bangladesh	To assess health facilities' readiness to manage CVD and DM	Quantitative; Countrywide	319 healthcare facilities	Survey; Modified WHO SARA questionnaire	CVD, DM	HSD, HW, MPK&T	58% DM, and 24.1% CVD services were available.
Islam et al. (2016) (29)	Bangladesh	To assess the availability and provision of NCD service delivery	Quantitative; One district	50 health facilities	Survey; Modified WHO SARA questionnaire	CRD, CVD, DM	HSD	52% CRD, 73% CVD and DM 52% services were available.
NIPORT++ (2020) (39)	Bangladesh	To assess health facilities' readiness to manage cancer, CRD, CVD, DM and HTN	Quantitative; Countrywide	1524 healthcare facilities	Survey; Modified DHS questionnaire	Cancer, CRD, CVD, DM, HTN	HSD, HW, MPK&T	Availability of services varied from CCs to UHCs: cervical cancer (0.4%-37.5%), CRD (34.1%-93.9%), CVD (1.4%-69.6%), DM (0.9%-84.5%), and, hypertension (3.5%-91.5%).
Nyame et al. (2019) (34)	Ghana	To assess health facilities' capacity to implement the WHO PEN pilot	Quantitative; Three regions	23 health facilities	Survey; Modified WHO PEN questionnaire	NCD focus was not specified	HSD, HW, HF	Health facilities had inadequate capacity to implement WHO-PEN interventions.
Elias et al. (2017) (43)	India	To investigate the local health system's preparedness for DM and HTN	Mixed-methods; One district	1,149 patients, 39 healthcare staff, 30 pharmacists, 14 FGDs±	Survey; Non-validated questionnaire; Interview; IDI and FGD guides	DM, HTN	HSD, MPK&T	Public healthcare facilities had insufficient capacity for HTN and DM service delivery due to inadequate diagnostic capacity and frequent medicine stockouts.
Pakhare et al. (2015) (35)	India	To identify facility-level gaps that affect CVD care and management	Quantitative; 24 districts	85 medical officers	Survey; Modified WHO PEN questionnaire	DM, HTN	HSD, HW, MPK&T	The community health centre had a relatively better CVD management capacity than the primary health centre but lacked sufficient equipment, medicine and human resources.
Panda et al. (2018) (42)	India	To describe the health system's response and preparedness to NCDs	Qualitative; One district	13 key stakeholders	Interviews; IDI guide	Cancer, CVD, DM and Stroke	HSD, HW, HF, L&G	Health facilities were overburdened and lacked trained staff, and resources to manage NCDs.
Van Dijk-de Vries et al. (2016) (46)	Netherlands	To examine patients' readiness to consult psychosocial problems with nurses	Mixed-methods; Primary care setting	217 diabetic patient participants	Survey; Non-validated questionnaire; IDI guide	DM	Patients' readiness	90% of respondents had positive attitudes towards the existing diabetes consultation.
Honey et al. (2016) (28)	New Zealand	To assess older people's readiness to e-health	Quantitative; Urban settings	263 patients in primary healthcare centres	Survey; Non-validated questionnaire	Cancer, CRD, DM, HTN, Mental Illness	HIS	36% of participants sought health information from an online platform.
Adinan et al. (2019) (25)	Tanzania	To assess health facilities' readiness to manage DM and HTN	Quantitative; Rural and urban districts	43 health facilities, 62 healthcare workers	Survey; Modified WHO SARA questionnaire	DM, HTN	HSD, HW, HIS, MPK&T	86% DM, and 79% HTN services were available.
Bintabara et al. (2018) (26)	Tanzania	To assess health facilities' readiness to manage HTN	Quantitative; Countrywide	725 healthcare facilities	Survey; Modified WHO SARA questionnaire	HTN	HSD	28% of the health facilities had outpatient HTN services.

Peck et al. (2014) (36)	Tanzania	To assess NCDs burden and investigate facilities' readiness to manage DM and HTN	Quantitative; Urban and rural settings	335 healthcare workers	Modified WHO SARA questionnaire	DM, HTN	HSD, MPK&T	Most first-line healthcare facilities lacked guidelines, diagnostic equipment, trained staff and effective reporting systems.
Aekplakorn et al. (2005) (40)	Thailand	To assess primary healthcare providers' readiness to manage CVD along with community members perception and knowledge	Qualitative; Rural district	18 CVD patients, 33 community members, 29 health workers/professionals	Semi-structured interview; IDI, KII and FGD guides	CVD	HSD, MPK&T	Community members lacked minimal knowledge of the symptoms and signs of heart attack or stroke. Healthcare workers had limited skills to manage heart disease, while emergency care hospitals were insufficiently equipped to treat CVD patients.
Katende et al. (2015) (30)	Uganda	To assess the readiness of CD-related services	Quantitative; Urban and rural settings	28 health facilities, 222 health workers	Survey; Modified WHO SARA questionnaire	CRD, CVD, DM, Epilepsy, HTN, HIV	HSD, HW, MPK&T	Most primary care facilities had inadequate capacity to manage CDs
Musinguzi et al. (2015) (32)	Uganda	To assess health facilities' capacity to manage hypertension	Quantitative; Two districts	126 public & private health facilities, 271 healthcare workers	Survey; Non-validated questionnaire	HTN	HSD, MPK&T	Nearly 93% health facilities managed HTN services and all of them lacked trained staff, guideline, supplies, and diagnostic equipment.
Volk et al. (2015) (37)	USA	To examine clinicians' readiness to implement lung cancer screening programmes	Quantitative; Medical attendees	350 participants	Survey; Non-validated questionnaire	Cancer	HSD (screening)	50% clinicians planned to refer eligible patients for lung cancer screening.
Duong et al. (2019) (27)	Vietnam	To explore NCD service delivery availability, readiness and utilisation	Quantitative; Rural settings	89 community health centres	Survey; Modified WHO SARA questionnaire	DM, Cancer, CRD, HTN, Mental Illness	HSD, HW	25% of the health facilities had NCD services.
Kien et al. (2018) (41)	Vietnam	To explore responsiveness of commune health stations in urban settings to NCDs	Qualitative; Two districts	19 healthcare staff	Interviews; IDI guide	NCD focus was not specified	HSD, HW, HIS, MPK&T, HF, L&G	Healthcare professionals had limited knowledge about the national NCD strategy and lacked NCD-specific training and skills.
Meiqari et al. (2020) (44)	Vietnam	To describe the delivery and organisation of HTN care in primary healthcare settings	Mixed-methods; Rural and urban setting	90 healthcare staff, 29 hypertensive patients	Survey; Modified WHO SARA questionnaire; Semi-structured interview guide	HTN	HW, MPK&T	District-level health facilities had HTN services; however, capacity of facilities across districts to monitor prescription refills and disease for HTN patients varied.
Thi Thuy Nga et al. (2017) (45)	Vietnam	To describe commune health stations' readiness for NCD prevention and control	Mixed-methods; One district	20 commune health stations	Survey; Modified WHO SARA questionnaire; IDI and FGD guides	Cancer, CRD, DM, HTN	HSD, HW, HIS, MPK&T, HF, L&G	Commune health stations (CHSs) had limited capacity for NCD screening, diagnosis and treatment services.
Van Minh et al. (2014) (47)	Vietnam	To describe the primary care system's readiness for NCDs	Mixed-methods; One district	Health facilities and staff±	Survey; Non-validated questionnaire; Interview; IDI guide	NCD focus was not specified	HSD, HW, HIS, MPK&T, HF, L&G	Primary healthcare facilities had limited NCD management capacity and service integration.
Mutale et al. (2018) (33)	Zambia	To assess the health system's readiness to address NCDs	Quantitative; Three districts	46 primary healthcare facilities	Survey; Modified WHO PEN questionnaire	NCD focus was not specified	HSD	Only the first-level hospitals had a mean readiness index score (=>70%) for managing NCDs.
Mendis et al. (2012) (31)	Multi-country	To evaluate primary care facilities' capacity for the major NCDs	Quantitative; Multi-country*	90 primary healthcare facilities	Survey; Modified WHO PEN questionnaire	Cancer, CRD, CVD, DM	HSD, HW, HIS, MPK&T, HF, RS	Primary care facilities had inadequate financing, basic technologies and medicines, medical information systems and health workforce

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Note. CVDs: Cardiovascular Diseases, DM: Diabetes Mellitus, DHS: Demographic and Health Surveys, FGD: Focus Group Discussion, HTN: Hypertension, IDI: In-depth Interviews, KII: Key Informant Interview, HSD: Health Service Delivery, HW: Health Workforce, HIS: Health Information System, MPK&T: Medical Products, Knowledge and Technologies, HF: Health Financing, CRDs: Chronic Respiratory Diseases, NCD: Non-communicable Disease, WHO: World Health Organization, LMIC: Low- and Middle-Income Countries, L&G: Leadership and Governance, RS: Referral System, WHO SARA: WHO Service Availability and Readiness Assessment, WHO PEN: WHO Package of Essential Non-communicable Disease Interventions

*Multi-country includes Benin, Bhutan, Eritrea, Sri Lanka, Sudan, Suriname, Syria and Vietnam

[±]The number of participants/sample size was not specified.

[++]National Institute of Population Research and Training

Health service delivery

Of the 23 studies, 18 addressed issues related to the health service delivery system's readiness in preventing and managing NCDs at the primary healthcare level. Eleven of the 18 studies were quantitative studies, assessing primary healthcare facilities' readiness in implementing the WHO SARA reference manual (25-27, 29, 30, 36, 38, 45) or WHO PEN interventions (33-35). Three papers adopted the qualitative approach (40-42), while another three used the mixed-method approach (43, 45, 47). Four studies focused on a single NCD: DM, CVD (40) or HTN (26, 32). Five papers studied two NCDs (25, 35, 36, 38, 43), while seven investigated multiple NCDs and risk factors (27, 30, 31, 39, 41, 42, 48). However, two articles did not specify the NCDs that were evaluated (34, 47). Most of the studies found that healthcare facilities had insufficient capacity to deliver NCD prevention, care and treatment at the primary level. Among the NCDs, a higher level of readiness at the primary healthcare level was reported for hypertension prevention and management. The availability of hypertension services at healthcare facilities was reported to be 92.9% in Uganda (32) and 86% in Tanzania (25); however, one study found that hypertension preparedness was only 28% in Tanzania's outpatient care (26). A mixed-methods study in Thailand revealed that commune health stations were significantly prepared to manage HTN (44). The services readiness for CVD (47.8%), and DM (50%), were reported at the upazila health complex (UHC) in 2014 in Bangladesh(29, 38). However, the most recent data reported the availability of services largely varied from community clinic (CC) to 'UHC' for cervical cancer (0.4%-37.5%), CRD (34.1%-93.9%), CVD (1.4%-69.6%), DM (0.9%-84.5%), and, hypertension (3.5%-91.5%) (39). In Vietnam, only 25% of commune health centres were equipped to prevent, diagnose and treat major NCDs, with a noticeably lower utilisation rate of services by the users (27). Capacity for managing DM was predominantly low across all studies; however, one study in Tanzania (25) found that care for diabetes mellitus was available in 79% of healthcare facilities. Moreover, a lower level of readiness for managing CVD was reported across countries (31, 40, 42, 45). Qualitative studies conducted in Thailand (40) and India (43) noted facilities' low-level preparedness to manage HTN, DM and CVD, with healthcare facilities/programmes lacking effective community engagements and limited support

from the national programmes. In Kien et al.'s 2018 study conducted in Vietnam, one of the district-level health staff shared the following:

> [In our district] we implemented the hypertension programme for only four communes and implemented the diabetes programme for four other communes [among 18 communes]. We do not have any NCD programmes for the rest of the communes (41).

In a cross-sectional study conducted in Madhya Pradesh, India, the preparedness level for DM and HTN was reported to be slightly high (35). However, inadequate capacity was found for managing the common NCDs in a qualitative study in Odisha and Kerala, India (42). Lower levels of readiness for major NCDs have also been commonly reported in Zambia (33) and Ghana (34).

Overall, the delivery of NCD services was affected by multiple factors and revealed to be insufficient at the primary healthcare level. Inadequate and ill-equipped healthcare facilities were the most common issues hampering service delivery (25, 27, 31-35, 43). Moreover, notable key barriers include patients' lack of self-management education and knowledge (25), primary-level healthcare professionals' limited NCD management skills and national NCD strategies (25, 41), insufficient NCD service management and implementation capacity of local-level healthcare organisations (26, 47), a weak referral and follow-up system (30, 31), poor adherence to clinical guidelines (25, 30, 32, 36), inadequate screening opportunity (45), lack of information-education-community material (45) and the healthcare facility's rural location.

Healthcare workforce

Twelve of the studies reviewed reported a healthcare workforce issue related to NCD services and care. According to these papers, a common bottleneck for NCD services is insufficient primary-level healthcare professionals. One cross-sectional study in Tanzania reported only 53% and 15% of healthcare facilities had trained health professionals to manage HTN and DM, respectively (25). In Thailand (40) and Vietnam (45, 47), there was an acute lack of trained healthcare staff to manage CVD.

Moreover, a study conducted in Uganda found that only 26% and 16% of primary healthcare staff had an adequate level of knowledge to manage DM and HTN outpatients, respectively (30). This study also revealed that medical doctors had a higher level of knowledge (85% for HTN and 8% for DM) than nurses (8% for HTN and 4% for DM) (30). One study in Vietnam reported that only 9% of primary healthcare facilities in rural and urban locations had five categories of human resources (medical doctor, assistant doctor, nurse, midwife and pharmacist) to deliver HTN services (44). The shortage of trained healthcare staff (at least one staff received in-service training in the last 24 months before the data collection date) was reported at the primary healthcare in Bangladesh (39). The trained staff for cervical cancer (29% trained staff at the UHCs, but no trained staff in CCs and union-level facilities), CRD (4% union-level facilities, 11% CCs, and 29% UHCs), CVD (7% union-level facilities, 15% CCs, and 40%, UHCs), DM (3% union-level facilities, 14% CCs, and 28% UHCs), and hypertension (6% union-level facilities, 10% CCs, and 39% UHCs) were reported (39). According to a multi-country study, physicians at primary healthcare facilities were only available in two of the eight participating nations, while nurses and healthcare assistants were the key professionals for NCD services in the remaining six countries (31). A study in Ghana found that more than half of the healthcare centres lacked at least one medical doctor and nurse trained in NCDs (34). In India, while two medical officers were available on average at community health centres to manage DM, CVD, HTN and cancer, this number was lowest (less than half) in primary healthcare centres (35). In qualitative studies conducted in India (42) and Vietnam (41), insufficient healthcare staff jeopardised NCD services in primary care facilities. An NCD programme officer in Odisha, India and a national-level health worker in Vietnam shared their respective thoughts:

> In a big community health centre like ours, there should be more health workforce, and there should be a special training programme for all the health workers (42).

> For the health workforce at commune health stations, some facilities lack human resources and/or capacity. They must be strengthened in their capacity to provide services for NCD prevention, consultation, early detection and management. The reason for this is that we have not implemented NCD services systematically at primary healthcare facilities (41).

Health financing

Seven studies found that inadequate funding/budget support from the national healthcare programme compromised effective NCD service and care at the primary healthcare level. Furthermore, the absence or limitation of healthcare insurance coverage jeopardised NCD services and care. One study in India reported that less than 3% of households had insurance coverage (43). A study in Ghana revealed that healthcare financing is organised by the government as the 'National Health Insurance Scheme', and only those who paid the premium received its benefits (34). Limited public financial/budgetary support has also been identified as a major barrier to NCD services in primary healthcare in Vietnam (45, 47). A national-level health worker in Vietnam conveyed the following to Kien et al. in 2018:

> The budget for NCD primary health care services is extremely limited; [funding is] mainly through national target programmes on NCDs, but the programmes have been reduced. There are some barriers to health insurance reimbursement for NCDs at the primary health care level (41).

Similarly, in a qualitative study, a medical officer from Odisha, India shared his observation:

> Since there is no existing system, funds do not reach the grassroots level. There is no funding (42).

Access to medical products, knowledge and technologies

Across countries and regions, a lack of supply-side factors, such as medical products and knowledge and technologies to prevent and manage NCDs, has been widely reported. Fifteen studies reported inadequate or interrupted access to supplies and technologies at the primary healthcare level, which are vital for diagnosing and treating NCDs. In Bangladesh, the availability of medicine widely varied at the UHCs based on their types for DM (metformin 38.1%, glibenclamide 7.4%), CRD (salbutamol 91.6%, epinephrine 0.3%), CVD (amiodipine/nifedipine 41.5%, aspirin 2.6%), and HTN

(amlodipine/nifedipine 44.7%, thiazide 1.4%), but no supply in the CCs were reported (39). In India, the essential drugs for the management of HTN (beta-blockers and calcium channel blockers) were available at most of the primary health centres (PHCs) and community health centres; however, other drugs (except metformin) were largely unavailable across facilities that resulted in 90% of NCD patients in India to rely on private providers/facilities for NCD service and care (35). More than 60% of PHC-level facilities faced a shortage of essential DM medicine, with over 30% of PHCs having a medicine stockout of more than six months. Only 38% of PHCs had functional laboratory facilities (43). According to a study conducted in Tanzania, 50% of health centres, 24% of dispensaries and 80% of hospitals had HTN and DM medicines on hand; however, more than one-third of these locations lacked basic laboratory facilities (25). A qualitative study in Vietnam (41) and a qualitative multi-country investigation (Benin, Bhutan, Eritrea, Sri Lanka, Sudan, Suriname, Syria and Vietnam) (31) likewise reported the shortage of medicine and basic diagnostic facilities at primary healthcare facilities. Moreover, basic amenities and equipment for NCDs were in short supply in Ugandan healthcare facilities (hospitals and healthcare centres), with more than half of them lacking the recommended antihypertensive drug and nearly 30% lacking a blood pressure device (32). Likewise, Tanzanian healthcare facilities reported a shortage of the recommended medicine and supplies required for HTN and DM service and care (36). Similarly, a mixed-method study found a scarcity of medical products and equipment for CRD, DM, cancer and HTN in Vietnam (45). However, basic equipment and diagnostic facilities such as stethoscope (93.2% CCs, 96.9% UHCs), blood pressure apparatus (85.6% CCs, 95.4% UHCs), adult scale (90.9% CCs, 82.9% UHCs), blood glucose testing (22.2% CCs, 48.9% UHCs), urine protein (0% CCs, 36.2 % UHCs), and urine glucose (0% CCs, 30.4 % UHCs) were available in Bangladesh (39).

Health information system

Studies that assessed the health information system's readiness were limited. Only five papers addressed the health information system required for optimising NCD care at the primary healthcare level (25, 31, 41, 45, 47). These studies extensively reported on weak health information systems for detecting,

treating and monitoring NCD patients in primary healthcare settings. Furthermore, only 52.9% of primary healthcare facilities in Tanzania were prepared to collect, analyse and use local-level data for HTN and DM services (25). According to a multi-country survey, 85% of healthcare facilities created paper-based (patient register) individual-level information for patients who attended the facilities, but only half of that information was used at the follow-up visit (31). Weak and ineffective health information system management and inadequate NCD information, such as a lack of population-based NCD-related data on risk factors, mortality, disability and referral systems at the primary healthcare level, have been identified as crucial barriers to managing NCDs in Vietnam (41, 45).

Leadership and governance

Four studies investigated issues of leadership and stewardship in the management of NCDs in primary healthcare (41, 42, 45, 47). The research reported a lack of coordination among stakeholders and departments in implementing nationally designed NCD programmes/interventions. A qualitative study in India discovered weak inter-departmental coordination between various government departments (e.g. mental health programme and tobacco control programme), which resulted in poor NCD outcomes at the primary care level (42). The primary care-level NCD managers lacked knowledge of Vietnam's national NCD strategy or policies affecting targeted interventions for cancer, CVDs and diabetes (41). Limited knowledge of NCD management strategy and insufficient leadership capacity were highlighted among front-line healthcare staff (41). Furthermore, a lack of interaction between private and public providers and stakeholders was reported for NCD prevention/management activities in Vietnam (45). A mixed-method study found that Vietnam's nationally targeted NCD management and control programme lacked leadership and governance capacity (47).

Community perspective

Only two studies, conducted in the Netherlands and New Zealand, explored community perspectives on patients' capacity for using healthcare information, self-management and sharing problems when

seeking aid to manage NCDs at the primary healthcare level. A mixed-method study in the Netherlands (46) showed that, during a consultation, people with diabetes had a low-level ability to share psychological issues with healthcare providers at the primary healthcare level. In New Zealand, the readiness of patients with NCDs (cancer, chronic pain, diabetes and mental health problems) was low, with only 36% of them seeking health-related information from digitalised sources (28). This demand-side perspective was not addressed in studies from low- and middle-income countries.

Quality of included studies / Quality assessment

Nearly three-fifth (61%) of the studies were of good quality (MMAT score of 75) (Table 1): one paper (4%) had an MMAT score of 25 (low quality), eight (35%) scored 50 (medium quality), eleven (48%) received 75 (good quality) and three (13%) reached 100 (high quality). No study had an MMAT score of 0 (poor quality).

Discussion

This review appraised available evidence on health system readiness for NCDs at the primary healthcare level. The key findings of this study were that health systems at the primary healthcare level were inadequately prepared for NCD prevention and management, and that readiness was poorly understood. Health system readiness was examined from the providers' perspectives, which is specifically focused on the availability of infrastructures and supply of resources (e.g. medicine, basic amenities, medical products and technologies) as devised in the WHO SARA methodology or WHO PEN interventions. This may have narrowed the 'systems thinking' approach, which is a core philosophical basis that incorporates various elements and their interactions and interconnectedness to function as a system (19). Viewing the health system from this constricted sense categorically failed to include people's (service users') dimensions, which is an essential consideration for a well-functioning and inclusive health system. One plausible reason for predominantly analysing the health system from the supply-side

perspective was the widespread acceptance of the WHO health system framework and its broader applications in individual studies. Over the past years, the 'building block' approach appeared as a dominant health system method globally (49), supporting the existing trend of assessing the health system from the supply-side perspective. Thus, the demand-side perspectives of health system readiness for NCDs warrant extensive investigation. Future research may focus on the demand-side aspects of the health system's readiness, such as community characteristics and associated determinants needed to establish an effective and inclusive health system to respond to the NCD epidemic.

This review demonstrated that almost all countries' primary healthcare systems have suffered from inadequate supply-side responses to medicine, technologies, equipment, amenities, trained healthcare professionals, health information and leadership and stewardship. The ill-equipped health system may result from insufficient financing mobilised through international and domestic channels and a lack of policy priority in responding to NCDs (50-52). Among the NCDs addressed by the studies in this review, DM and HTN received the most attention in the current literature. Hence, other major NCDs such as CVD, CRD and cancer, which are prioritised by the WHO, remain largely under-researched. The focus on DM and HTN may be due to multiple factors, including increasing prevalence and associated determinants/risk factors for other NCDs in low- and middle-income countries, a nationwide vertical programme, individual-level professional capacity and greater resource mobilisation (53-55), all of which have facilitated DM and HTN care, management and research. Moreover, the integrated model for DM and HTN care has widely been considered in the low-and middle-income countries that accelerated the provision of effective and equitable health service delivery at the primary healthcare level, which would have helped to address the rising burden of them with accessible, equitable, and cost-effective interventions (56-58). This review revealed that at the primary healthcare level, health system readiness for major NCDs was primarily concentrated on the diagnosis and treatment aspects. However, readiness for health promotion and preventive interventions, provision of palliative care, screening, identification of risk factors, self-management and health education have remained under-investigated and of less priority (59, 60). As such, primary and secondary prevention of NCDs was

emphasised in the WHO's NCD prevention and control strategy in 2011 (61) and has been highlighted in the current literature to reduce NCD-related morbidities and deaths (62-64). Preventive and health promotional activities on key NCD risk factors, (61, 65) such as tobacco consumption, salt intake, physical inactivity, harmful alcohol use and unhealthy diet, stress that these can be addressed at the primary healthcare level to improve NCD outcome. The potential for a well-prepared health system is realised when promotional and preventive services are adequately provided at the primary healthcare level (66, 67). Lack of a comprehensive prevention and management approach led us to hypothesise that the full potential of the health system's response to NCDs may have been hindered at the primary healthcare level. Majority of the studies in this review had good or high quality. However, a large proportion of the study reflected inexplicit evidence due to the methodology, small sample size, bias, and incomplete information. A few quantitative studies lacked sufficient details about the participants' selection criteria, standard criteria for minimizing bias, and use of non-validated questionnaires with a relatively small sample size that might affect the scope of generalizability of the findings (27, 29, 32, 34, 35). One mixed-method study was rated low quality due to the homogeneous sample and insufficient information about the data analysis (47). The rest of the mixed-method studies included in the review had a more representative sample size and methodological rigors. The majority of the included studies used the WHO's health system framework as an analytical basis to identify the health system components. However, some studies lacked a deeper analysis of the interplay and interconnectedness between different health system components. Despite these limitations, this study provides important information regarding current evidence on the readiness of the primary healthcare system for NCDs. Additionally, most of the selected studies in this review were conducted in resource-poor settings, primarily in sub-Saharan African and South East Asian countries. The smaller number of studies in developed countries may be explained by their adoption of a specialised disease management strategy, which lessens the focus on comprehensive management of NCDs at the primary healthcare level (68). An extensive investigation of community characteristics and associated factors may be necessary for establishing a well-functioning and more responsive health system to respond to NCDs (24).

Strengths and limitations

This review's main strength was an inclusive data synthesis informed by the health system dynamics framework, which offers a deeper and more comprehensive (both supply-side and demand-side factors) understanding of primary healthcare system readiness for NCDs. Conducting An extensive systematic search of literature with hand-searching references and expert advice increased the validity and trustworthiness of this review's findings. On the other hand, one of its limitations was that a few studies that reported health system readiness at combined primary and secondary healthcare levels were excluded. Moreover, the selected studies had heterogeneous study designs, methods and techniques, and focused on a variety of health system components, preventing meta-analysis. Another limitation was that studies containing relevant information published in languages other than English have been excepted, which may have influenced the results of this review.

Conclusion and future direction

This review demonstrated that health systems at the primary healthcare level are insufficiently prepared for NCD prevention and management, especially for CVD, CRD and cancer. The existing health system response was characterised by insufficient 'supply-side' factors (i.e. supply of medicine, equipment and technology), a lack of appropriate NCD management strategies and guidelines, a weak health information system, limited resources, uncoordinated local-level stewardship and leadership and a shortage of human resources. One of the notable findings was that the primary healthcare system's readiness over the years was evaluated from the 'supply-side' perspective; hence, there is a significant knowledge gap in the literature from the 'demand-side' standpoint. This observation may be useful for future research into users' views on NCD management at the primary healthcare level, including NCD management practice, knowledge, attitude, care-seeking behaviour, adherence to treatment, self-management and coping strategies.

Author Contributions

AK, NK and BB created the manuscript. AK and LR led the literature search. AK, NK, RI and BB screened the literature and completed the mapping. AK led the drafting process, while NK, RI and BB provided substantial input. All authors read and approved the final manuscript.

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Data availability statement

No additional data are available.

Competing interest

The authors declare that they have no competing interests.

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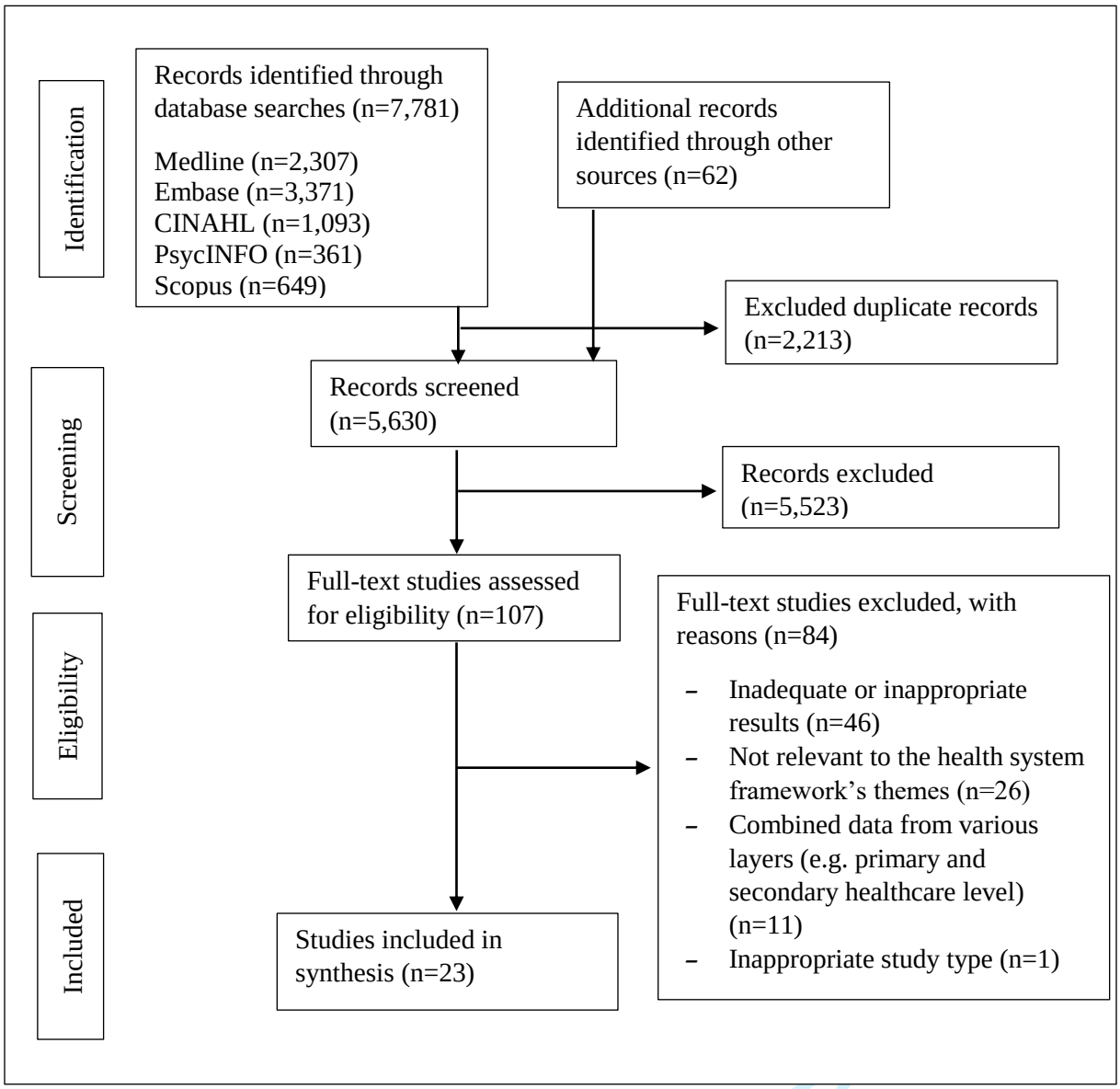
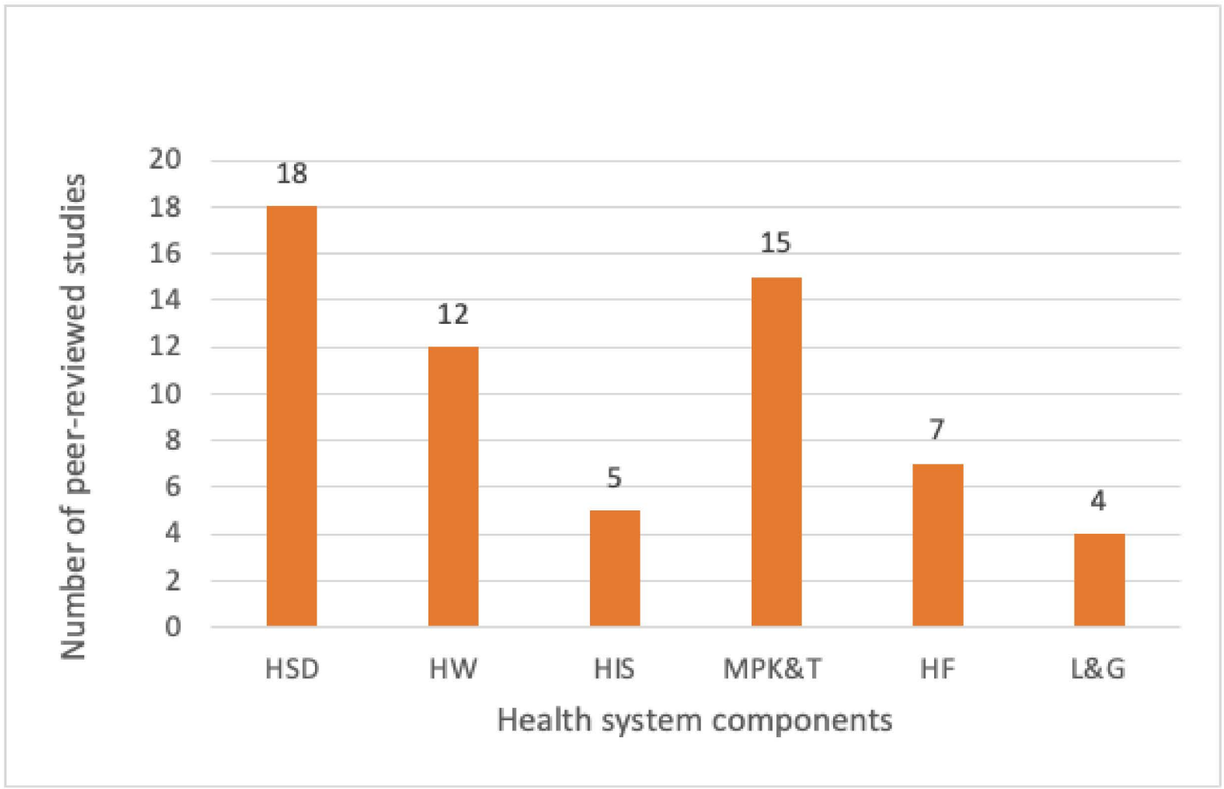


Figure 1 PRISMA flowchart for study inclusion.

a



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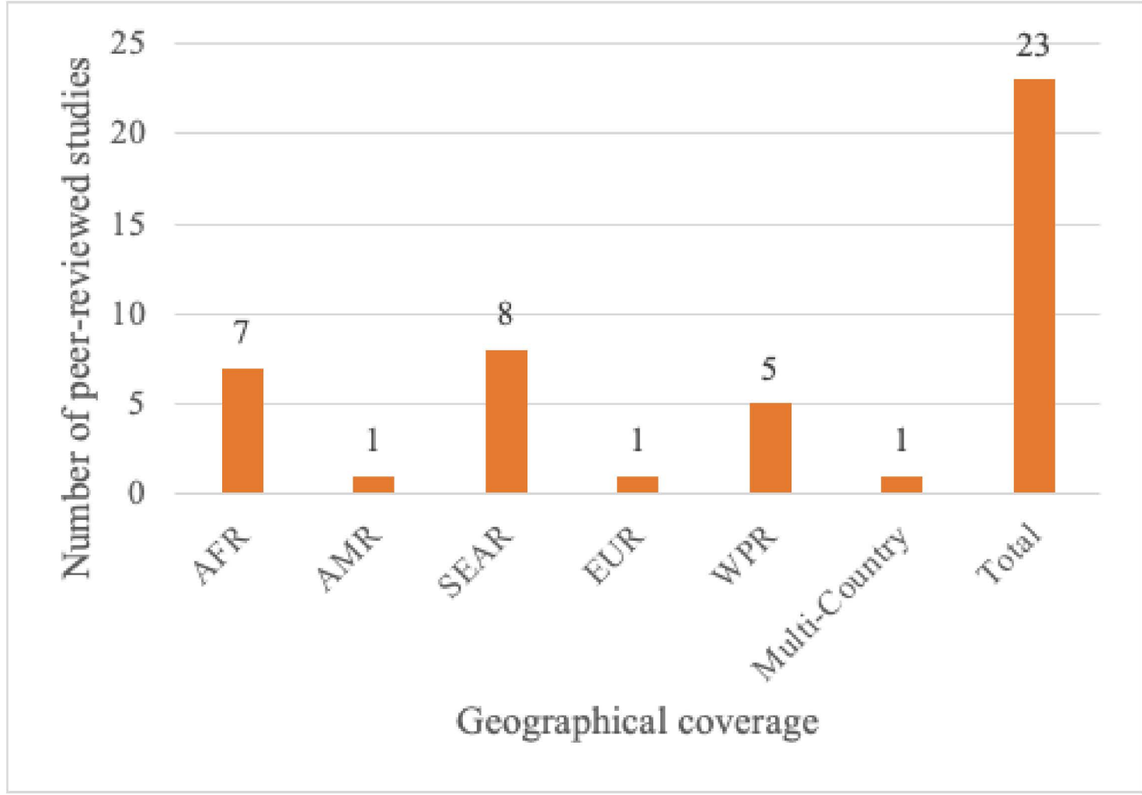

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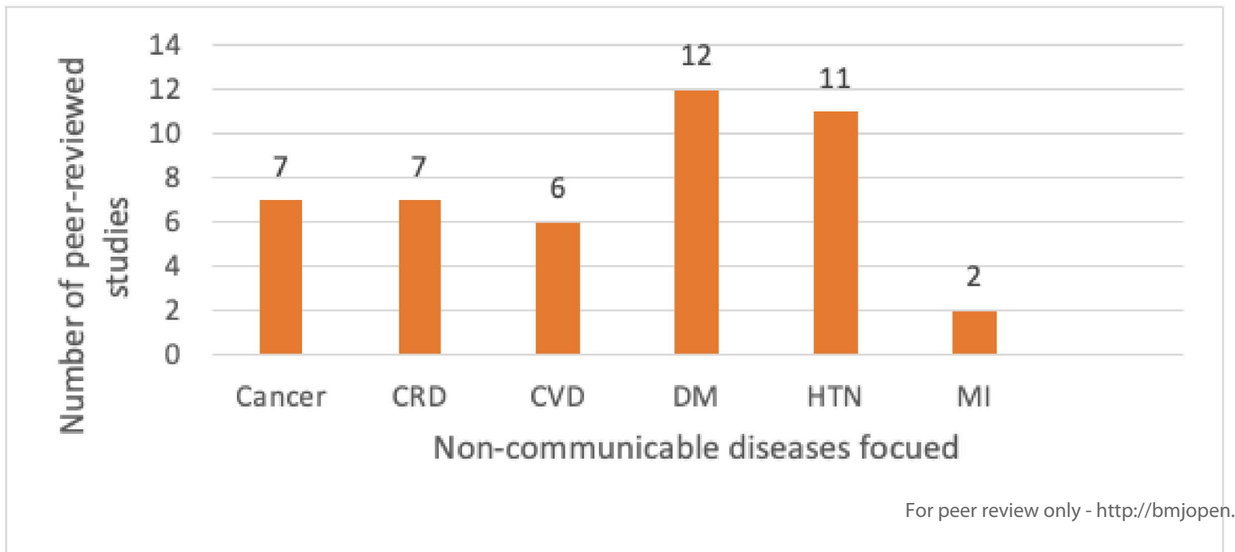

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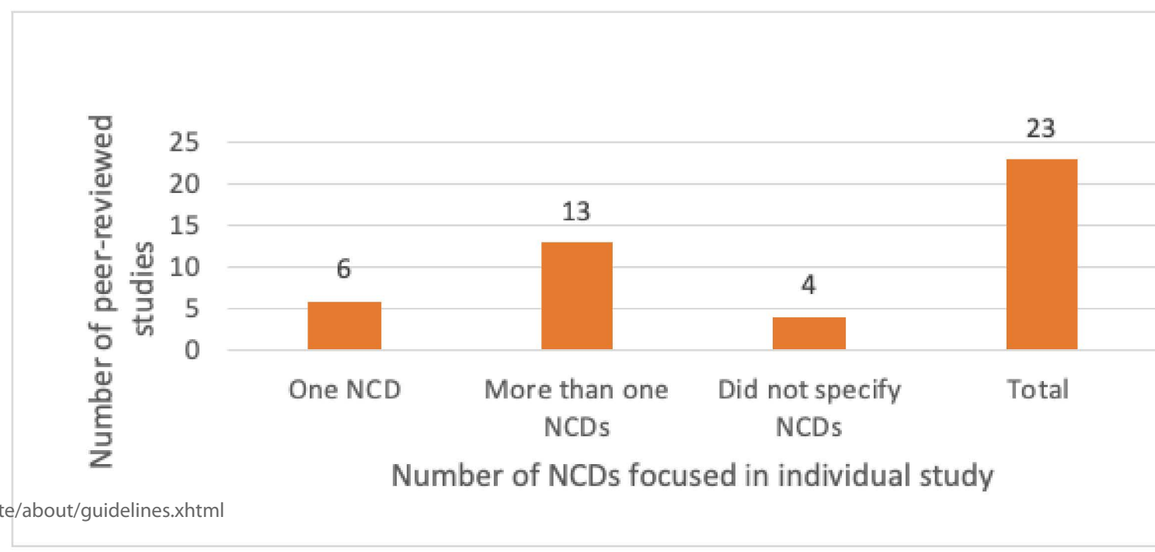

Supplementary appendix

Table S1. Literature search strategy

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)** Search Strategy:**1st of January 1984 to July 30th 2021**

#	Searches
1	chronic disease/ or multiple chronic conditions/ or non communicable disease/
2	(chronic disease* or chronic disorder* or chronic* sick* or chronic health condition* or chronic medical condition* or chronic* ill* or long term condition* or multimorbidit* or mult imorbidit*).mp.
3	(non-communicable disease* or non-infectious disease* or noncommunicable disease* or noninfectious disease*).mp.
4	(cardiovascular disease* or coronary artery disease* or myocardial isch?emia or myocardial infarct* or pulmonary disease* or chronic obstructive pulmonary or chronic obstructive lung or chronic obstructive respiratory or diabetes or coronary heart disease* or neoplasm* or cancer*).mp.
5	(hypertension or hypertriglycerid?emi* or hyper triglycerid?emi* or high triglyceride* or high cholesterol or hypercholesterol?emi* or hyperlipid?emia* or hyperlipidemi*).mp.
6	(diastolic pressure or systolic pressure or blood pressure or cardiometabolic syndrome*).mp.
7	(copd or asthma or renal disease* or kidney disease*).mp.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	Primary Health Care/
10	Delivery of Health Care/
11	(primary health system or primary health service or primary healthcare system or primary health care system or primary healthcare service or primary health care service or primary medical service delivery or primary medical care service or primary care service or primary care system).mp.
12	(first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*).mp.
13	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*)).mp.
14	9 or 10 or 11 or 12
15	8 and 14
16	(readiness or preparedness or capacity or quality improvement or quality of Improvement).mp.
17	15 and 16
18	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj5 (accessibility or availability)).mp.
19	8 and 18
20	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj (need* or demand*)).mp.
21	8 and 20
22	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*) adj3 (need* or demand*)).mp.

23	8 and 22
24	17 or 19 or 21 or 23
25	limit 24 to english language
26	limit 25 to (case reports or comment or editorial or letter or news)
27	25 not 26

Database(s): Embase Classic+Embase

Search Strategy:

#	Searches
1	exp antineoplastic agent/ or cancer therapy/ or bone marrow purging/ or bone marrow rescue/ or exp cancer adjuvant therapy/ or exp cancer chemotherapy/ or cancer gene therapy/ or cancer hormone therapy/ or exp cancer immunotherapy/ or exp cancer radiotherapy/ or multimodality cancer therapy/ or oncolytic virotherapy/ or target cell destruction/ or immunotherapy/ or adoptive immunotherapy/ or exp chimeric antigen receptor immunotherapy/ or radioimmunotherapy/ or exp radiotherapy/ or exp bone marrow transplantation/ or exp hematopoietic stem cell transplantation/ or stem cell transplantation/ or cancer patient/ or cancer survivor/
2	exp neoplasm/dt, rt [Drug Therapy, Radiotherapy]
3	(anti-cancer* or anti-neoplas* or anticancer* or antineoplas* or anticancerogen* or anticarcinogen* or anti-carcinogen* or anti-tumo?r* or antitumor?r* or cancer inhibitor* or tumo?r inhibitor* or anti-leukemi* or antileukemi* or oncotherap* or antimetastatic* or anti-metastatic* or antimetastas#s or anti-metastas#s).mp.
4	((cancer* or tumo?r* or neoplas* or carcinoma* or malignan* or adenocarcinoma* or sarcoma* or lymphoma* or leukemi* or blastoma* or carcinostatic or oncolog* or carcinocidal or oncocidal or oncostatic) adj3 (therap* or drug* or agent* or chemotherap* or electrochemotherap* or treat* or medication* or compound* or immunotherap* or immunological or immunomodul* or immunomodurat*)).mp.
5	((adenoma* or chondrosarcoma* or osteosarcoma* or rhabdomyosarcoma* or astrocytoma* or ependymoma* or glioma* or neuroblastoma* or medulloblastoma* or oligodendroglioma* or pheochromocytoma* or retinoblastoma* or cholangiocarcinoma* or melanoma* or mesothelioma* or pheochromocytoma* or paraganglioma* or craniopharyngioma* or esthesioneuroblastoma* or myeloma*) adj (therap* or treatment* or drug* or agent* or medication* or vaccine*)).mp.
6	((cancer or tumo?r) adj (cure* or healing or remed* or vaccin* or adjuvant therap* or multichemotherap* or polychemotherap* or gene therap* or hormon* therap* or radiation or irradiation or ablation or immun* therap*)).mp.
7	((cancer or carcinoma or adenocarcinoma or sarcoma or lymphoma or leukemia or blastoma or adenoma or chondrosarcoma or osteosarcoma or rhabdomyosarcoma or astrocytoma or ependymoma or glioma or neuroblastoma or medulloblastoma or oligodendroglioma or pheochromocytoma or retinoblastoma or cholangiocarcinoma or melanoma* or mesothelioma or pheochromocytoma or paraganglioma or craniopharyngioma or esthesioneuroblastoma or myeloma or oncolog*) adj (patient* or survivor* or sufferer*)).mp.
8	(alkylating adj (agent* or chemical* or compound* or cytostatic*)).mp.
9	(((angiogenesis or neovascularisation or tumo?r vascularisation) adj inhibitor*) or ((angiostatic or anti-angiogenesis or antiangiogenesis or anti-angiogenic or antiangiogenic or antimutagenic) adj (agent* or drug*))).mp.
10	(abecomotide or abemaciclib or abexinostat or abieslactone or abivertinib or abrotanone or aburatubolactam A or aburatubolactam C or abyssinone V or acalabrutinib or acalisib or aceglatone or acodazole or adaphostin or adarotene or adavosertib or aderbasib or afamitresgene autoleucel or afatinib or afuresertib or Agaricus blazei extract or agatolimod or agerafenib or aglatimagene or besadenovec or albicanyl acetate or aldesleukin or alectinib or alicdamotide or alisertib or adozelesin or alkanesulfonic acid or amsacrine or amsacrine derivative or asulacrine isethionate or busulfan or dimethylbusulfan or mesylic acid or mesylic acid derivative or mesylic acid ethyl ester or mesylic acid methyl ester or mesylmesylic acid 2 chloroethyl ester or methylene dimesylate or treosulfan or ametantrone or anaxirone or aziridine derivative or apaziquone or azimexon or aziridine or aziridinylbenzoquinone or azirine derivative or carboquone or ciamexon or diaziquone or dipin or pumitepa or

	thiotepa or tretamine or tretazicar or triaziquone or uredepa or banoxantrone or bisantrene or bizelesin or brostallicin or carboplatin or carzelesin or chlormethine derivative or acridine mustard or aldophosphamide or alestramustine or ambamustine or amustaline or aniline mustard or bendamustine or benzoquinone mustard or bestrabucil or canfosfamide or chlorambucil or chlormethine or chlornaphazine or cloturin or cortifen or cyclophosphamide or cydrin or dichlorodiethylamine or dopan or estramustine or evofosfamide or galamustine or glufosfamide or gonadorelin or ifosfamide or laromustine or mafosfamide or mafosfamide cyclohexylamine or mafosfamide lysine or mannomustine or melphalan or mepacrine mustard or palifosfamide or peptichemio or perfosfamide or phenesterin or phosphoramide mustard or sarcolysin or sufosfamide or tallimustine or tinostamustine or trofosfamide or uramustine or xylamine or cisplatin or cyclodisone or dacarbazine or dianhydrogalactitol or etoglucid or imidacrine or irofulven or ledoxantrone or losoxantrone or mitoxantrone or nitrosourea derivative or bofumustine or butylnitrosourea or carmustine or chloroethylnitrosourea or chloroethylnitrosourea derivative or cystemustine or ecomustine or elmustine or estradiol 17 or ethylnitrosourea or fotemustine or lomustine or methylnitrosourea or nimustine or nitrosourea or prednimustine or ranimustine or semustine or spirazidine or spiromustine or streptozocin or tauromustine or nortopixantrone or oxanthrazole or pentamethylmelamine or pixantrone or procarbazine or teloxantrone or temozolomide or topixantrone or alobresib or alpelisib or alpha sarcin or altemicidin or alteminostat or altiratinib or altretamine or ambazone or amcasertib or amidox or aminothiadiazole or amonafide or amphethinile or amphidinolide A or amphidinolide B or amphidinolide D or amsilarotene or amuvatinib).mp.
11	(acrizanib or aflibercept or aganirsen or alofanib or anecortave or anginex or angiostatic protein or angiostatin or angiozyme or atiprimod or avadomide or axitinib or beloranib or bermekimab or bevasiranib or brivanib or cabozantinib or canstatin or caplostatin or carlumab or carotuximab or cediranib or cenupatide or cetuximab or cilengitide or combretastatin A1 phosphate or conbercept or conendostatin or crenolanib or crizotinib or dalantercept or depudecin or dovitinib or endostatin or endothelial monocyte activating polypeptide II or fexapotide or foretinib or foslinanib or fruquintinib or fumagillol chloroacetylcarbamate or glesatinib or infigratinib or lapatinib plus pazopanib or lenalidomide or lenvatinib or linifanib or lucitanib or maspin or monoclonal antibody DC101 or monoclonal antibody imc 1c11 or motesanib or muparfostat or dicarboxamide or navicixizumab ornintedanib or ofranergene obadenovec or oglufanide or orantinib or paclitaxel or pazopanib or pegaptanib or pegdinetanib or pegpleranib or pixatimod or pomalidomide or ranibizumab or recombinant endostatin or regorafenib or relzomostat or rinucumab or risuteganib or roneparstat or semaxanib or "siRNA 027" or sonepcizumab or sorafenib or squalamine or sunitinib or tanomastat or tasquinimod or tesevatinib or thalidomide or thrombospondin 1 or thrombospondin 2 or tigapotide or tiomolibdate choline or tirbanibulin or tivozanib or toceranib or trabedersen or trebananib or tumstatin or vandetanib or varisacumab or vascular endothelial growth inhibitor or vascular endothelial cell growth inhibitor or vascular endothelial growth factor antagonist vascular endothelial growth factor inhibitor or VEGF inhibitor or vasculotropin inhibitor or abicipar pegol or bevacizumab or brolucizumab or catequentinib or dilpacimab or faricimab or olinvacimab or pamufetinib or ramucirumab or rivoceranib or sintilimab or vulinacimab vatalanib or volociximab or vorolanib or metastasis inhibitor or carcinostatic alkaloid or acronine or afeletecan or atiratecan or becatecarin or belotecan or camptothecin or topotecan or cephalotaxine or coralyne or cositecan or cyclopamine or datelliptium chloride or deacetylvinblastine or demecolcine or diazepinomicin or diflomotecan or ellipravin or ellipticine or elliptinium or elomotecan or etirinotecan pegol or etoposide or exatecan or exatecan alideximer or fagaronine or firtecan or gimatecan or govitecan).mp.
12	(harringtonine or homoharringtonine or indicine n oxide or indirubin or irinotecan or lorvotuzumab mertansine or lurbinectedin or maytansine or mitopodozide or mureletecan or namitecan or napavin or narciclasine or nitidine or olivacine or patidegib or pazelliptine or pegamotecan or retelliptine or rubitecan or senecionine or sinococuline or solamargine or swainsonine or tenifatecan or teniposide or thalicarpine or trabectedin or trewiasine or trimethylcolchicinic acid or vinblastine or vincristine or vindesine or vinflunine or vinfosiltine or vinleucinol or vinleurosine or vinorelbine tartrate or vintafolide or vintriptol or vinzolidine or withanolide or carcinostatic antibiotic or 21 aminoepothilone B or 3 deazaaristeromycin or actinobolin or 7 aminodactinomycin or actinomycin derivative or adozelesin or alanosine or alvespimycin or ankinomycin or anthracycline antibiotic agent* or 11 deoxydaunorubicin or 2 fluoroidarubicin or 2 pyrrolinodoxorubicin or 4 demethoxy 11 deoxydaunomycinone or 4 demethoxydaunomycinone or 4 demethoxydoxorubicin or 4 iodoesorubicin or 5 iminodaunorubicin or 9 deacetyl 9 methylidarubicin or 9 deoxydoxorubicin or aclacinomycin or aclacinomycin B or aclarubicin or adriamycinone or aklavinone or aldoxorubicin or amrubicin or annamycin or anthracycline or anthracyclinone derivative or barminomycin I or berubicin or camsirubicin or carubicin or cinerubin A or

	cinerubin B or daunomycinone or daunorubicin or monoclonal antibody conjugate or daunorubicinol or decilorubicin or detorubicin or ditrisarubicin B or doxorubicin or doxorubicinol or epirubicin or epirubicinol or epsilon rhodomycinone or esorubicin or galarubicin or gancotamab or idarubicin or idarubicinol or ladirubicin or leurubicin or n benzyldoxorubicin 14 valerate or n trifluoroacetyldoxorubicin or n trifluoroacetyldoxorubicin 14 hydrogen adipate or nemorubicin or obelmycin or oxaunomycin or pirarubicin or pyrromycinone or rhodomycin A or rodorubicin or ruboxyl or sabarubicin or valrubicin or viriplanin A or zoptarelin doxorubicin or zorubicin or anthramycin or arasangivamycin or asperlin or auromomycin or azaserine or bactobolin or bizelesin or blasticidin S or bleomycin or bleomycinic acid or liblomycin or pepleomycin or cactinomycin or cadeguomycin or calicheamicin or gemtuzumab or inotuzumab ozogamicin or calphostin or caplostatin or carzelesin or chartreusin or chlorozotocin or chromomycin or chrysomycin or colabomycin A or congocidine or cordycepin or dactinomycin or dehydrodidemnin B or dehydroxysparsomycin or didemnin or distamycin A derivative or duocarmycin or duocarmazine or duocarmycin SA or dynemicin A or echinomycin or echinosporin or elsamicin A or epothilone or esperamicin or formycin or fostriecin or fredericamycin A or fumagillin or fumagillol).mp.
13	(geldanamycin or gilvocarcin V or glidobactin or granaticin or hadacidin or herbimycin or himastatin or illudin or irofulven or ixabepilone or kapurimycin or kedarcidin or leinamycin or lidamycin or luzopeptin or macbecin I or macromomycin or marcellomycin or menogaril or mithramycin or 7 n acetylmitomycin C or mitomycin or porfiromycin or musettamycin or mycophenolic acid or n bromoacetyldistamycin A or neothramycin or neplanocin A or nogalamycin or olivomycin or oxanosine or ozogamicin or pactamycin or pibenzimol or pibrozelesin or pirazofurin or prodigiosin or puromycin or pyrindamycin A or pyrindamycin B or quinocarcin or rachelmycin or rebeccamycin or resorthiomycin or retaspimycin or reumycin or rodaplutin or romidepsin or rubomycin or rufocromomycin or saframycin or sagopilone or sangivamycin or sapurimycin or sarkomycin or showdomycin or sibiromycin or sparsomycin or spergualin orspicamycin or spongistatin 1 or spongistatin 2 or streptonigrin derivative or tallysomycin or tanespimycin or tetracenomycin C or thiocoraline or thrazarine or tomaymycin or tubercidin or tuftsin or vicenistatin or yunnanmycin or zinostatin or buthionine sulfoximine or folic acid antagonist or folic acid antimetabolite or pteroylglutamic acid antimetabolite or 10 deazaaminopterin or 7 hydroxymethotrexate or aminopterin or arfolitixorin or bromebric acid or dichloromethotrexate or edatrexate or gamma fluoromethotrexate or homofolic acid or lometrexol or metesind or methotrexate or metodiclorofen or nolatrexed or pelitrexol or pemetrexed or piritrexim or plevitrexed or pralatrexate or raltitrexed or talotrexin or triazinate or trimetrexate or oxythiamine or purine antagonist or 4 carbamoylimidazolium 5 olate or 6 methylthioinosine or 6 n benzyladenosine or 8 azaguanine or azaguanosine or azathioprine or cladribine or clofarabine or cloturin or deoxythioguanosine or dezaguanine or fludarabine or guanine 7 oxide or guanine arabinoside or mercaptopurine or nelarabine or pentostatin or selenazofurin or sulfenosine or sulfinosine or sulfonosine or thioguanosine or tiazofurin or tioguanine or pyrimidine antagonist or 3 deazauridine or 3 ethynylcytidine or 5 chlorodeoxycytidine or 5 hydroxymethyldeoxyuridine or 5 aminothymidine or 5 deoxy 5 fluorocytidine or 6 azacytidine or ancitabine or azacitidine or azauracil or azauridine or brequinar or bromodeoxycytidine or capecitabine or carmofur or cloxuridine or cytarabine or cytarazid or decitabine or dihydrofluorouracil or doxifluridine or elacytarabine or emitefur or enocitabine orfazarabine or fiacitabine or floxuridine or flucytosine deoxyriboside or fluorouracil or fluorouridine or fosfluridine tidoxil or fosgemcitabine palabenamide or fosifloxuridine nafalbenamide or galocitabine or gemcitabine or gimeracil plus oteracil potassium plus tegafur or guadecitabine or orzel or ropidoxuridine or sapacitabine or tegafur or tezacitabine or tipiracil plus trifluridine or troxacitabine or uracil arabinoside).mp.
14	(4 hydroxytoremifene or abiraterone or acetylsalicylic acid plus aluminum hydroxide plus ascorbic acid plus prednisone or acetylsalicylic acid plus caffeine plus phenacetin plus prednisolone or acetylsalicylic acid plus calcium carbonate plus methylprednisolone or acetylsalicylic acid plus calcium carbonate plus prednisolone or acetylsalicylic acid plus methylprednisolone or acetylsalicylic acid plus prednisolone or acolbifene or afimoxifene or aluminum hydroxide plus ascorbic acid plus prednisone plus salicylamide or aluminum hydroxide plus calcium ascorbate plus calcium carbonate plus pantothenate calcium plus potassium salicylate plus prednisone or aluminum hydroxide plus magnesium trisilicate plus pantothenate calcium plus prednisolone or aluminum hydroxide plus magnesium trisilicate plus prednisone or amcenestrant or angiopeptin or apalutamide or aromatase inhibitor or estrogen synthetase inhibitor or oestrogen synthetase inhibitor or steroid aromatase inhibitor or abyssinone II or aminoglutethimide or anastrozole or atamestane or exemestane or fadrozole or finrozole or formestane or leflutrozole or letrozole or liarozole or minamestane or plomestane or pyridoglutethimide or testolactone or vorozole or arzoxifene or ascorbic acid plus chlorpheniramine maleate plus prednisone or ascorbic acid plus chlorpheniramine plus prednisone or avorelin or bestrabucil or bicalutamide or buserelin or calcium

	phosphate dibasic plus cyanocobalamin plus ethinylestradiol plus methylphenidate plus methyltestosterone plus nicotinamide plus pyridoxine plus riboflavin plus thiamine or calusterone or carisoprodol plus prednisolone or chloramphenicol plus prednisolone or chlorbutol plus phenylephrine plus prednisolone acetate or chlorotrianisene or chlorpheniramine gluconate plus prednisolone acetate or chlorzoxazone plus paracetamol plus prednisolone or conjugated estrogen or cyproterone or deslorelin or diethylstilbestrol derivative or dienestrol or diethylstilbestrol or fosfestrol or hexestrol or methestrol or dimethylstilbestrol or droloxifene or drostanolone or ectylurea plus ethoxzolamide plus medroxyprogesterone acetate or endoxifen or enzalutamide or ephedrine plus phenobarbital plus prednisone plus theophylline or estradiol undecylate or ethinylestradiol or fluoxymesterone or flutamide or fulvestrant or galeterone or gentamicin plus prednisolone acetate or gestonorone or goserelin or gramicidin plus neomycin plus phenylephrine plus prednisolone acetate or hydroxyflutamide or hydroxyprogesterone or hydroxytamoxifen or hydroxyzine plus prednisolone or idoxifene or leuprorelin or medroxyprogesterone or megestrol or melengestrol or mephenesin plus methylphenobarbital plus prednisone or mepitiostane).mp.
15	(methoxyphenamine plus methylprednisolone or methylprednisolone or methyltestosterone or miproxifene or nafarelin or nandrolone or neomycin plus phenylephrine plus phenylpropanolamine plus prednisolone sodium phosphate or neomycin plus phenylephrine plus prednisolone or neomycin plus phenylephrine plus prednisolone acetate or neomycin plus polymyxin B plus prednisolone acetate or neomycin plus prednisolone or neomycin plus prednisolone acetate or neomycin plus prednisolone sodium phosphate or nilutamide or nortamoxifen or ormeloxifene or orteronel or ospemifene or ozarelix or panomifene or phenylephrine plus prednisolone or pipendoxifene or polyestradiol or prednisolone or prednisone or raloxifene or seviteronel or sivifene or tamoxifen or tesmilifene or testololactone or testosterone propionate or toremifene or trioxifene or triptorelin or zanoterone or zindoxifene or zoptarelin doxorubicin or antineoplastic metal complex or amminebisbutyratodichloro cyclohexylamine platinum or bleomycin cobalt or bleomycin copper or budotitane or capecitabine plus oxaliplatin or carboplatin or carboxyethylgermanium sesquioxide or cisplatin or clivatuzumab tetraxetan or cycloplatam or doxorubicin copper or doxorubicin iron or enloplatin or epratuzumab tetraxetan yttrium y 90 or eptaplatin or imifoplatin or iproplatin or labetuzumab tetraxetan yttrium y 90 or lilotomab satetraxetan lutetium lu 177 or lintuzumab satetraxetan actinium ac 225 or lobaplatin or malopen or miboplatin or miriplatin or nedaplatin or oxaliplatin or oxoplatin or pasireotide tetraxetan gallium ga 68 or picoplatin or platinum ammine cyclohexylamine dichloride or platinum ethylenediamine dichloride or satoreotide tetraxetan or satraplatin or sebriplatin or spirogermanium or spiroplatin or tacatuzumab tetraxetan yttrium y 90 or tetrachloroplatinate potassium or tetrachloroplatinum fast black or tetraplatin or tetulomab tetraxetan lutetium lu 177 or titanocene or triplatin tetranitrate or vipivotide tetraxetan or zeniplatin or antroquinonol or apicidin or apitolisib or aplysianin E or apoptin or apoptosis inducing factor or 2 hydroxymethyl 2 methoxymethyl 3 quinuclidinone or arsenic trioxide or clezutoclax or daratumumab or genistein or isotretinoin or lisavanbulin or moxetumomab pasudotox or otenaproxesul or rimiducid or tapotoclax or apricoxib or arenastatin A or asciminib or aspacytarabine or asparaginase or asunercept or atuveciclib or audencel or avanbulin or avapritinib or avi 4126 or aviscumine or axicabtagene ciloleucel or bafetinib or balamapimod or barasertib or bardoxolone or batabulin or batracylin or beclanorsen or beclin 1 or belapectin or belinostat or belizatinib or belvarafenib or belzupacap sarotalocan or belzutifan or bemcentinib or bempegaldesleukin or benfluron or bersanlimab or berzosertib or beta elemene or beta lapachone or bexarotene or bifikafusp alfa or bimiralisib or binimetinib or birabresib or biricodar or birinapant or bisnafide or bistratene or bomedemstat or borofalan b 10 or bortezomib or bosutinib or briciclib or brigatinib or brilanestrant or bropirimine or bryostatin or bullatacin or bullatacinone or buparlisib or cabazitaxel or calaspargase pegol or camelliin B or camidanlumab).mp.
16	(adagloxad simolenin or adegramotide or algenpantucel L or autogene cevumeran or axalimogene filolisbac or baloramotide or baltaleucel T or belagenpumatucel L or biropepimut S or bizalimogene ralaplasmid or cadalimogene ixalentivec or dasiprotimut T or dorgenmeltucel L or eltrapuldencel T or falimarev or galinpepimut S or imm 101 or inalimarev or lapuleucel T or lovaxin b or maveropepimut S or mavilimogene ralaplasmid or mesmulogene ancovacivec or mitumprotimut T or modified vaccinia virus Ankara 5T4 vaccine or nelatimotide or nelipepimut S or olvimulogene nanivacirepvec or ombipepimut S or onamelatucel L or opolimogene capmilisbac or pemlimogene merolisbac or ranagengliotucel T or rasdegafusp alfa or rindopepimut or rocapuldencel T or rovaleucel or ruxotemitide or seviprotimut L or sipuleucel T or tecemotide or tergenpumatucel L or tertomotide or theratope or tipapkinogene sovacivec or tisagenlecleucel T or vadacabtagene leraleucel or vesigenurtucel L or viagenpumatucel L or vitespen or zastumotide or canertinib or capivasertib or capmatinib or caracemide or carbetimer or carfilzomib or carlecortemcel L or carmethizole or ceclazepide or cedazuridine or cemadotin or cenersen or cenisertib or ceralasertib or cerdulatinib or cergutuzumab amunaleukin or ceritinib or cevipabulin or

	chloroquine or ciforadenant or ciltacabtagene autoleucel or cintirorgon or citarinostat or clervonafusp alfa or clofazimine or cobimetinib or cobomarsen or colloidal gold or combretastatin or conteltinib or contusugene ladenovec or copanlisib or corynebacterium parvum extract or crenigacestat or crisnatol or cryptophycin or curcumin or custirsen or cyclophosphamide plus doxorubicin plus taxane or cysteine ethyl ester methylcarbamate or cytostatic agent or cytotoxic agent or emtansine or mafodotin or mertansine or ravtansine or soravtansine or tafasitamab or dabrafenib or dacinostat or dacomitinib or dactolisib or damistimagene matitucel or danusertib or danvatirsen or daporinad or darinaparsin or darleukin or darolutamide or dasatinib or davamotecan pegadexamer or decernotinib or defactinib or degarelix or dehydroxymethylepoxyquinomicin or delanzomib or delimotecan or delolimogene mupadenorepvec or demethoxycurcumin or demplatin pegraglumer or denileukin diftitox or derazantinib).mp.
17	(azintuxizumab or balstilimab or belantamab or bemarituzumab or benufutamab or bexmarilimab or bintrafusp alfa or bivatuzumab or blinatumomab or blontuvetmab or brentuximab vedotin or brontictuzumab or budigalimab or camrelizumab or cantuzumab or catumaxomab or cemiplimab or cergutuzumab or cetrelimab or cetuximab or cevostamab or cibisatamab or cinrebafusp alfa or cixutumumab orclivatuzumab tetraxetan or cobolimab or codrituzumab or cofetuzumab or coltuximab or conatumumab or cosibelimab or cudarolimab or cusatuzumab or dacetuzumab or dalotuzumab or daratumumab or datopotamab or demcizumab or demupitamab or denintuzumab or denosumab or depatuxizumab or derlotuximab biotin i 131 or detumomab or dilpacimab or dinutuximab or disitamab or dostarlimab or drozitumab or duligotuzumab or durvalumab or dusigitumab or duvortuxizumab or ecromeximab or edrecolomab or efizonerimod alfa or elgemtumab or elotuzumab or emactuzumab or emibetuzumab or enapotamab or enavatuzumab or encelimab or enfortumab or enoblituzumab or enoticumab or ensituximab or envafolimab or epcoritamab or epitumomab or epratuzumab or ertumaxomab or etaracizumab or ezabenlimab or farletuzumab or feladilimab or felzartamab or fianlimab or ficlatuzumab or figitumumab or flanvotumab or flotetuzumab or fresolimumab or futuximab or galiximab or gancotamab or ganitumab or gatipotuzumab or gatralimab or giloralimab or gilvetmab or girentuximab or glembatumumab or glofitamab or hyaluronidase plus rituximab or hyaluronidase plus trastuzumab or ibritumomab tiuxetan or icrucumab or ieramilimab or ifabotuzumab or iladatuzumab or imalumab or imgatuzumab or immunoliposome or immunotoxin or anatumomab mafenatox or cintredekin besudotox or citatuzumab bogatox or moxetumomab pasudotox or nacolomab tafenatox or naptumomab estafenatox or taplitumomab paptox or telimomab aritox or indatuximab or indusatumab or inebilizumab or intetumumab or ipilimumab or iratumumab or isatuximab or istiratumab or ivuxolimab or labetuzumab or lacnotuzumab or lacutamab or ladiratuzumab or laprituximab or lenzilumab or lexatumumab or lifastuzumab or lilotomab or lintuzumab or lirilumab or lodapolimab or loncastuximab or lorukafusp alfa or lorvotuzumab or losatuxizumab or lucatumumab or lumiliximab or lumretuzumab or lupartumab or magrolimab or manelimab or mapatumumab or margetuximab or matuzumab or mavezelimab or mezagitamab or milatuzumab or minretumomab or miptenalimab or mirvetuximab or mirzotamab or mitumomab or modakafusp alfa or modotuximab or mogamulizumab or monalizumab).mp.
18	(deruxtecan or devimistat or dexniguldipine or dexverapamil or dezapelisib or diacetyldianhydrogalactitol or diaspirin crosslinked haemoglobin or didemethoxycurcumin or diglycoaldehyde or dihydroambazone or dilanubicel or dinaciclib or dinaline or discodermolide or disufenton sodium or ditercalinium or docetaxel or dociparstat or dofequidar or dolastatin or domatinostat or dubermatinib or dulanermin or duvelisib or ebifuramin or edelfosine or edicotinib or edotecarin or edotreotide ga 68 or edotreotide lu 177 or edotreotide y 90 or efaprinermin alfa or efatutazone or efgivanermin alfa or efineptakin alfa or eflornithine or eftozanermin alfa or elacestrant or elacridar or elafibranor or elagolix or elesclomol or eleutherobin or elinafide or elisidepsin or eltanexor or empesertib or enasidenib or encequidar or encorafenib or enistimgene setitucel or ensartinib or entasobulin or entinostat or entospletinib or entrectinib or enzastaurin or epertinib or epipodophyllotoxin or erbulozole or erdafitinib or eribulin or erlotinib or erucin or ethazolastone or etidaligide or everolimus or exicorilant or factor AF2 or fadraciclib or falnidamol or fedratinib or felezonexor or fenebrutinib or fenretinide or ferritin antibody i 131 or fetindomide or fibromun or filanesib or filgotinib or fimepinostat or fisogatinib or flavopiridol or flumatinib or fluorocyclopentenylcytosine or forodesine or fosciclopirox or fosquidone or fumitremorgin C or futibatinib or gallium nitrate or galunisertib or gandotinib or gataparsen or gedatolisib or gefitinib or geiparvarin or gendicine or gene expression modulator 231 or ghilanten or gilteritinib or girolline or givinostat or glasdegib or glucopyranosyl lipid A or glycoprotein P inhibitor or golnerminogene pradenovec or golvatinib or goniofufurone or granulocyte macrophage colony stimulating factor vaccine or grifolan or guanazole or gusacitinib or halichondrin B or heat shock protein 27 inhibitor or apatorsen or heat shock protein 90 inhibitor or alvespimycin or celastrol or gambogic acid or gamendazole or ganetespib or geldanamycin or

	luminespib or onalespib or pimitespib or retaspimycin or tanespimycin or hepsulfam or HER dimerization inhibitor or hexamethylenebisacetamide or hydroxymethylpentamethylmelamine or hydroxyurea or hypericin or hypothemycin or iadademstat or ibrutinib or icotinib or idasanutlin or idecabtagene vicleucel or idelalisib or idetrexed or idronoxil or ilixadencel or ilmofosine or ilorasertib or imaradenant or imatinib or imetelstat or imlatoclax or abagovomab or abituzumab or actimab a or adebrelimab or adecatumumab or alacizumab pegol or alemtuzumab or alsevalimab or amatuximab or amivantamab or andecaliximab or anetumab or apolizumab or aprutumab or aprutumab ixadotin or ascrinvacumab or astegolimab or atezolizumab or avdoralimab or avelumab or axatilimab).mp.
19	(monoclonal antibody J591 or mosunetuzumab or murlentamab or nadunolimab or naratuximab or narnatumab or naxitamab or necitumumab or nesvacumab or nimotuzumab or nivolumab or nurulimab or obinutuzumab or ocaratuzumab or odronextamab or ofatumumab or olaratumab or oleclumab or olinvacimab or omburtamab or onartuzumab or ontuxizumab or onvatilimab or oportuzumab monatox or opucolimab or oregovomab or otlertuzumab or pacmilimab or panitumumab or parsatuzumab or pasotuxizumab or patritumab or pembrolizumab or pemtumomab or pepinemab or pertuzumab or petosemtamab or pidilizumab or pimurutamab or pinatuzumab vedotin or plamotamab or polatuzumab vedotin or praluzatamab or pritumumab or prolgolimab or quavonlimab or racotumomab or radretumab or ragifilimab or ramucirumab or rasdegafusp alfa or relatlimab or retifanlimab or revdofilimab or rilotumumab or ripertamab or rituximab or robatumumab or rolinsatamab or rosmantuzumab or rosopatamab or rovalpituzumab or rovalpituzumab tesirine or sabatolimab or sacituzumab or samalizumab or samrotamab or sasanlimab or selicrelumab or serclutamab or seribantumab or serplulimab or sibrotuzumab or siltuximab or simlukafusp alfa or simtuzumab or sintilimab or sirtratumab or sofituzumab or solitomab or sontuzumab or spartalizumab or sugemalimab or tabalumab or tabituximab or tacatuzumab or tetraxetan yttrium y 90 or tacatuzumab y 90 or tafasitamab or talacotuzumab or talquetamab or tamrintamab or tamtuvetmab or tarextumab or tavolimab or tebotelimab or teclistamab or telisotuzumab or tenatumomab or tepoditamab or teprotumumab or tetulomab tetraxetan lutetium lu 177 or ticilimumab or tidutamab or tigatuzumab or tilogotamab or tilvestamab or timigutuzumab or tinurilimab or tiragolumab or tislelizumab or tisotumab or tomuzotuximab or toralizumab or toripalimab or tositumomab or tovetumab or trastuzumab or ublituximab or ulocuplumab or upifitamab or urabrelimab or urelumab or utomilumab or vadastuximab or vandortuzumab vedotin or vantictumab or vanucizumab or varlilumab or veltuzumab or vesencumab or vibecotamab or vibostolimab or vofatamab or vonlerolizumab or vopratelimab or vorsetuzumab or vulinacimab or xentuzumab or zalifrelimab or zalutumumab or zanidatamab or zanolimumab or zolbetuximab or zuberitamab).mp.
20	(inavolisib or inbakicept or incyclinide or indibulin or indisulam or indoximod or ingenol disoxate or ingenol mebutate or inodiftagene vixteplasmid or interferon regulatory factor 2 or intiquinatine or intoplicine or ipafricept or ipatasertib or irosustat or isoswinholide A or ispinesib or itacitinib or itraconazole or ivaltinostat or ivosidenib or ixazomib or kahalalide F or krestin or laetrile or laniquidar or lapachol or lapatinib or lapretolimod or larifan or larotaxel or larotrectinib or laulimalide or lefitolimod or lerociclib or lestaurtinib or letetresgene autoleucel or lexidronam samarium sm 153 or lifileucel or lifirafenib or linperlisib or linrodostat or lisocabtagene maraleucel or litenimod or litronesib or lonafarnib or lonidamine or lorlatinib or ltvax or lurtotecan or maltose tetrapalmitate or masitinib or mavelertinib or mavorixafor or melacine or merbarone or merestinib or methanol extraction residue or metirosine or mevociclib or midostaurin or mifamurtide or milademetan or milataxel or milciclib or miltefosine or mipetresgene autoleucel or mipsagargin or miralimogene ensolisbac or miransertib or mirdametinib or mirostipen or mitazalimab or mitindomide or mitobronitol or mitoflaxone or mitoguazone or mitolactol or mitonafide or mitoquidone or mitotane or mitozolomide or mivavotinib or mivebresib or mivobulin or mobocertinib or mocemestrocel or mocetinostat or molibresib or momelotinib or monastrol or mosedipimod or motixafortide or motolimod or mubritinib or mucocin or murizatoclax or mycalamide or myeloablative agent or nabiximols or nadofaragene firadenovec or namodenoson or nanatinostat or napabucasin or naquotinib or nastorazepide or navitoclax or navoximod or nazartinib or necuparanib or nemiralisib or neratinib or netazepide or nevanimibe or nilotinib or niraparib or nirogacestat or nitracrine or nitrocaphane or noscapine or numidargistat or nutlin or obafistat or obatoclax or oblimersen or oblongifolin C or oblongixanthone A or obovatal or obtusilactone A or oclacitinib or olafertinib or olaparib or olaptesed pegol or olcorolimus or olitresgene autoleucel or olmutinib or olutasidenib or olverembatinib or omidubicel or omipalisib or omtriptolide or onatasertib or oncolytic virus or oncolytic adenovirus or enadenotucirev or lontucirev or tasadenoturev oroncolytic herpes virus or canerpaturev or seprehvir or talimogene laherparepvec or teserpaturev or oncolytic paramyxovirus or oncolytic parvovirus or oncolytic reovirus or pelareorep or pexastimogene devacirepvec or onfekafusp alfa or ontorpacept or onvansertib or opaganib or opigolix or oprozomib or oracin or orelabrutinib or

	ortataxel or orvacabtagene autoleucel or osimertinib or oxamflatin or oxodotreotide lu 177 or paclitaxel ceribate or paclitaxel derivative or paclitaxel poliglumex or paclitaxel tocosol or paclitaxel trevatide or pacritinib or palbociclib or palmerolide A or pamiparib or panaxytriol or panduratin A or panobinostat or panulisib or parsaclisib or pasireotide or paxalisib or pegargiminase or pegcantratinib or pegcrisantaspase or pegilodecakin or pegvorhyaluronidase alfa or pelcitoclax or pelidotin or pelitinib or pemigatinib or penclomedine or peposertib or peretinoin).mp.
21	(perifosine or pevonedistat or pexidartinib or phenethyl isothiocyanate or phomopsin A or phorboxazole or phyllanthocin or phyllanthoside or picibanil or pictilisib or pilaralisib or pimasertib or pinometostat or pipobroman or pivaloyloxymethyl butyrate or plocabulin or plusonermin or podophyllotoxin or polyerga or ponatinib or poziotinib or pracinostat or pralsetinib or prexasertib or prexigebersen or prospidium or ptilocaulin or pyran copolymer or pyrazine diazohydroxide or quarfloxin or quisinostat or quizartinib or rabacfosadine or rabusertib or radiosensitizing agent or radio-sensitizing agent or bromodeoxycytidine or broxuridine or chloroaluminum phthalocyanine or cloxuridine or crocetin ordeclopramide or doranidazole or efaproxiral or etanidazole or etiopurpurin or fimaporfin or gadolinium texaphyrin or gilvocarcin V or hematoporphyrin derivative or isometronidazole or lemuteporfin or lutetium texaphyrin or merocyanine or misonidazole or motexafin or napavin or nimorazole or nocodazole or normisonidazole or padeliporfin or padoporfin or photofrin I or photofrin II or photosan III or phthalocyanine or pimonidazole or porfimer or redaporfin or senazole or talaporfin or temoporfin or tetrachloroplatinum fast black or tetraphenylporphyrin or tetrasulfophthalocyanine or tirapazamine or tretazicar or troquidazole or verteporfin or radium chloride ra 223 or radotinib or ralimetinib or ranpirnase or rapamycin or ravoxertinib or razoxane or rebastinib or recombinant asparaginase or recombinant interleukin 21 or denenicokin or recombinant methionine gamma lyase or recombinant tumor necrosis factor related apoptosis inducing ligand or refametinib or remetinostat or repotrectinib or resminostat or rezivertinib or rhizoxin or rhodamine 6G or ribociclib or ribonucleotide reductase R2 specific phosphorothioate oligonucleotide or ricolinostat or ridaforolimus or rigosertib or rilimogene galvacirepvec or rilimogene glafolivec or ripretinib or riviciclib or rivogenlecleucel or robaveron or roblitinib or rocakinogene sifuplasmid or rociletinib or roniciclib or roridin A or rosabulin or rosomidnar or rucaparib or ruxolitinib or salinosporamide A or salirasib or samotolisib or samuraciclib or sapanisertib or sapitinib or saracatinib or sarcodictyin A or sarcophytol A or sarcophytol B or sardomozide or satoreotide trizoxetan or savolitinib or Sclerotinia sclerotiorum extract or seclidemstat or selectikine or selinexor or selitrectinib or selpercatinib or selumetinib or seocalcitol or sepantronium bromide or serabelisib or serdemetan or serpentine or shikonin derivative or silmitasertib or simotaxel or simurosertib or siremadlin or sitimagene ceradenovec or sitravatinib or sobuzoxane or solcoderm or sonermin or sonidegib or sonolisib or sparfosic acid or spebrutinib or spirobromine or squamocin or ssioriside or stapuldencel T or starch microsphere or sulfatinib or sulforaphane or sulindac sulfone or sulofenur or suramin or swinholide A or swinholide B).mp.
22	(tacedinaline or tafluposide or tagraxofusp or talabostat or talactoferrin or taladegib or talazoparib or talirine or taltobulin or tamibarotene or taminadenant or tandutinib or tanshinone IIA or tanurmotide or tariquidar or tarloxotinib or taselisib or tasidotin or tasisulam or tasonermin or tavokinogene telseplasmid or tazemetostat or tebentafusp or tebrocabtagene autoleucel or tecogalan or tefinostat or tegavivint or teglarinad chloride or telaglenastat or teleukin or telomestatin or telotristat or telratolimod or temarotene or temsirolimus or tenalisib or tengonermin or tepotinib or teprasiran or terameprocol or teroxirone or tesetaxel or tetramethylmelamine or tetravil or thioglucose or tian xian wan or tigilanol tiglate or tilomisole or tilsotolimod or timcodar or timonacic derivative or tipifarnib or tirabrutinib or tivantinib or tomivosertib or topsalysin or tosedostat or tozasertib or trametinib or transferrin aldifitox or trichlormethine or trichosanthin or trichostatin A or triciribine or triciribine phosphate or trilaciclib or trimelamol or tubacin or tubulozole or tucatinib or tucidinostat or tucotuzumab celmoleukin or tumo?r suppressor protein or inhibitor of growth protein 1 or ubiquitin carboxyl terminal hydrolase CYLD or tuvatexib or tylophorine or ulicyclamide or ulipristal or ulithiacyclamide or ulixertinib or umbralisib or upamostat or uproleselan or uprosertib or uzansertib or vaccinia oncolysate or vactosertib or valecobulin or valemetostat or valspodar or varlitinib or vascular targeting agent or anginex or bavituximab or crolibulin or denibulin or lexibulin or n acetylcolchinol phosphate or ofranergene obadenovec or ombrabulin or plinabulin or soblidotin or vadimezan or vecabrutinib or vedotin or velimogene aliplasmid or veliparib or vemurafenib or venetoclax or verdinexor or verrucarin A or verubulin or vesatolimod or virus oncolysate or vismodegib or vistusertib or vocimagene amiretrorepvec or volasertib or vorasidenib or vorinostat or voruciclib or vosaroxin or vosilasarm or voxtalisib or withaferin A or WW domain containing oxidoreductase or xanthone 4 acetic acid or xevinapant or xiaochaihu tang or xiliertinib or zafiride or zandelisib or zanubrutinib or

	zenocutuzumab or zerumbone or zibotentan or zilascorb or zoledronic acid or zoligratinib or zorifertinib or zosuquidar or zotatifin or zotiraciclib).mp.
23	(protein tyrosine kinase inhibitor or tyrosine kinase inhibitor or tyrosine protein kinase inhibitor or anaplastic lymphoma kinase inhibitor or bruton tyrosine kinase inhibitor or adaphostin or alofanib or alpha cyanothiocaffeic acid amide or altiratinib or alvespimycin or amivantamab or amuvatinib or alectinib or brigatinib or ceritinib or crizotinib or ensartinib or entrectinib or lorlatinib or repotrectinib or asciminib or avapritinib or axitinib or bafetinib or belizatinib or bemcentinib or bosutinib or brivanib or brivanib alaninate or acalabrutinib or branebrutinib or dasatinib or elsubrutinib or evobrutinib or ibrutinib or orelabrutinib or poseltinib or remibrutinib or rilzabrutinib or spebrutinib or tolebrutinib or vecabrutinib or zanubrutinib or cabozantinib or capmatinib or catequentinib or cediranib or cerdulatinib or cevidoplenib or conteltinib or crenolanib or damnacanthal or decernotinib or defactinib or derazantinib or dovitinib or dubermatinib or edicotinib or elafibranor or emodin or epidermal growth factor receptor kinase inhibitor or erbstatin or focal adhesion kinase inhibitor or Janus kinase inhibitor or baricitinib or brepocitinib or delgocitinib or fedratinib or fosifidancitinib or gusacitinib or ifidancitinib or ilginatinib or itacitinib or izencitinib or abrocitinib or filgotinib or lorpucitinib or momelotinib or ruxolitinib or tofacitinib or upadacitinib or lavendustin A or lazertinib or linsitinib or lorecivivint or mitogen activated protein kinase kinase inhibitor or peficitinib or pexmetinib or protein kinase Syk inhibitor or fostamatinib or lanraplenib or piceatannol or radicicol or recifercept or ritlecitinib or seralutinib or solcitinib or suppressor of cytokine signaling 1 or telatinib or tilvestamab or tyrphostin).mp.
24	(abscopal effect or bone marrow purging or bone marrow rescue or chemoradiotherap* or chemoradiation or antibody directed enzyme prodrug therap* or chemoembolization or graft versus tumo?r effect or graft versus leuk?emia effect or graft versus lymphoma effect or oncolytic viral therap* or oncolytic virus therap* or target cell destruction or biologic* response modifier therap* or BRM therap* or chimeric antigen receptor immunotherap* or chimeric antigen receptor natural killer cell immunotherap* or chimeric antigen receptor T-cell immunotherap* or CAR immontherap* or CAR T cell therap* or CAR T cell immunotherap* or CAR T therap* or CAR NK cell immunotherap* or CAR NK cell therap* or chimeric antigen receptor T cells or immune checkpoint inhibitor* or immune checkpoint blockade* or radioimmunotherap* or immunoradiotherap* or radiotherap* or bioradiant therap* or hemibody irradiation or irradiation therap* or irradiation treatment* or radiation therap* or radiation treatment* or radio therap* or radiotreatment or beam therap* or blood radiation or brachytherap* or interstitial radiation or radioisotope therap* or radium therap* or electron therap* or gamma irradiation or gamma knife radiosurgery or body radiation or photon beam therap* or proton beam therap* or radioimmunotherap* or stereotactic radiosurgery or teleradiotherap* or bone marrow transplant* or bone marrow cell transfer or bone marrow graft* or bone marrow transfusion* or h?ematopo?etic stem cell* or HSC therap* or HSC transplant* or stem cell transplant* or stem cell based therap* or stem cell therap* or allogeneic stem cell* or autologous stem cell* or peripheral blood stem cell* or allogen?ic HSCT or allogen?ic HSCTs or auto-HSCT or auto-HSCTs or autologous HSCT or autologous HSCTs or tumo?r killing activit* or tumo?r killing effect* or tumo?r killing action* or log cell kill or metastatic* inhibit* or metastas* inhibit*).mp.
25	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
26	blood vessel parameters/ or arterial stiffness/ or arterial wall thickness/ or artery diameter/ or augmentation index/ or blood vessel diameter/ or carotid-femoral pulse wave velocity/ or endothelial dysfunction/ or artery compliance/ or blood vessel compliance/ or vascular remodeling/ or artery blood flow/ or pulse wave/ or blood vessel function/ or blood vessel reactivity/ or vascular resistance/ or vasoconstriction/ or vasodilatation/ or vascular endothelium/ or artery endothelium/ or artery dilatation/ or blood flow velocity/ or blood vessel capacitance/
27	(tunica intima/ or endothelium, vascular/ or tunica media/ or muscle, smooth, vascular/ or Endothelial Cells/) and (cellular senescence/ or telomere shortening/ or Aging/)
28	arteriosclerosis/ or arteriolosclerosis/ or artery intima proliferation/
29	(endothelial function or endothelial vascular function).mp.
30	((vascular* or vasculature or endotheli* or vessel*) adj4 (ag?ing or aged or stiff* or dysfunction* or impair* or deficit* or defect* or change* or alteration* or remode?ling or dilat* or degenerat* or thick* or elasticit* or elastance or distens*)).mp.
31	((vascular* or vasculature or endotheli* or blood vessel*) adj (inflammation or senescen* or cell senescence or damage or dyshomeostasis or measurement* or compliance or calcification or reactivity)).mp.

32	((artery or arteries or arteria* or aorta* or aortic*) adj4 (ag?ing or stiff* or thick* or compliance or distens* or wave reflection or reflection index or elasticit* or elastance or defect* or change* or impair* or diameter* or dilat* or measurement* or dysfunction* or alteration* or remode?ling or calcification)).mp.
33	((Intima* media* or intimamedia* or tunica intima or tunica media) adj3 thick*).mp.
34	(pressure wave transmission or pressure wave reflection or pulse pressure or pulse wave velocity or pulse wave analys#s or pulse wave amplitude or arterial pulsatility or flow mediated dilation or blood flow velocit* or arter* flow velocit*).mp.
35	(aortic blood pressure* or aortic pressure* or aortic pulse pressure* or aortic tension* or central aortic blood pressure* or central aortic pressure*).mp.
36	(central BP or arterial BP or aortic BP or (central SBP or arterial SBP or aortic SBP) or (central PP or arterial PP or aortic PP)).mp.
37	(aortic blood pulse wave* or aortic pulse wave* or aortic tension* or arterial blood pulse wave* or arterial pulse wave* or arterial tension* or central aortic blood pulse wave* or central aortic pulse wave* or carotid to femoral pulse wave* or pulse wave*).mp.
38	(augmentation adj (index* or indice*)).mp.
39	((augmentation or amplification) adj6 (pressure* or pulse* or wave* or aortic or central)).mp.
40	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39
41	25 and 40
42	clinical trial/ or randomized controlled trial/ or randomization/ or single blind procedure/ or double blind procedure/ or crossover procedure/ or placebo/ or prospective study/
43	(randomi?ed controlled or RCT or randomly allocated or allocated randomly or random allocation or (allocated adj2 random) or (single adj1 blind*) or (double adj1 blind*) or ((treble or triple) adj1 blind*) or placebo*).mp.
44	((cross-sectional or prevalence or disease frequency) adj (analys#s or study or studies or survey)).mp.
45	((cohort or incidence) adj (analys#s or study or studies or survey)).mp.
46	((follow-up or followup or longitudinal or prospective or retrospective) adj (study or studies)).mp.
47	42 or 43 or 44 or 45 or 46
48	41 and 47
49	(exp animal/ or exp invertebrate/ or animal.hw. or nonhuman/) not exp human/
50	48 not 49
51	limit 50 to english language
52	limit 51 to (editorial or letter or note)
53	51 not 52
54	53 not (case report* or news or newspaper*).mp,pt.
55	limit 54 to conference abstract
56	54 not 55
57	limit 56 to conference abstracts
58	56 not 57

#	Query
S15	S11 OR S13 Limiters - Publication Year: 1990-2020; English Language; Exclude MEDLINE records
S14	S11 OR S13
S13	S5 AND S12
S12	(((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) N4 (accessibility or availability))) OR (((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) N0 (need* or demand*))) OR (((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*) N2 (need* or demand*)))
S11	S9 AND S10
S10	(readiness or preparedness or capacity or quality improvement or quality of Improvement)
S9	S5 AND S8
S8	S6 OR S7
S7	((primary health system or primary health service or primary healthcare system or primary health care system or primary healthcare service or primary health care service or primary medical service delivery or primary medical care service or primary care service or primary care system)) OR ((first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) OR (((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*)))
S6	(MH "Primary Health Care") OR (MH "Health Care Delivery")
S5	S1 OR S2 OR S3 OR S4
S4	((diastolic pressure or systolic pressure or blood pressure or cardiometabolic syndrome*)) OR ((copd or asthma or renal disease* or kidney disease*))
S3	((cardiovascular disease* or coronary artery disease* or myocardial isch?emia or myocardial infarct* or pulmonary disease* or chronic obstructive pulmonary or chronic obstructive lung or chronic obstructive respiratory or diabetes or coronary heart disease* or neoplasm* or cancer*)) OR ((hypertension or hypertriglycerid?emi* or hyper triglycerid?emi* or high triglyceride* or high cholesterol or hypercholesterol?emi* or hyperlipid?emia* or hyperlipidemi*))
S2	((chronic disease* or chronic disorder* or chronic* sick* or chronic health condition* or chronic medical condition* or chronic* ill* or long term condition* or multimorbidit* or mult imorbidit*)) OR ((non-communicable disease* or non-infectious disease* or noncommunicable disease* or noninfectious disease*))
S1	(MH "Chronic Disease") OR (MH "Noncommunicable Diseases") OR (MH "Chronic Pain")

CINAHL Search

Database(s): APA PsycInfo
Search Strategy:

#	Searches	Results
1	chronic illness/ or chronic fatigue syndrome/ or chronic pain/	27358
2	(chronic disease* or chronic disorder* or chronic* sick* or chronic health condition* or chronic medical condition* or chronic* ill* or long term condition* or multimorbidit* or mult imorbidit*).mp.	48956
3	(non-communicable disease* or non-infectious disease* or noncommunicable disease* or noninfectious disease*).mp.	1052
4	(cardiovascular disease* or coronary artery disease* or myocardial isch?emia or myocardial infarct* or pulmonary disease* or chronic obstructive pulmonary or chronic obstructive lung or chronic obstructive respiratory or diabetes or coronary heart disease* or neoplasm* or cancer*).mp.	121105
5	(hypertension or hypertriglycerid?emi* or hyper triglycerid?emi* or high triglyceride* or high cholesterol or hypercholesterol?emi* or hyperlipid?emia* or hyperlipidemi*).mp.	20201
6	(diastolic pressure or systolic pressure or blood pressure or cardiometabolic syndrome*).mp.	24127
7	(copd or asthma or renal disease* or kidney disease*).mp.	13056
8	1 or 2 or 3 or 4 or 5 or 6 or 7	207978
9	primary health care/	18474
10	health care delivery/	20844
11	(primary health system or primary health service or primary healthcare system or primary health care system or primary healthcare service or primary health care service or primary medical service delivery or primary medical care service or primary care service or primary care system).mp.	511
12	(first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*).mp.	338
13	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*)).mp.	2322
14	9 or 10 or 11 or 12	38723
15	8 and 14	4987
16	(readiness or preparedness or capacity or quality improvement or quality of Improvement).mp.	118317
17	15 and 16	312
18	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj5 (accessibility or availability)).mp.	148
19	8 and 18	19
20	((primary care or primary health care or primary healthcare or primary health system* or primary medical service* or primary medical care or (first-level healthcare or first-level health care or first-level health system* or first-level health facilit* or local health system* or local health care or local healthcare or local-level health*)) adj (need* or demand*)).mp.	290
21	8 and 20	55
22	((primary or first-level or local) adj3 health* adj3 (clinic* or center* or centre* or setting*) adj3 (need* or demand*)).mp.	17
23	8 and 22	2
24	17 or 19 or 21 or 23	387

25	limit 24 to english language	380
26	limit 25 to yr="1990 -Current"	380
27	limit 26 to ("column/opinion" or "comment/reply" or dissertation or editorial or letter)	41
28	26 not 27	339

Scopus

Search Strategy:

((((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND ((TITLE-ABS-KEY (("primary health system" OR "primary health service" OR "primary healthcare system" OR "primary health care system" OR "primary healthcare service" OR "primary health care service" OR "primary medical service delivery" OR "primary medical care service" OR "primary care service" OR "primary care system"))) OR (TITLE-ABS-KEY (("first-level healthcare" OR "first-level health care" OR "first-level health system*" OR "first-level health facilit*" OR "local health system*" OR "local health care" OR "local healthcare" OR "local-level health*"))) OR (TITLE-ABS-KEY ((primary OR "first-level" OR local) W/2 health* W/2 (clinic* OR center* OR centre* OR setting*)))))) AND (TITLE-ABS-KEY ((readiness OR preparedness OR capacity OR "quality improvement" OR "quality of Improvement"))))) OR (((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND (TITLE-ABS-KEY ((("primary care" OR "primary health care" OR "primary healthcare" OR "primary health system*" OR "primary medical service*" OR "primary medical care" OR "first-level healthcare" OR "first-level health care" OR "first-level health system*" OR "first-level health facilit*" OR "local health system*" OR "local health care" OR "local healthcare" OR "local-level

health*") W/4 (accessibility OR availability))))) OR (((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND (TITLE-ABS-KEY ((("primary care" OR "primary health care" OR "primary healthcare" OR "primary health system*" OR "primary medical service*" OR "primary medical care" OR "first-level healthcare" OR "first-level health care" OR "first-level health system*" OR "first-level health facilit*" OR "local health system*" OR "local health care" OR "local healthcare" OR "local-level health*") W/0 (need* OR demand*))))) OR (((TITLE-ABS-KEY (("chronic disease*" OR "chronic disorder*" OR "chronic* sick*" OR "chronic health condition*" OR "chronic medical condition*" OR "chronic* ill*" OR "long term condition*" OR multimorbidit* OR "mult imorbidit*"))) OR (TITLE-ABS-KEY (("non-communicable disease*" OR "non-infectious disease*" OR "noncommunicable disease*" OR "noninfectious disease*"))) OR (TITLE-ABS-KEY (("cardiovascular disease*" OR "coronary artery disease*" OR "myocardial isch?emia" OR "myocardial infarct*" OR "pulmonary disease*" OR "chronic obstructive pulmonary" OR "chronic obstructive lung" OR "chronic obstructive respiratory" OR diabetes OR "coronary heart disease*" OR neoplasm* OR cancer*))) OR (TITLE-ABS-KEY ((hypertension OR hypertriglycerid?emi* OR "hyper triglycerid?emi*" OR "high triglyceride*" OR "high cholesterol" OR hypercholesterol?emi* OR hyperlipid?emia* OR hyperlipidemi*))) OR (TITLE-ABS-KEY (("diastolic pressure" OR "systolic pressure" OR "blood pressure" OR "cardiometabolic syndrome*"))) OR (TITLE-ABS-KEY ((copd OR asthma OR "renal disease*" OR "kidney disease*")))) AND (TITLE-ABS-KEY (((primary OR "first-level" OR local) W/2 health* W/2 (clinic* OR center* OR centre* OR setting*) W/2 (need* OR demand*))))) AND (LIMIT-TO (LANGUAGE , "English")) AND (EXCLUDE (DOCTYPE , "ch") OR EXCLUDE (DOCTYPE , "no") OR EXCLUDE (DOCTYPE , "bk") OR EXCLUDE (DOCTYPE , "ed")) AND (EXCLUDE (SUBJAREA , "AGRI") OR EXCLUDE (SUBJAREA , "CENG") OR EXCLUDE (SUBJAREA , "ARTS") OR EXCLUDE (SUBJAREA , "BUSI") OR EXCLUDE (SUBJAREA , "EART") OR EXCLUDE (SUBJAREA , "VETE")) View less

Table S2. A list of the excluded studies and reasons for their exclusion

SL	Study	Reason for exclusion
01	Abolhassani N, Santos-Eggimann B, Chiolero A, Santschi V, Henchoz Y. Readiness to accept health information and communication technologies: A population-based survey of community-dwelling older adults. *International Journal of Medical Informatics* 2019; **130**: 103950.	Not relevant to the theme for review
02	Acton KJ, Shields R, Rith-Najarian S, et al. Applying the diabetes quality improvement project indicators in the Indian Health Service primary care setting. *Diabetes Care*; **24**(1): 22-6.	Inadequate or inappropriate results
03	Ahmed S, Chowdhury MA, Khan MA, Huq NL, Naheed A. Access to primary health care for acute vascular events in rural low income settings: a mixed methods study. *BMC Health Services Research*; **17**(1): 47.	Inadequate or inappropriate results
04	Allenby A, Kinsman L, Tham R, Symons J, Jones M, Campbell S. The quality of cardiovascular disease prevention in rural primary care. *Australian Journal of Rural Health*; **24**(2): 92-8.	Inadequate or inappropriate results
05	Armour CL, Reddel HK, Lemay KS, et al. Feasibility and Effectiveness of an Evidence-Based Asthma Service in Australian Community Pharmacies: A Pragmatic Cluster Randomized Trial. *Journal of Asthma* 2013; **50**(3): 302-9.	Not relevant to the theme for review
06	Alzubaidi HT, Chandir S, Hasan S, McNamara K, Cox R, Krass I. Diabetes and cardiovascular disease risk screening model in community pharmacies in a developing primary healthcare system: A feasibility study.	Inadequate or inappropriate results
07	Ahmedov M, Green J, Azimov R, Avezova G, Inakov S, Mamatkulov B. Addressing the challenges of improving primary care quality in Uzbekistan: a qualitative study of chronic heart failure management. *Health Policy & Planning*; **28**(5): 458-66.	Inadequate or inappropriate results
08	Aryal BK, Daud M, Thapa A, Mahotra A, Ale Magar S, Malla CK. Assesssment of Health Facilities for Implementation of Non-communicable Disease Package. *Journal of Nepal Health Research Council*; **16**(2): 149-55.	Combined data on primary and secondary healthcare level
09	Banasiak NC. Implementation of the Asthma Control Test in Primary Care to Improve Patient Outcomes. *Journal of Pediatric Healthcare* 2018; **32**(6): 591-9.	Not relevant to the theme for review
10	Barcelos MRB, Nunes BP, Duro SMS, et al. Utilization of Breast Cancer Screening in Brazil: An External Assessment of Primary Health Care Access and Quality Improvement Program.	Not relevant to the theme for review
11	Bello AK, Ronksley PE, Tangri N, et al. Quality of Chronic Kidney Disease Management in Canadian Primary Care. *JAMA Network Open*; **2**(9): e1910704.	Inadequate or inappropriate results
12	Baeza JI, Fitzgerald L, McGivern G. Change capacity: the route to service improvement in primary care. *Quality in Primary Care*; **16**(6): 401-7.	Inadequate or inappropriate results
13	Bawazir AA, Al-Surimi K, Suwaidan SD, AlShehri AM, AlFarhan AI, Aboulfotouh MA. Capacity and readiness of primary health care centers for implementation of the basic strategy for prevention and control of non-communicable diseases in Saudi Arabia. A case study from the Ministry of National Guard-Health Affairs, Riyadh, Saudi Arabia. *Saudi Medical Journal*; **40**(6): 614-8.	Inappropriate study type (n=1)
14	Boehmer KR, Kyriacou M, Behnken E, Branda M, Montori VM. Patient capacity for self-care in the medical record of patients with	Not relevant to the theme for review

	chronic conditions: a mixed-methods retrospective study. *BMC family practice* 2018; **19**(1): 164.	
15	Bindman AB, Grumbach K, Osmond D, Vranizan K, Stewart AL. Primary care and receipt of preventive services.	Inadequate or inappropriate results
16	Birabwa C, Bwambale MF, Waiswa P, Mayega RW. Quality and barriers of outpatient diabetes care in rural health facilities in Uganda - a mixed methods study. *BMC Health Services Research*; **19**(1): 706.	Combined data on primary and secondary healthcare level
17	Brownson CA, Miller D, Crespo R, et al. A quality improvement tool to assess self-management support in primary care. *Joint Commission Journal on Quality & Patient Safety*; **33**(7): 408-16.	Inadequate or inappropriate results
18	Casalino LP, Wu FM, Ryan AM, et al. Independent practice associations and physician-hospital organizations can improve care management for smaller practices. *Health Affairs*; **32**(8): 1376-82.	Inadequate or inappropriate results
19	Chavannes NH. Integrated chronic obstructive pulmonary disease management in primary care. *Disease Management & Health Outcomes* 2008; **16**(5): 315-8.	Inadequate or inappropriate results
20	Chen M, Patel T, Chang F. The impact of a primary care, pharmacist-driven intervention in patients with chronic non-cancer pain-A pilot study. *Pharmacy* 2020; **8**(8): 113.	Not relevant to the theme for review
21	Chen XRC, Leung SH, Li YC. Chronic Obstructive Pulmonary Disease (COPD) management in the community: how could primary care team contribute? *BMC family practice* 2020; **21**(1): 184.	Not relevant to the theme for review
22	Collins S. Primary care shortages: Strengthening this sector is urgently needed, now and in preparation for healthcare reform. *American Health and Drug Benefits* 2012; **5**(1): 40-7.	Inadequate or inappropriate results
23	Chen LW, Nguyen AT, Jacobson J, Palm D. Assessment of workforce capacity for Local Health Departments in Nebraska: a perspective from public health programmatic areas. *Journal of Public Health Management & Practice*; **18**(6): 595-601.	Not relevant to the theme for review
24	Chen LM, Sakshaug JW, Miller DC, Rosland A-M, Hollingsworth J. The association among medical home readiness, quality, and care of vulnerable patients. *Am J Manag Care* 2015; **21**(8): e480-e6.	Inadequate or inappropriate results
25	Day A, Oldroyd C, Godfrey S, Quinn T. Availability of cardiac equipment in general practice premises in a cardiac network: A survey. *British Journal of Cardiology* 2008; **15**(3): 141-4.	Inadequate or inappropriate results
26	Deckard GJ, Borkowski N, Diaz D, Sanchez C, Boisette SA. Improving timeliness and efficiency in the referral process for safety net providers: Application of the lean six sigma methodology. *Journal of Ambulatory Care Management* 2010; **33**(2): 124-30.	Not relevant to the theme for review
27	Depatie A, Bigbee JL. Rural Older Adult Readiness to Adopt Mobile Health Technology: A Descriptive Study. *Online Journal of Rural Nursing & Health Care* 2015; **15**(1): 150-84.	Inadequate or inappropriate results
28	Due TD, Thorsen T, Waldorff FB, Kousgaard MB. Role enactment of facilitation in primary care - a qualitative study. *BMC Health Services Research*; **17**(1): 593.	Not relevant to the theme for review
29	Fleck S. Unified health services and family focused primary care.	Not relevant to the theme for review
30	Foo KM, Sundram M, Legido-Quigley H. Facilitators and barriers of managing patients with multiple chronic conditions in the community: a qualitative study. *BMC public health* 2020; **20**(1): 273.	Inadequate or inappropriate results
31	Fortin M, Chouinard M-C, Diallo BB, Bouhali T. Integration of chronic disease prevention and management services into primary care (PR1MaC): findings from an embedded qualitative study. *BMC Family Practice* 2019; **20**(1): 1-8.	Inadequate or inappropriate results

32	Fox CH, Brooks A, Zayas LE, McClellan W, Murray B. Primary care physicians' knowledge and practice patterns in the treatment of chronic kidney disease: an Upstate New York Practice-based Research Network (UNYNET) study. *Journal of the American Board of Family Medicine: JABFM*; **19**(1): 54-61.	Not relevant to the theme for review
33	Fuchs S, Jaffe DM, Christoffel KK. Pediatric emergencies in office practices: prevalence and office preparedness. *Pediatrics*; **83**(6): 931-9.	Not relevant to the theme for review
34	Furno M. The primary role: How the availability of primary care physicians affects diabetes care management.	Inadequate or inappropriate results
35	Galaviz KI, Narayan KMV, Manders OC, et al. The Public Health Leadership and Implementation Academy for Noncommunicable Diseases. *Preventing Chronic Disease*; **16**: E49.	Inadequate or inappropriate results
36	Ghimire U, Shrestha N, Adhikari B, Mehata S, Pokharel Y, Mishra SR. Health system's readiness to provide cardiovascular, diabetes and chronic respiratory disease related services in Nepal: analysis using 2015 health facility survey. *BMC Public Health* 2020; **20**(1): 1163.	Combined data on primary and secondary healthcare level
37	Gerbert B, Maurer T, Berger T, et al. Primary care physicians as gatekeepers in managed care. Primary care physicians' and dermatologists' skills at secondary prevention of skin cancer. *Archives of Dermatology*; **132**(9): 1030-8.	Inadequate or inappropriate results
38	Gordon NP, Hornbrook MC. Older adults' readiness to engage with eHealth patient education and self-care resources: a cross-sectional survey. *BMC health services research* 2018; **18**(1): 220.	Not relevant to the theme for review
39	Goytia EJ, Rapkin B, Weiss ES, Golub D, Guzman V, O'Connor M. Readiness and capacity of librarians in public libraries to implement a breast cancer outreach and screening campaign in medically underserved communities. *Cancer control : journal of the Moffitt Cancer Center* 2005; **12 Suppl 2**: 13-20.	Not relevant to the theme for review
40	Gujral UP, Johnson L, Nielsen J, et al. Preparedness cycle to address transitions in diabetes care during the COVID-19 pandemic and future outbreaks. *BMJ Open Diabetes Research & Care* 2020; **8**(1): 07.	Not relevant to the theme for review
41	Haileamlak A. Preparedness to Respond to the Ever-increasing Cancer Cases. *Ethiopian Journal of Health Sciences*; **25**(4): 293-4.	Not relevant to the theme for review
42	Hanusaik N, O'Loughlin JL, Kishchuk N, Paradis G, Cameron R. Organizational capacity for chronic disease prevention: a survey of Canadian public health organizations. *European Journal of Public Health*; **20**(2): 195-201.	Combined data on primary and secondary healthcare level
43	Henderson KH, DeWalt DA, Halladay J, et al. Organizational Leadership and Adaptive Reserve in Blood Pressure Control: The Heart Health NOW Study. *Annals of Family Medicine*; **16**(Suppl 1): S29-S34.	Inadequate or inappropriate results
44	Heslop L, Power R, Cranwell K. Building workforce capacity for complex care coordination: a function analysis of workflow activity. *Human Resources for Health [Electronic Resource]*; **12**: 52.	Not relevant to the theme for review
45	Geboers et al.	Inadequate or inappropriate results
46	Inrig SJ, Higashi RT, Tiro JA, Argenbright KE, Lee SJ. Assessing local capacity to expand rural breast cancer screening and patient navigation: An iterative mixed-method tool. *Evaluation and program planning* 2017; **61**: 113-24.	Inadequate or inappropriate results
47	Jayanna K, Swaroop N, Kar A, et al. Designing a comprehensive Non-Communicable Diseases (NCD) programme for hypertension	Inadequate or inappropriate results

	and diabetes at primary health care level: evidence and experience from urban Karnataka, South India. *BMC Public Health* 2019; **19**(1): 409.	
48	Jigjidsuren A, Byambaa T, Altangerel E, et al. Free and universal access to primary healthcare in Mongolia: the service availability and readiness assessment. *BMC Health Services Research*; **19**(1): 129.	Inadequate or inappropriate results
49	Jin Y, Zhu W, Yuan B, Meng Q. Impact of health workforce availability on health care seeking behavior of patients with diabetes mellitus in China.	Combined data on primary and secondary healthcare level
50	Joffres C, Heath S, Farquharson J, et al. Defining and operationalizing capacity for heart health promotion in Nova Scotia, Canada. *Health Promotion International* 2004; **19**(1): 39-49.	Not relevant to the theme for review
51	Jones D, West R, Lester C. Evaluation of changes in primary health care availability and provision from the patient perspective.	Inadequate or inappropriate results
52	Jones R, Ostrem A. Optimising pharmacological maintenance treatment for COPD in primary care. *Primary Care Respiratory Journal* 2011; **20**(1): 33-45.	Inadequate or inappropriate results
53	Kayser L, Rossen S, Karnoe A, et al. Development of the Multidimensional Readiness and Enablement Index for Health Technology (READHY) Tool to Measure Individuals' Health Technology Readiness: Initial Testing in a Cancer Rehabilitation Setting. *Journal of medical Internet research* 2019; **21**(2): e10377.	Inadequate or inappropriate results
54	Khunti K, Baker R, Rumsey M, Lakhani M. Approaches to the organization of multi-practice audits in primary health care in the UK. *International Journal for Quality in Health Care*; **11**(3): 221-6.	Inadequate or inappropriate results
55	Kaufman ND, Rajataramya B, Tanomsingh S, Ronis DL, Potempa K. Nurse preparedness for the non-communicable disease escalation in Thailand: a cross-sectional survey of nurses. *Nursing & Health Sciences* 2012; **14**(1): 32-7.	Inadequate or inappropriate results
56	Laatikainen T, Inglin L, Collins D, et al. Implementing Package of Essential Non-communicable Disease Interventions in the Republic of Moldova-a feasibility study. *Eur J Public Health* 2020.	Inadequate or inappropriate results
57	Landon BE, Hicks LS, O'Malley AJ, et al. Improving the management of chronic disease at community health centers. *New England Journal of Medicine* 2007; **356**(9): 921-34.	Inadequate or inappropriate results
58	Langer S, Chew-Graham CA, Drinkwater J, et al. A motivational intervention for patients with COPD in primary care: qualitative evaluation of a new practitioner role. *BMC Family Practice*; **15**: 164.	Inadequate or inappropriate results
59	Liu J, Yin H, Zheng T, et al. Primary health institutions preference by hypertensive patients: Effect of distance, trust and quality of management in the rural Heilongjiang province of China.	Inadequate or inappropriate results
60	Maarse JA, Ruwaard D, Spreeuwenberg C. The governance of quality management in dutch health care: new developments and strategic challenges. *Quality Management in Health Care*; **22**(3): 236-47.	Not relevant to the theme for review
61	Madueno A, Martin A, Peculo JA, Anton E, Paravisini A, Leon A. Usefulness of inspiratory capacity measurement in COPD patients in the primary care setting. *International Journal of General Medicine* 2009; **2**: 219-25.	Combined data on primary and secondary healthcare level
62	Main DS, Cohen SJ, DiClemente CC. Measuring physician readiness to change cancer screening: Preliminary results. *American Journal of Preventive Medicine* 1995; **11**(1): 54-8.	Inadequate or inappropriate results
63	Monaghan M, Hilliard M, Sweenie R, Riekert K. Transition readiness in adolescents and emerging adults with diabetes: the role	Inadequate or inappropriate results

	of patient-provider communication. *Current Diabetes Reports*; **13**(6): 900-8.	
64	Moynihan M, Saewyc E, Whitehouse S, Paone M, McPherson G. Assessing readiness for transition from paediatric to adult health care: Revision and psychometric evaluation of the Am I ON TRAC for Adult Care questionnaire. *Journal of Advanced Nursing*; **71**(6): 1324-35.	Inadequate or inappropriate results
65	Neher M, Landen Ludvigsson M, Enblom A. Preparedness to Implement Physical Activity and Rehabilitation Guidelines in Routine Primary Care Cancer Rehabilitation: Focus Group Interviews Exploring Rehabilitation Professionals' Perceptions. *Journal of cancer education : the official journal of the American Association for Cancer Education* 2020.	Inadequate or inappropriate results
66	Nilsson GH, Skånér Y, Krakau I, Hassler E, Sundquist K. Primary prevention of first-ever stroke in primary health care: A clinical practice study based on medical register data in sweden.	Inadequate or inappropriate results
67	Nuno-Solinis R. Are Healthcare Organizations Ready for Change? Comment on "Development and Content Validation of a Transcultural Instrument to Assess Organizational Readiness for Knowledge Translation in Healthcare Organizations: The OR4KT". *International Journal of Health Policy & Management*; **7**(12): 1158-60.	Inadequate or inappropriate results
68	Nyarko KM, Ameme DK, Ocansey D, Commeh E, Markwei MT, Ohene SA. Capacity assessment of selected health care facilities for the pilot implementation of Package for Essential Non-communicable Diseases (PEN) intervention in Ghana. *The Pan African medical journal*; **25**(Suppl 1): 16.	Combined data on primary and secondary healthcare level
69	Ogbimi RI. Leadership in Nigerian health system for cancer prevention and control. *African Journal of Medicine & Medical Sciences*; **38 Suppl 2**: 49-53.	Inadequate or inappropriate results
70	Ostroff JS, Copeland A, Borderud SP, Li Y, Shelley DR, Henschke CI. Readiness of lung cancer screening sites to deliver smoking cessation treatment: Current practices, organizational priority, and perceived barriers. *Nicotine & Tobacco Research* 2016; **18**(5): 1067-75.	Not relevant to the theme for review
71	Oyewole EY, Ojewale LY, Abimbola OO. Primary Health Care Nurses' Competencies and Resources Availability for Diabetes Mellitus Care at Local Government Areas of Ibadan. *International Journal of Caring Sciences* 2020; **13**(1): 368-80.	Not relevant to the theme for review
72	Parchman ML, Anderson ML, Coleman K, et al. Assessing quality improvement capacity in primary care practices. *BMC Family Practice*; **20**(1): 103.	Not relevant to the theme for review
73	Pilkerton CS, Singh SS, Bias TK, Frisbee SJ. Healthcare resource availability and cardiovascular health in the USA. *BMJ Open* 2017; **7**(12): e016758.	Not relevant to the theme for review
74	Radin A, Cote C. Primary care of the patient with chronic obstructive pulmonary disease-part 1: frontline prevention and early diagnosis. *American Journal of Medicine*; **121**(7 Suppl): S3-12.	Inadequate or inappropriate results
75	Rathish D, Premarathna I, Jayathilake T, et al. Availability of essential medicines in selected public, primary and secondary health care institutions of a rural Sri Lankan district: A spot survey.	Combined data on primary and secondary healthcare level
76	Rogers HE, Akiteng AR, Mutungi G, Ettinger AS, Schwartz JI. Capacity of Ugandan public sector health facilities to prevent and	Combined data on primary and secondary healthcare level

	control non-communicable diseases: an assessment based upon WHO-PEN standards. *BMC Health Services Research*; **18**(1): 606.	
77	Roper KL, Thomas AR, Hieronymus L, Brock A, Keck J. Patient and Clinician Perceptions of Prediabetes: A Mixed-Methods Primary Care Study. *Diabetes Educ* 2019; **45**(3): 302-14.	Inadequate or inappropriate results
78	Schwartz R, Smith C, Speers MA, et al. Capacity building and resource needs of state health agencies to implement community-based cardiovascular disease programs. *Journal of Public Health Policy* 1993; **14**(4): 480-94.	Inadequate or inappropriate results
79	Shaw RJ, Kaufman MA, Bosworth HB, et al. Organizational factors associated with readiness to implement and translate a primary care based telemedicine behavioral program to improve blood pressure control: the HTN-IMPROVE study. *Implementation Science*; **8**: 106.	Inadequate or inappropriate results
80	Sorensen A, Le LW, Swami N, et al. Readiness for delivering early palliative care: A survey of primary care and specialised physicians. *Palliative Medicine* 2020; **34**(1): 114-25.	Combined data on primary and secondary healthcare level
81	Soylu TG, Cuellar AE, Goldberg DG, Kuzel AJ. Readiness and Implementation of Quality Improvement Strategies Among Small- and Medium-Sized Primary Care Practices: an Observational Study. *Journal of General Internal Medicine* 2020.	Not relevant to the theme for review
82	Tanjasiri SP, Tran JH. Community capacity for cancer control collaboration: weaving an Islander Network for Cancer Awareness, Research and Training for Pacific Islanders in Southern California. *Cancer Detection & Prevention*; **32 Suppl 1**: S37-40.	Inadequate or inappropriate results
83	Tompkins JW, Mequanint S, Barre DE, et al. National Survey of Indigenous primary healthcare capacity and delivery models in Canada: the TransFORmation of IndiGEnous PrimAry HEAlthcare delivery (FORGE AHEAD) community profile survey. *BMC Health Services Research*; **18**(1): 828.	Combined data on primary and secondary healthcare level
84	Weeks DL, Polello JM, Hansen DT, Keeney BJ, Conrad DA. Measuring primary care organizational capacity for diabetes care coordination: the Diabetes Care Coordination Readiness Assessment. *Journal of General Internal Medicine*; **29**(1): 98-103.	Not relevant to the theme for review

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Lines 2-3, Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Lines 25-48, Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Lines 90-117, Page 4-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Lines 121-122, Page 45
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Lines 132-137, Page 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Lines 146-161, Page 7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary materials
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 192-208, Page 8-9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Lines 181-190, Page 8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Lines 209-218, Page 9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Lines 209-218, Page 9
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 192-202, Page 8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Result was thematically presented in descriptive manner. Therefore, no effect measure was presented.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Lines 192-202, Page 8

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Lines 192-202, Page 8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Lines 192-202, Page 8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	No meta-analysis performed
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	No meta-analysis performed
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	No sensitivity
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Lines 192-202, Page 8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable in this review
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Lines 229-246, Page 10
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary materials
Study characteristics	17	Cite each included study and present its characteristics.	Lines 229-246, Page 10
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Lines 192-202, Page 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Result was presented thematically. Therefore, no table/confidence interval was presented.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not exactly relevant in this review as reported was described under themes
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not exactly relevant in this review as

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
			reported was described under themes
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Lines 473-481, Page 24
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not exactly relevant in this review as reported was described under themes
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not exactly relevant in this review as reported was described under themes
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not exactly relevant in this review as reported was described under themes
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Lines 420-468, Page 22-24
	23b	Discuss any limitations of the evidence included in the review.	Lines 473-481, Page 24
	23c	Discuss any limitations of the review processes used.	Lines 473-481, Page 24
	23d	Discuss implications of the results for practice, policy, and future research.	Lines 473-481, Page 24
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Lines 128-130, Page 6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Protocol was not prepared
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	No amendment done
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Lines 511, Page 25

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Competing interests	26	Declare any competing interests of review authors.	Lines 505, Page 25
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Lines 507, Page 25

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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