SYSTEMATIC REVIEW

Patient pathways for cardiovascular diseases in Malaysia and the Philippines: a systematic review [version 1; peer review: 1 approved]

Maureen Seguin1*, Gideon Lasco2*, Khairuddin Bin Idris3, Jhaki Mendoza4, N.H. Hanani Mohd Kadri3, Steven Krauss4, Jeffrey D'Silva3, Hayrol Mohamed Shaffril3, Mohd Fauzi Fadzil3, Benjamin Palafox1, Alicia Renedo5, Mat-Nasir Nafiza6, Fadhлина Majid6, Azlina A. Razak7, Khalid Yusoff6,7, Lia Palileo-Villanueva4, Antonio Dans4, Eunice Mallari4, Dina Balabanova1, Martin McKee1

1Centre for Global Chronic Conditions, London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK
2Department of Anthropology, University of the Philippines Diliman, Quezon City, Philippines
3Institute for Social Science Studies, University Putra Malaysia, Serdang, Malaysia
4College of Medicine, University of the Philippines Manila, Manila, Philippines
5Department of Social and Environmental Health Research, London School of Hygiene & Tropical Medicine, London, WC1H 9SH, UK
6Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia
7UCSI University, Kuala Lumpur, Malaysia

* Equal contributors

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Abstract

Background: Cardiovascular diseases (CVDs) are the leading cause of premature mortality in the world and are a growing public health concern in low- and middle-income countries (LMICs), including those in South East Asia. Their management requires coordinated responses by a range of healthcare providers, which should preferably be based on knowledge of the national context. We systematically review evidence on the pathways followed by patients with CVD in Malaysia and the Philippines to understand patient journeys, along with the barriers at each stage.

Methods: We searched seven bibliographic databases and grey literature sources to identify material focused on the pathways followed by patients with CVD in Malaysia and the Philippines, and performed a narrative synthesis.

Results: The search yielded 25 articles, 3 focused on the Philippines and 22 on Malaysia. Most articles were quantitative analyses that focused on hypertensive patients. Three examined secondary prevention post myocardial infarction, and one each examined acute
Corresponding author: Maureen Seguin (maureen.seguin@lshtm.ac.uk)

Author roles: Seguin M: Conceptualization, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; Lasco G: Conceptualization, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; Bin Idris K: Conceptualization, Supervision, Writing – Review & Editing; Mendoza J: Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; Krauss S: Methodology, Writing – Review & Editing; D’Silva J: Methodology, Writing – Review & Editing; Shaffril HM: Methodology, Writing – Review & Editing; Fadzil MF: Methodology, Writing – Review & Editing; Palfox B: Conceptualization, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; Renedo A: Conceptualization, Writing – Original Draft Preparation, Writing – Review & Editing; Nafiza MN: Methodology, Writing – Review & Editing; Majid F: Writing – Review & Editing; Razak AA: Writing – Review & Editing; Yusoff K: Conceptualization, Writing – Review & Editing; Palileo-Villanueva L: Conceptualization, Writing – Review & Editing; Dans A: Conceptualization, Writing – Review & Editing; Mallari E: Methodology, Writing – Review & Editing; Balabanova D: Conceptualization, Methodology, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; McKee M: Conceptualization, Supervision, Writing – Review & Editing

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Myocardial infarction, heart failure, and atrial fibrillation. Reported barriers reflected capability (knowledge of behaviours to achieve control or the capacity to conduct these behaviours), intention (attitudes or motivations toward the behaviours to achieve control), and aspects of the health care system (availability, accessibility, affordability and acceptability of services).

Conclusions: There are large gaps in our understanding of patient pathways in Malaysia and the Philippines that limit the development of evidence-based strategies to effectively address the CVD burden in South East Asian countries and in LMICs more broadly. Addressing these evidence gaps will require longitudinal mixed-methods studies following patients from initial diagnosis to long-term management.

Keywords
Cardiovascular diseases, Patient pathways, Barriers to care, Health systems, Malaysia, Philippines, South East Asia, Systematic review
Introduction
Cardiovascular diseases (CVD) are now the leading contributor to the burden of disease in South East Asia and lost Disability Adjusted Life Years per 100,000 attributed to these diseases have increased by 22.2% between 1970 and 2017. Yet much of this burden is avoidable. Western countries have seen steep falls in the CVD burden in this period, as in Canada (-25.8%), Finland (-35.6%), and the United Kingdom (-53.3%). Typically, between a quarter and a third of these declines can be attributed to improvements in acute disease treatment and secondary prevention, and a further third to a half to reductions in risk factors, such as hypertension, smoking, and high cholesterol, although the contributions varied depending on the initial risk factor profile. If these successes are to be replicated in middle-income countries, such as those in South East Asia, concerted action will be needed to reduce risk factors in the population and ensure that those who can benefit from treatment and secondary prevention receive it.

This paper has been written to inform a study on barriers to effective care of CVDs in two countries in this region, Malaysia and the Philippines, and how they might be overcome. These are neighbouring countries in South East Asia, in which cardiovascular disease are the leading cause of death. Malaysia has universal health care coverage provided by public sector services and lower out of pocket expenditure than in the Philippines (38% vs. 53% respectively in 2016). Yet both face considerable challenges. In Malaysia, only 7.6% of patients with CVD are taking three or more of the drugs recommended for secondary prevention, and only 2.3% in The Philippines. Corresponding figures for the percentage of individuals with hypertension that is controlled are 12.5% and 13.5%, respectively. Effective policy responses are clearly needed but must be informed by a detailed understanding of the barriers that patients with CVD face on their journey through the health system in each country, alongside accounting for socio-cultural contexts that also influence patients’ conceptions of – and responses to – illness.

As we explore opportunities to intervene in Malaysia and the Philippines, we must first: (1) identify and analyze existing research on how patients with CVD move through each health system and (2) summarize what is known about barriers and enabling factors that are specific to each stage of the patient pathway. Here we report a systematic review of the published evidence, drawing on our two earlier systematic reviews, where we categorized barriers to effective management of hypertension into those at the level of the health system and in the clinical encounter and then analyzed barriers in Malaysia and Colombia. Although the findings are of immediate relevance to Malaysia and the Philippines, we envisage that our review can be used to inform similar approaches elsewhere. The paper presents the barriers we identified according to different stages in the patient pathway, and discusses the implications of the findings in the context of existing literature.

Methods
Eligibility criteria
We included primary research (both quantitative and qualitative) undertaken in Malaysia or the Philippines, excluding editorials and commentaries, which focused on the patient pathways (and related barriers and facilitators) related to any CVD (including hypertension, ischemic heart disease, myocardial infarction, heart failure, coronary artery disease, and excluding cerebrovascular disease). We included articles that involve patient pathways, which we define as patient’s interactions with different forms of care through the following phases: symptoms, diagnosis, treatment, long-term management, and any contact with secondary and tertiary care. We included papers that contained findings on two or more phases, as well as papers focused on one phase reporting data captured at two or more points in time (i.e., management over time). We excluded intervention studies, as these by definition impose a particular pathway which would not otherwise occur. We also excluded studies which reported preliminary results superseded by subsequent papers, papers reporting individuals in institutionalized care and studies published prior to 2000.

Search strategy
Medline, Embase, Global Health, International Bibliography of the Social Sciences, Scopus, ISI-Web of Science and PsycINFO were searched in February 2018, with a repeat search conducted in July 2020 to update the results. Grey literature was sought through relevant websites, Google, and hand searches of university libraries and online periodicals. No limits were placed on initial publication date or the age range of the included participants. Final search terms were informed by exploratory Medline searches conducted in September-December 2017 within the scope of the ‘Responsive and Equitable Health Systems – Partnership on Non-communicable Diseases’ (RESPOND) Study. Search terms pertained to two areas: CVD (including signs and symptoms such as elevated blood pressure and angina) and treatment patterns (including such terms as ‘patient navigation’ and ‘care pathway’). The detailed Medline search strategy is provided in the Extended data.

Selection process
Studies were selected according to the preferred reporting items for systematic reviews and meta-analyses (see Reporting guidelines for a completed PRISMA checklist). Two reviewers (MS and GL) independently reviewed titles and abstracts against inclusion/exclusion criteria, with disagreements resolved by a third reviewer. Full texts of included articles were screened independently by MS and GL, with those fulfilling the inclusion criteria retained. Reference lists of included studies were manually searched for additional relevant articles.

Data extraction and analytic approach
Location, sample characteristics, methodology, particular CVD, pathway portion(s), and barriers and facilitators along the
pathway were extracted from each article to an Excel spreadsheet. A narrative synthesis was conducted rather than a meta-analysis or meta-synthesis due to study heterogeneity.

Findings are reported by condition, where possible extracting information on different segments (including symptoms, diagnosis, management, hospitalization, and post-discharge) of each pathway are described, along with associated barriers and facilitators. Barriers were extracted and organized according to a framework suggested by Khatib et al. on hypertension control\textsuperscript{11} which drew upon earlier theoretical work by Michie et al.\textsuperscript{17} Khatib et al. define three types of barrier to hypertension control, including capability barriers (knowledge of behaviors required to achieve control, or the capacity to conduct these behaviors), intention barriers (attitudes or motivations toward the behaviors necessary to achieve control), and health care system-related barriers (availability of resources, affordability of care, and/or acceptability of services).

Quality assessment
A quality assessment of included articles was completed by NHHMK, using the RATS guidelines\textsuperscript{18} and STROBE checklist\textsuperscript{19} for qualitative and quantitative articles respectively. The quality assessment was not used to exclude articles, but to appraise the quality level of the evidence base.

Results
Study selection
The results of the search are summarized in Figure 1. The main database search yielded 784 records, and a further eight were identified via complementary search strategies. After duplicates were removed, the titles and abstracts of the remaining 635 articles were independently screened by GL and MS. Of these articles, GL and MS agreed on inclusion/exclusion on 623 (IIR = 98.1%). Disagreements on 12 articles were resolved in discussion with DB, leading to a full article screen of 82 articles. In total, 64 articles were excluded due to insufficient focus on the patient pathway, leaving 18 studies selected for final review. A manual review of reference lists yielded three additional studies, leading to a total of 21 (Table 1).

Of the 21 studies, 15 focused on hypertension, of which 8 were quantitative, 6 qualitative, and 1 mixed method. Three examined secondary prevention post myocardial infarction, all quantitatively, and there were one each studying atrial fibrillation (quantitative), heart failure and acute myocardial infarction (both qualitative). The final quantitative study focused on modifiable CVD risk factors. Only three studies were set in the Philippines, compared to 18 in Malaysia.

Risk of bias and quality assessment
The quality assessment of included studies is available in the Extended data\textsuperscript{15}. Common weaknesses in the quantitative articles included a lack of discussion of sources of bias, study limitations, and source of funding, along with a lack of validity measures. Few qualitative articles reported details on participant recruitment and informed consent procedures.

Hypertension
Initial presentation. A community-based survey in the Philippines\textsuperscript{20} found high rates of undiagnosed hypertension (HT), and the same conclusion was reached in Malaysia by a study using a nationally-representative household health survey\textsuperscript{21}. Four papers examined how patients found to have HT entered the health system\textsuperscript{13,22–24}. In studies of those with known HT, most patients presented at clinics with non-specific symptoms, including headaches or dizziness, causing them to seek medical advice. A minority attended after checking their own blood

Figure 1. Results of the screening processes in Malaysia and the Philippines.
<table>
<thead>
<tr>
<th>Author (year), reference</th>
<th>CVD</th>
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<th>Study design &amp; methodology</th>
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<tr>
<td><strong>Quantitative studies</strong></td>
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<td>Ahmad, Ramesh and Zambahari (2011)</td>
<td>ACS</td>
<td>525 adults aged 21 years or older, 75% male, diagnosed unstable angina or NSTEMI, mean age 58 years.</td>
<td>17 Hospitals in Malaysia</td>
<td>Prospective observational study which collected data at discharge and then followed-up on patients four times over a one-year period.</td>
<td>Following hospitalisation, a minority (16.4%) were advised coronary angiogram. Of these patients, 14.0% had only angiograms done, 76.7% had PCI, 8.1% had CABG, and 1.2% had PCI followed by CABG. However, the majority (83.6%) were managed medically. Among the medically managed branch, 62.7–77.6% of received aspirin only, 5.0–6.8% received clopidogrel only and 15.6–32.3% received dual antiplatelet medications. The prescription of dual antiplatelet therapy (aspirin and clopidogrel) decreased from 32.3% at visit-2 to 15.6% at visit-5. Among patients treated with aspirin only, 2.9%–6.5% discontinued the treatment permanently. Among those treated with clopidogrel only, the compliance was &gt; 80% of prescribed tablets in &gt; 88% of subjects. With regard to combined aspirin and clopidogrel medications, &gt; 90% of the patients had clopidogrel compliance for &gt; 80% of the prescribed tablets.</td>
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<td>Ahmad et al. (2013)</td>
<td>HT</td>
<td>520 adults aged 18 to 80, 58.5% male, diagnosed HT, mean age 61 years, 49.8% Chinese, 32.3% Malay, 15.6% Indian, and 2.3% other.</td>
<td>Pulau Pinang Hospital, Penang, Malaysia</td>
<td>Cohort study tracking patients’ prescriptions at two points in time, and blood pressure at the second point in time.</td>
<td>67.1% of patients received guidelines-compliant pharmacotherapy. 51% were at goal BP on visit 2.</td>
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<td>Beshir, Chee and Lo (2016)</td>
<td>AFib</td>
<td>192 patients, 51% male, diagnosed Afib, 29% under 65 years, 71% aged 65 or older, 64 Chinese, 25% Malay, 9% Indian, 2% other.</td>
<td>Tertiary hospital in Kuala Lumpur, Malaysia</td>
<td>Retrospective longitudinal cohort study. The clinical and demographic data of a cohort who started dabigatran were reviewed until date of death or on 31st December 2013. Those patients who discontinued dabigatran were further followed up until 31st December 2015 to determine the occurrence of any thromboembolic event.</td>
<td>26 (14 %) patients discontinued dabigatran therapy during a median follow-up period of 20 (range 3–45) months. About one-half of the discontinuation occurred within the first 6 months of dabigatran use. Patients who discontinued dabigatran received warfarin (38 %), antiplatelet agents (16 %) or no alternative antithrombotic therapy (46 %).</td>
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<td>Hanafi et al. (2015)</td>
<td>HT</td>
<td>1060 patients, 59.2% female, diagnosed HT, mean age 62.0 years, 30.5% Malay, 48.0% Chinese, 20.6% Indian, and 10.9% other.</td>
<td>University of Malaya Medical Centre, Malaysia</td>
<td>Retrospective longitudinal cohort study. A retrospective review of medical records was conducted on randomly selected patients with HT who had been followed up for at least 1 year in a primary care clinic. Continuity of care was determined via the ratio of patient visits to the usual provider to the total number of visits to all providers in 1 year. A score of 0 indicates no continuity and 1 perfect continuity.</td>
<td>A total of 72 doctors provided consultations (55 postgraduate family medicine trainees, 8 non-trainee doctors and 9 academic staff). The majority of patients were seen by postgraduate trainees (n = 795, 75%). The number of visits ranged from one to 13 with a mean of 3.85 (SD 1.36) visits. The majority of patients had a total of three visits in past 1 year (n = 352, 33.2%). A total of 144 patients (13.6%) had perfect personal continuity, with total visits ranging from 1 to 6. However, the mean continuity score was 0.43 (SD 0.34). There was no association between continuity and BP control.</td>
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<tr>
<td>Hasamnis et al. (2010)</td>
<td>HT and ISHD</td>
<td>54 patients with chronic diseases, including HT (70.37%) and ISHD (5.6%).</td>
<td>Households in Village Banggol, State Kedah, Malaysia</td>
<td>Cross sectional survey reported in letter to the editor. A three-day community-based drug utilization survey (completed by the head of households) was undertaken in 2008. Medicines for chronic illness present in the house at the time of interview were recorded.</td>
<td>The majority used WM (46, 85.2%). Two (3.7%) sought treatment from a traditional practitioner (Bomoh in local language) and the rest (6 patients, 11.1%) had discontinued or never commenced treatment.</td>
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## Quantitative studies

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<th>Author (year), reference</th>
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<td>Hassan et al. (2014)⁴⁴</td>
<td>HT</td>
<td>400 patients aged 25 or older, 51.5% female, diagnosed HT, 32.3% aged 55-64, 39.6% Malay, 36.0% Chinese, 24.5% Indian, 0.3% other.</td>
<td>Public tertiary hospital in Penang, Malaysia</td>
<td>Prospective cohort study. Drawing on medical records, patients were followed from their admission day until discharge.</td>
<td>Patients admitted for high BP were followed from admission to discharge at a public tertiary hospital, with BP readings taken at admission, day 1, and discharge. BP was controlled in 24% on admission and 54% upon discharge. Hypertension was poorly controlled among in-patients. BP control was better on discharge than on admission. The number of patients not on treatment decreased significantly to 1% upon discharge.</td>
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<td>Kassab et al. (2015)⁴⁵</td>
<td>ACS</td>
<td>190 patients (151 retained at follow-up) who had been discharged on a regimen of secondary preventive medications, 69.5% male, diagnosed ACS (58.4% USA, 21.1% NSTEMI, and 20.5% STEMI), mean age 59 years, 34.7% Malay, 38.9% Chinese, 26.3% Indian.</td>
<td>Cardiac clinics at Hospital Pulau Pinang, Malaysia</td>
<td>Prospective cross sectional study. A random sample of patients who had discharged on a regimen of secondary preventive medications were followed up over a three appointments at 8, 16, and 23 months post discharge. At each appointment, patients were interviewed and given a questionnaire to complete to compare their level of adherence to the prescribed regimens across the three consecutive time periods.</td>
<td>The majority of patients reported either medium (60.3%) or low (39.7%) adherence across the three time periods with none reporting high adherence. There was a significant downward trend in the level of adherence to cardio protective medications during the study period.</td>
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<td>Lee et al. (2013)⁴⁶</td>
<td>ACS</td>
<td>210 clinically stable patients who experienced ACS within a year prior to the study (50.0% diagnosed USA, 26.2% STEMI, 23.8% NSTEMI), 72.4% male, 51.4% 60 years or older, 48.6% younger than 60, 40.0% Malay, 34.8% Indian, 22.9% Chinese, and 2.4% other.</td>
<td>Cardiac clinic and wards of a large public tertiary teaching hospital in Kuala Lumpur, Malaysia</td>
<td>Cross-sectional survey using consecutive sampling. A questionnaire was administered in a clinical setting within one year of the ACS hospitalisation to measure patient adherence to cardiac-enhancing recommendations including medication taking, dietary modification, regular physical exercise, stress reduction, gathering social support, and not abusing substances.</td>
<td>Rates of recall of recommendation varied from 38.1% to 95.3%. The overall suboptimal adherence rate was 65.2%. In ascending order, adherence rates varied from 22.1% (use of relaxation techniques), 30.2% (regular exercise), 37.9% (cut down on stress), 48.3% (diet modification), 52.5% (gathering social support), 62.6% (taking prescribed medication), 68.3% (decreasing alcohol consumption), to 95.1% (carrying a medicine supply) across the six aspects of health recommendations. Those adhering to more than three aspects of the recommendations, smokers, and Malay patients had higher odds of suboptimal adherence.</td>
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<td>Opina (2008)⁴⁷</td>
<td>HT</td>
<td>187 hypertensive outpatients who had at least one anti-hypertensive prescribed for at least a month, 68% female, mean age 57 years. 94% of patients have comorbidity.</td>
<td>Primary care clinic at the Philippine General Hospital, Philippines</td>
<td>Cross-sectional survey examining the association between patient factors and adherence.</td>
<td>65% of subjects were adherent to prescribed anti-hypertensive medication in the week preceding the survey. 25% of patients were initially diagnosed as hypertensive by local health center personnel, 29% by a private practitioner and the rest by a government hospital physician. Most of them have been hypertensive for at least a year. Many patients were asymptomatic (43%) before the diagnosis. Among those with symptoms, dizziness was the most frequent presenting symptom. Of the symptomatic (n=107), 44 (41%) visited a health facility within hours, 15 (14%) within days, 11% within weeks, and 36% within months or years. 42% have been consulting Philippine General Hospital for less than a year, with a mean of 3.3 years, the longest at 34 years. Each patient usually had 2 to 3 medicines prescribed, commonly aspirin, anti-diabetes medication and lipid lowering agents. ACE-I were the most frequent type of anti-hypertensive prescribed. The most frequent non-pharmacologic treatment employed by the patients was low fat and low salt diet. Aside from the hospital, patients usually consult the local health centre for blood pressure monitoring.</td>
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<td>Ramli et al. (2010)⁴⁸</td>
<td>HT</td>
<td>400 hypertensive outpatients on pharmacological treatment for 1 year or less, 52.8% female, mean age 59.5 years.</td>
<td>Public primary care clinics in Selangor, Malaysia</td>
<td>Cross sectional survey to assess the prescribing pattern of antihypertensive medications. Appropriate prescribing of antihypertensive medication was based on current evidence and the 2008 recommendations by the Malaysian Clinical Practice Guidelines on the Management of Hypertension.</td>
<td>The prescribing pattern of antihypertensive agents was not in accordance with current evidence and guidelines. β-blockers and short-acting preparations were commonly used both as monotherapy and combination treatment. Thiazide diuretics, ACE inhibitors and long acting calcium channel blockers were underutilised.</td>
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<td>Reyes-Gibby &amp; Aday (2000)</td>
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<td>20</td>
<td>HT</td>
<td>336 residents aged 30 or older, 63% females, 23% screened in as hypertensive.</td>
<td>Households in rural area on Luzon island, Philippines</td>
<td>Cross sectional study using cluster sampling.</td>
<td>Of the 78 (23%) survey participants who were found to have HT, only 33 (42%) had been diagnosed prior to the survey by a physician. All of those diagnosed (33), and 4 additional participants, were on treatment (4 were self-medicating). However, control was very low: 17% of those discovered by the screening process to be hypertensive had controlled BP, and 35% of those on treatment and controlled their BP.</td>
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<td>Tong et al. (2012)</td>
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<td>34</td>
<td>HT</td>
<td>4076 patient records of adults aged 29 or older who were followed up for at least 1 year, 58.8% male, diagnosed HT, 62.1% Malay, 26.2% Indian, 10.9% Chinese, and 0.8% other.</td>
<td>Public and private primary care clinics, Malaysia</td>
<td>Cross sectional survey comparing the prescribing practices of the public and private systems.</td>
<td>Process of care and prescription of antihypertensive medications fell short of guidelines in both private and public clinics. The average number of antihypertensive medications used per patient was higher at the public than private clinics. Though rates of documentation of recommended clinical and laboratory assessments were poor in both settings, they were lower in public than private clinics. In public clinics, the most common group of medication prescribed was BB (56.2%), CCB (45.2%), ACE-I (31.5%) and DU (31.5%). In private clinics, BB were prescribed 40.2% of the time, followed by ARB (19.8%), DU (18.3%), CCB (17.0%) and ACE-I (13.0%). There were significantly more ARB and fixed-dose combination antihypertensive medications such as ARB/DU and BB/DU prescribed at private versus public clinics.</td>
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<td>Qualitative studies</td>
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<td>24 HT patients using home blood pressure monitoring.</td>
<td>Primary care clinics in urban areas of Petaling Jaya, Selangor, Malaysia</td>
<td>Thematic analysis informed by grounded theory, drawing on interviews and focus group discussions to explore the influence of self-initiated home blood pressure readings on primary care patients with hypertension. Purposive sampling.</td>
<td>Patients used home blood pressure readings as a tool for managing their HT, influencing their adherence to diet and exercise and providing reassurance while experiencing symptoms. Discussing readings with health care professionals enhanced the patient-physician relationship. The readings sometimes caused confusion and led patients to make medical decisions based on their own guidelines.</td>
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<td>Chai, Putit &amp; Siop (2016)</td>
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<td>18 patients with AMI who were stable and free of chest pain for at least 48 hours. 17 participants were male, mean age 47 years, 7 Chinese, 6 Malay, 4 Iban, and 1 Indian.</td>
<td>Coronary care unit, Sarawak Heart Centre, Malaysia</td>
<td>Descriptive thematic analysis of individual in-depth interviews to explore barriers amongst patients to seek care for AMI covering experiencing symptoms and seeking treatment at hospital.</td>
<td>Participants delayed seeking treatment as they felt uncertain whether their symptoms were serious enough to warrant treatment, as they were unfamiliar with them and believed they could bear them. Some patients persuaded themselves that their symptoms were not life threatening or would subside without treatment. Some patients did not want to seek treatment because of their work responsibilities, which provided income for the entire family. Some did not seek treatment due to a belief in fate; that if God decided that they should die, then there was nothing anyone could do to prevent this. Conversely, some patients believed that it was not their fate to die, and so no matter how intense their symptoms, they would survive. Some patients tried their own remedies such as drinking warm water, taking a bath, resting, applying topical ointment, getting a massage or taking Chinese herbs. Some who sought help at general practitioner clinics were misdiagnosed as suffering from gastritis and were prescribed inappropriate medication. Taking the medication and deciding whether it was working to relieve symptoms also caused a delay. On average, patients took 204 minutes to decide to seek care at hospital. Once this decision was made, it took an average of 24 minutes to arrive at the hospital.</td>
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<td>Lee et al. (2010)&lt;sup&gt;94&lt;/sup&gt;, HT</td>
<td>10 patients, 5 female, aged 40-56, either Malay, Chinese, or Indian, who 1) have been diagnosed with hypertension and been on medication for at least one year; 2) their main diagnosis is hypertension; 3) have been discharged from hospital; &amp; 4) clinically stable.</td>
<td>Medical clinic of Kuala Lumpur General Hospital, Malaysia</td>
<td>Semi-structured face-to-face interviews to understand and conceptualise experiences of persons on long-term antihypertensive treatment. Participants recruited via purposive sampling followed by theoretical sampling.</td>
<td>When participants were first diagnosed as having hypertension, they denied the fact and refused to take medication. They wanted to challenge and maintain their original self – a person without hypertension. Fear of death and disease complications caused some to decide to take medication after initial refusal. Nine out of ten patients were not totally adherent to medication, minimizing dosages, taking 'breaks' from medication, or using TCAM. They rationalised these modifications by the belief that they knew their body best.</td>
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<td>Lee et al. (2014)&lt;sup&gt;77&lt;/sup&gt;, HT</td>
<td>23 participants, 12 male, aged between 38 and 64, 9 Malay, 9 Chinese, and 5 Indian.</td>
<td>Ministry of Health community health clinic in Selangor, Malaysia</td>
<td>Content analysis drawing on in-depth semi-structured interviews, purposively selecting participants. A social constructivist epistemological position is adopted.</td>
<td>The majority of patients had a negative perception of WM. These participants reduced their WM, took TCAM instead or in addition to WM, alternated between WM and TCAM, and/or only took medication (including TCAM and WM) when their symptoms were elevated. Such self-adjustment of WM was not disclosed to GPs. Participants using TCAM typically used jelly gamat, ginseng, red yeast rice, spirulina, akar kayu, jamu, Herbalife, Chinese traditional herbs, and 'Teh Orang Kampung.' One participant engaged in Tai Chi to control HT. Those who had a positive perception of WM were largely adherent to prescribed medication.</td>
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<td>Lee et al. (2015)&lt;sup&gt;60&lt;/sup&gt;, HT</td>
<td>35 healthcare professionals (policy makers, doctors, pharmacists and nurses), 62.9% female, 45.7% aged 24-35 and 22.9% aged 36-45, 51.4% Malay, 22.9% Chinese, 20.0% Indian and 5.7% other.</td>
<td>University teaching hospital in Kuala Lumpur, Malaysia</td>
<td>Thematic analysis drawing on in-depth interviews (n=7) and FGDs (n=6), purposively sampling participants.</td>
<td>The Clinical Practice Guideline of HT management bears upon the treatment initiation and long term management of HT. Physicians perceived that patients resisted the initiation of treatment, which caused non-adherence to the guideline. The guideline stipulates that ACE-I must be prescribed before ARB, which was perceived as overly rigid by the physician participants. Combination drugs were not available (appropriate for non-adherent patients) due to lack of storage space and cost constraints. Policy-maker participants perceived that physicians often wanted greater power to prescribe novel drugs not routinely used in practice, which could not be accommodated due to budget constraints. Physicians often could not offer advice on diet and lifestyle factors within the context of a busy caseload.</td>
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<td>Ming et al. (2011)&lt;sup&gt;29&lt;/sup&gt; HF</td>
<td>20 HF patients, 15 male.</td>
<td>Penang General Hospital, Malaysia.</td>
<td>Thematic analysis drawing on semi-structured interviews, purposively sampled for ethnicity.</td>
<td>Patients perceived HF medications and limiting fluid intake as important factors to managing HF. There was less awareness of the importance of limiting sodium intake. Participants required clarification on ways to reduce sodium intake and improve adherence to lifelong medications and healthy diet. Individualized patient self-care, disease, and medication counselling may enhance adherence. Barriers to adherence included lack of communication with health care practitioners, misinformation on medications and HF, difficulty in remembering medications, complexity of regimens, and lack of noticeable HF symptoms.</td>
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### Qualitative studies

<table>
<thead>
<tr>
<th>Author (year), reference</th>
<th>CVD</th>
<th>Sample &amp; demographics</th>
<th>Setting &amp; country</th>
<th>Study design &amp; methodology</th>
<th>Description of pathway</th>
</tr>
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</table>
| Ramiro et al. (2000)
| HT, HTD, HLD | 502 residents, 60% female, aged 10 to 65. | Households in urban communities in Metro Manila, Philippines | Ethnography using content analysis purposively sampling participants by age, gender, socio-economic status, area, body size, smoking status, and health status, using semi-structured interviews, FGDs, narratives or storytelling, projective techniques such as drawings and free associations and photo descriptions. | The majority of respondents with hypertension found out about their condition from a doctor or nurse. Others suspected they had hypertension prior to seeing a medical professional because of headaches, palpitations, breathing difficulty, pain or numbness in the nape of neck and dizziness. HT was believed to lead to stroke, heart disease and kidney disease, and that it can paralyze and be fatal. Preventive measures for HT include eating less fat and salt, exercising, weight-watch, resting and sleeping well, praying, meditating, relaxing, and having a good philosophy in life. Aside from drugs, respondents with HT follow indigenous ways of controlling their condition such as consuming garlic, garlic with vinegar and tofu, garlic with apple and celery, garlic with honey, pito-pito (tea from seven types of leaves), ginseng tea, Vitamin C drinks, and bathing at night. |
| Shima, Farizah & Majid (2014) | HT | 25 patients, 56% female, diagnosed HT, mean age 49 years, 32% Malay, 28% Chinese, 28% Indian, 12% other. | Government primary care clinics in Hulu Langat and Klang, Malaysia | Thematic analysis drawing on in-depth semi-structured interviews, purposive sampling of non-adherent patients. | Participants experienced symptoms at first diagnosis, such as dizziness and headaches, as well as poor sleeping due to stress and overwork. Only 6 of the 25 participants were first diagnosed during a routine medical screening not specifically undergone to check for HT. The majority were diagnosed when they sought medical advice specifically for their symptoms. At diagnosis, patients and health care professionals agreed on treatment commencement, but then most participants did not adhere to antihypertensive medication or change their physical activity level or diet. Roughly half were referred to a dietician, but no follow-up was offered after the initial visit. |

### Mixed method studies

<table>
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<tr>
<th>Author (year), reference</th>
<th>CVD</th>
<th>Sample &amp; demographics</th>
<th>Setting &amp; country</th>
<th>Study design &amp; methodology</th>
<th>Description of pathway</th>
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<tbody>
<tr>
<td>Risso-Gill et al. (2015)</td>
<td>HT</td>
<td>73 respondents (12 Key informants, 24 health professionals, and 37 patients).</td>
<td>Urban and rural locations, Malaysia</td>
<td>Health systems assessment including document review and semi-structured interviews, purposive sampling.</td>
<td>Most patients with HT were diagnosed after presenting to a clinic with symptoms. Some are diagnosed at community health promotion sessions, though these patients rarely seek out a confirmation of the diagnosis after an initial high BP reading. Of those diagnosed at the clinic, due to patient denial of their condition, some do not return to the clinic for follow-up and end up in tertiary care after an acute event. Patients tend to visit multiple health care centres, sometimes switching between public and private, and Western and TCAM, impacting negatively upon continuity of care. Patient frequently supplement their HT medication with traditional or complementary medicine, using the latter to treat the side effects of the former. Some patients started taking TCAM when they felt that western medication was not working or they experienced side effects. Patients tend to stop coming in for follow-up once their BP is controlled, only to return later with dangerously high readings.</td>
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</table>

ACE-I = angiotensin-converting-enzyme inhibitor, ACS = acute coronary syndrome, AFib = atrial fibrilation, AMI = acute myocardial infarction, ARB = angiotensin II receptor blockers, BB = beta blockers, BP = blood pressure, CABG = coronary artery bypass graft, CCB = calcium channel blockers, CVD = cardiovascular disease, DBP = diastolic blood pressure, DI = diuretics, HCL = hypercholesterolaemia, HF = heart failure, HLD = hyperlipidaemia, HT = hypertension, IHD = Ischemic heart disease, LDL-C = low-density lipoprotein cholesterol, NSTEMI = Non-ST-elevation myocardial infarction, PCI = percutaneous coronary intervention, SBP = systolic blood pressure, STEMI = ST - elevation myocardial infarction, TCAM = traditional, complementary and alternative medicine, USA = unstable angina, WM = western medicine
pressure in their homes. An ethnographic study in the Philippines explored health beliefs that may delay seeking care. Hypertension was viewed as “blood that had gone to the head,” associated with menstruation or menopause among women, and stress, gambling losses, or difficulties at work among men. While the majority of participants recognized the role of prescribed drugs in treatment, almost as many placed their faith in the power of prayer, a balanced diet, and food such as garlic.

**Treatment initiation.** As noted above, most studies included patients who had attended clinics where they were diagnosed, with treatment initiated at the time or soon after. One Malaysian study reported that when HT was detected at a community outreach event, few are actually followed up. Qualitative studies in Malaysia reported patients who declined treatment, which the authors attributed to being in denial of or being confused about treatment, although some overcame denial when faced with adverse health implications. Studies in both countries reported patient concerns about the cost of lifelong treatment and side effects. In particular, some were concerned that they might become dependent on medication, or suspected that prolonged use of medication might harm them, concerns often perpetuated by family members and friends of patients. This points to a failure of communication of the nature of HT and its treatment creating an intention barrier. The complexity of medication regimes and reluctance to adopt a ‘hypertensive’ label created capability and intention barriers to adherence respectively. Healthcare barriers related mainly to the doctor-patient relationship and, with patients expecting more information from their doctors about HT and medication use.

**Long term management.** Common themes in many of the papers include frequent discontinuation or changes in treatment, self-management, combined use of western medicine (WM) and traditional and complementary medicine (TCAM), and uneven adherence by health professionals to treatment guidelines. Adherence to medication was variable but often poor, although it is not meaningful to calculate summary measures as the samples differed regarding inclusion criteria and measurement of adherence.

One Malaysian study examined continuity of care. Most patients attended a clinic three times per year but this varied from 1 to 13. Only 13% saw the same doctor each time. A cluster of qualitative studies on choices for treating HT reported widespread patient self-management, in terms of drug types and dosages.

Several Malaysian studies examined the use of traditional medicines. One, using mixed methods, including interviews with health workers and patients, concluded that use of TCAM, either to supplement or replace WM, was common. This view was supported in two further studies, one comprising in-depth interviews with 10 patients in a university clinic and another in a community clinic. In both, many patients rejected WM, at least initially, reducing their prescribed dosage of western drugs and taking TCAM instead or in addition to the western ones, and/or taking medication (both TCAM and WM) only when symptoms were evident. They justified this practice by asserting they ‘knew their body the best’ or that the body needs to ‘take a break’ from medications. However, another study, in a Malay village, found that almost all patients taking treatment for HT used WM, with fewer than 5% attending traditional practitioners. Thus, it is plausible that there is considerable variation within the country.

Though HT requires long-term monitoring, attendance at follow-up appointments was low. Some patients in both countries visited multiple clinics, switching between public and private facilities. Among patients who initially attended follow-up visits, attendance often decreased over time, with some patients eventually presenting with dangerously high blood pressure readings. One Malaysian study, following patients with HT over a year, reported that only 13.6% always saw the same health professional, but this was undertaken in a university clinic that would be expected to have a high turnover of junior staff.

The advent of automated sphygmomanometers has made it possible for patients to monitor their blood pressure at home. One Malaysian study found mixed effects, leading some participants to become more engaged in HT management (improving adherence), but others to became confused about their treatment. Some participants used the readings to adjust their medications, stopping or decreasing medication if readings were low. While unable to find associations between patient satisfaction and clinical outcomes, one study nonetheless suggests that satisfied patients are more likely to follow physician advice.

A cluster of four studies assessed professional adherence to published HT treatment guidelines in Malaysia. One found that prescribing of antihypertensive agents in primary care clinics was largely inconsistent with current guidelines, with some treatments under-utilized. Medication costs, a shortage of storage space for medications, and a lack of time to discuss diet and lifestyle were identified as barriers to guideline adherence, with one study finding that only two-thirds of Malaysian patients with HT received guideline-compliant pharmacotherapy. One survey found that the care provided in both public and private clinics in Malaysia, including prescription of antihypertensive medications, failed to meet standards set out in guidelines though adherence was worse in public clinics. Barriers include the failure by health professionals to motivate patients to attend follow up, a lack of patient trust in their doctor, and long distances between patients and clinics.

**Other conditions**

While most of the literature focused on HT, a few studies examined care pathways for other CVDs or conditions. Even as we recognize that it is unreasonable to draw firm conclusions from so few studies, we have included them in the interest of completeness.
Initial presentation. One qualitative study examined delays in seeking care by patients with acute myocardial infarction (AMI) in Malaysia. On average, patients took 204 minutes to decide to seek care at hospital after experiencing AMI symptoms. Delays were due to uncertainty over where to seek help, whether symptoms justified medical attention, and denial, with patients persuading themselves that symptoms were controllable and non-life threatening. These factors constitute both capability (individuals were not able to recognize the severity of their condition) and intention barriers (a sense of obligations to employers or family prevented them seeking care).

Long term management. Most studies of maintenance treatment addressed hypertension but one cohort study reported that 14% of Malaysian patients with atrial fibrillation discontinued dabigatran (an anticoagulant) by 20 months following commencement of therapy, with about a half discontinuing within the first 6 months of treatment. 38% transferred to warfarin and 16% to antiplatelet agents but 46% were on no therapy.

Three articles from Malaysia examined management following acute coronary syndrome/myocardial infarction. Follow-up ranged from 1 year to 23 months after discharge. 83.6% of 525 patients admitted to 17 Malaysian hospitals with unstable angina or non-ST elevation myocardial infarction (NSTEMI) were managed medically. Three-quarters of those managed surgically had percutaneous coronary interventions (PCI), 14% had angiograms only, and the remainder had coronary bypass grafting.

While one study reported high adherence to secondary prevention medication, the others showed downward trends over time. One of those studies reported much greater adherence to regimens that included medications (95.1%) than one that only involved relaxation techniques (22.1%).

One Malaysian study examined capability barriers to effective treatment of patients with heart failure, based on a small sample of inpatients. These patients had some knowledge of how to manage their conditions, in particular the importance of medication and limiting fluid intake as important to managing heart failure, there was less awareness of advice on limiting sodium. Intention barriers arose from lack of communication with health care practitioners, difficulty in remembering medications, complexity of regimens, and lack of noticeable symptoms.

Discussion

Despite the growing burden of CVD in Malaysia and the Philippines, as well as in Southeast Asia as a whole, we found relatively few papers that described the pathways to effective treatment and follow up for patients with CVD (n=21), and most of them are from Malaysia. They typically examine discrete stages in the pathway (e.g. entry or start of medication), providing an incomplete picture of the patient journey. Few consider how the health system might facilitate the patient’s journey or how it might take account of their social context, as well as local, cultural conceptions of illness. There are few qualitative or mixed methods studies that could aid interpretation of behavior of patients and providers. Many papers are descriptive and do not seek to conceptualize the different steps on the patient pathway.

The vast majority of the research is on hypertension, with very little on pathways to care and subsequent management of acute coronary syndrome or other cardiovascular conditions. Barriers identified in both Malaysia and the Philippines involve all three of the categories described by Khatib et al., intention, capability, and health system. They challenge a simplistic view that financial constraints are the sole barrier for healthcare. They also highlight the challenges of managing conditions that are lifelong and asymptomatic, for instance, the view that they require treatment only when they have symptoms and that the ‘body needs rest’ from medicines (capability barriers), and forgetfulness that is inherent to diseases that require daily medication for long, if not indefinite, periods of time. More in-depth longitudinal studies with a qualitative component are needed to understand the nuances of how patients’ socio-cultural contexts interact with healthcare services or healthcare system components in the pathway. The influence of TCAM, foregrounded in some of the Malaysian studies, also needs further exploration.

The lack of studies that span the entire patient pathway, or that addresses issues beyond the health system, reflect a limited conceptualization of “patient pathways.” To understand why interventions for effective management of HT work, for instance, it would be useful to know how patients’ wider social and material contexts contribute to success or failure to progress along these pathways. Patient pathways should be examined over time and space to truly capture their dynamic nature and should be examined alongside other aspects of their life such as routes out of employment due to illness, family dynamics after diagnosis, and local beliefs about disease. Qualitative investigation can help to capture how wider social and material dimensions facilitate or hinder HT control but it should include a longitudinal component to capture pathways in the long-term and engage with the experiences and voices of those affected by CVD. This can then be related and used to complement existing literature in the Asia Pacific region that, while likewise inadequate in characterizing patient pathways, generally reports adequate knowledge of CVDs among patients, but nonetheless identifies various patient-related motivation barriers including ‘low desire’, ‘ambivalence’, and a sense of lack of urgency, as well as health care system barriers including the failure of doctors to motivate their patients and the ‘cynicism’ among health care providers with long term management.
their conditions. We would encourage those in other countries, many also facing challenges in delivering proven interventions to their population, to ensure that what information does exist on the management of cardiovascular (and other) diseases in their populations are brought together to inform future research and policy. We hope that our conceptualization of the patient pathway and the identification of barriers as relating to intention or capability of patients and providers and the health system will be useful in these endeavors.

Conclusion
Cardiovascular diseases are the leading contributor to the burden of disease in South East Asia. Studies on CVD patient pathways in South East Asia are critical in order to understand and lessen the burden. The literature we have identified reveal important gaps in our understanding of the entire patient pathway. Additional research is especially needed in the Philippines, using longitudinal mixed methods approaches. One such initiative is the ‘Responsive and Equitable Health Systems – Partnership on Non-communicable Diseases’ (RESPOND) Study, currently underway in both countries, is doing this.

Data availability
Underlying data
All data underlying the results are available as part of the article and no additional source data are required.

Extended data

This project contains the following extended data:
- Detailed Malaysia Medline search strategy;
- Quality assessment of included articles.

Reporting guidelines

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

References


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Sandra C Thompson

Western Australian Centre for Rural Health, School of Population and Global Health, University of Western Australia, Crawley, WA, Australia

Thanks for the opportunity to review this systematic review looking at cardiovascular disease pathways in Malaysia and the Philippines. The issue is an important one and the authors have described the rationale for the review – that is, to inform a study on barriers to effective care. The review is well conceived, thorough and seems well executed. It is nicely written and I am pleased to see it published. The points below are largely minor considerations.

The authors have not registered their review protocol though it seems unlikely that others would be concurrently undertaking a review on this topic.

Critical to a systematic review are details of the search strategy. Some information (an example of the search) is available in Supplemental data 1, the detailed search strategy for Ovid Medline for Malaysia only. This was not stated as having been replicated for the Philippines, but it is presumed that the identical approach was used also for the Philippines and modified as necessary for the other databases which were reported. However, this information should be stated with the reference to Supplemental data 1 referring to it as an example. Supplemental files would not normally be listed as a reference in the article (ref 15) as they are part of the article. This should be removed as a reference.

The concept of a patient pathway is challenging in terms of identifying relevant terms for a search strategy. The terms used and approach seem to be appropriate, although I did wonder about whether terms such as integrated care, transfer of care, models of care, patient journey could have yielded relevant additional papers. The description of the pathway as reported in Table 1 seems primarily seems to describe compliance with evidence-based recommendations (compliance is another term not included in the search). The report of Ramiro et al seems to report on beliefs about the disease which is important to shaping patient experiences and willingness to take up care and recommended treatments (health literacy and care seeking were not included as relevant search terms). I would not necessarily have thought of this as part of the
care pathway but in fact, care seeking is relevant. Why is cardiac rehabilitation not part of the care pathway? This highlights the challenge of looking for papers that describe the care pathway overall; there are papers that look at components of the care pathway. Ultimately the conclusion of the review about the dearth of studies that have examined the whole pathway is very likely to be correct.

It may be helpful if there was a figure summarising the conceptual model of the pathway to care using the model of Khatib and colleagues (and Michie et al). This could then also identify where the relevant research has been undertaken and where there are gaps in the different parts of the pathway. While this information is in the text, there could be value in presenting what is known and highlighting the gaps through synthesis into a figure.

The authors have included quite detailed information on each of the studies included in the review. These are reported by the methodological approach of the study and then in alphabetical order by the first author. This means that studies of different types of CVD and setting including country are not grouped. There may be more meaningful groupings of condition or setting even within the current headings used in the table. Perhaps even more useful to a reader with an interest in the status of knowledge of CVD in these two countries would be the presentation with a summary matrix which simplifies limited relevant information related to the nature of the study – e.g. CVD condition, country, setting, nature of study. This comment is made for consideration – it is not essential as there are many ways in which the data could be presented.

It is evident that for all the elements of access, education and care/treatment, resourcing is a major issue. Some assessment of where effort needs to be prioritised for investment should be a conclusion of the review, even though all areas of patient intention, capability and health system are considered to need attention. Is there a conclusion from the review that suggests where focus is most needed?

**Are the rationale for, and objectives of, the Systematic Review clearly stated?**
Yes

**Are sufficient details of the methods and analysis provided to allow replication by others?**
Yes

**Is the statistical analysis and its interpretation appropriate?**
Not applicable

**Are the conclusions drawn adequately supported by the results presented in the review?**
Yes

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* Public health, health services, chronic diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.