Annex 18A. Systematic Review Methods and Complete Search Results

Systematic literature review method

Information Sources and Search Strategy

Two chapter authors (EL and AEM) designed an electronic search of MEDLINE and EMBASE electronic databases for the purpose of capturing published reports of vascular disease care quality improvement studies carried out in low- and middle-income countries (LMICs) and published in English between January 2000 and June 2014. Pertinent conditions selected for the search were myocardial infarction, acute coronary syndrome, hypertension, cardiovascular disease, diabetes, stroke, cerebrovascular disease, obesity, heart failure, and rheumatic heart disease. Based on key words identified in an informal review of publications already known to the authors and a survey of the other chapter authors, a second set of search terms related to quality improvement was identified (tables 18A.2 and 18A.3). Study designs were limited to controlled clinical trials, comparison studies, systematic reviews, and meta-analyses. Studies were limited to those published in peer-reviewed journals or in reports from institutes with rigorous internal reviews. The electronic search was refined and structured by a research librarian. Search results were considered valid if all of five key papers identified a priori by the chapter authors were retrieved by the electronic search[1-5]. The review adhered to PRISMA recommendations for the conduct and reporting of systematic reviews (table 18A.1).

Eligibility Criteria and Study Selection

Two authors (EL and AEM) independently assessed identified studies for eligibility based on the title and abstract. Selected full text papers were then independently reviewed by both authors. Eligibility criteria included: 1) LMIC setting; 2) patient/provider or system level intervention aimed at improving vascular disease quality of care; 3) outcome included risk factor or disease screening, case-finding, clinic-based vascular disease prevention (medication adherence, clinic visits, vital signs, laboratory results, mortality), behavioral changes (diet or exercise), improved access to medical care, or clinical guideline implementation; and 4) study design involved a comparison between a clinical quality improvement intervention and usual care, regardless of whether the intervention group served as its own control ("before and after" study) or a separate control group was used.

Data Collection/Data Items/Summary Measures

Data were abstracted and each study was categorized into one or more quadrants of the chapter rubric (Figure 18A.1). The following information was extracted from each study: study characteristics (setting, targeted disease, study design, participant number and baseline characteristics), type of intervention, observation interval, and outcome measures. The main summary measures were differences in means, proportions of the outcome, and outcome risk reduction. Three study types were

observed most frequently and were therefore identified for potential pooling in a quantitative analysis: task-shifting in hypertension control, mobile health in diabetes management, and ACS clinical pathway interventions. Four out of eight task-shifting hypertension control studies did not report variance around the most common main effect estimate—systolic blood pressure (SBP) change[6-13]. Only three out of six studies analyzing mobile health in diabetes management reported variance around mean hemoglobin A1c (HbA1c) change[14-19]. Too few studies reported on changes in fasting plasma glucose or percent adherence to medications. ACS clinical pathways studies did not consistently report on the same quality improvement metrics[1, 3, 20]. Because of heterogeneity of outcomes and lack of reporting on measures of dispersion about main effect estimates (variance), the authors were unable to per- form a quantitative analysis.

Study Selection and Characteristics

The search yielded 847 unique references and all five key papers identified a priori were captured. Based on a review of titles and abstracts, 273 potentially eligible papers were identified. Of these, two authors (EL and AEM) concurred that 49 papers reported population-based studies with clinically meaningful outcomes. The papers were selected for the detailed review (Figure 18A.2).

Table 18A.1. PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Eligibility criteria/Study selection
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Information sources
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Eligibility criteria/Study selection
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Data collection/Data Items/Summary Means
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Data collection/Data Items/Summary Means
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Data collection/Data Items/Summary Means
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Study selection/Characteristics
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Study selection/Characteristics
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Results, Tables 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Conclusion, Figure 4
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Conclusions
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Funding

Figure 18A.1. Quality conceptual framework for vascular diseases, the DCP3

	Acute phase	**Chronic phase**
Health system level	**Examples of system level/acute phase:** • Strategically locate hospitals in order to reduce treatment delays • Improve provider skills to deliver high quality care. Provide salary support for health care providers • Improve access to revascularization services • Improve transportation to hospital • Improve population awareness of acute symptoms and means to access acute care • Formulate and disseminate clinical practice guidelines and standards	**Examples of system level/chronic phase:** • Formulate and disseminate clinical practice guidelines and standards • Improve access to health care and medicines • Training of health care providers • Financial support for quality improvement • Infrastructure improvements: health care facilities; electronic and telephonic communications
Patient-provider level	**Examples of patient/provider-acute phase:** • Implement clinical practice guidelines using clinical pathways algorithms • Improve hospital discharge planning and transition to chronic care	**Examples of patient/provider-chronic phase:** • Provider and patient education • Implement clinical practice guidelines • Improve risk factor monitoring • Improve treatment adherence

Annex Figure 18A.2. Flow diagram describing the systematic literature review process

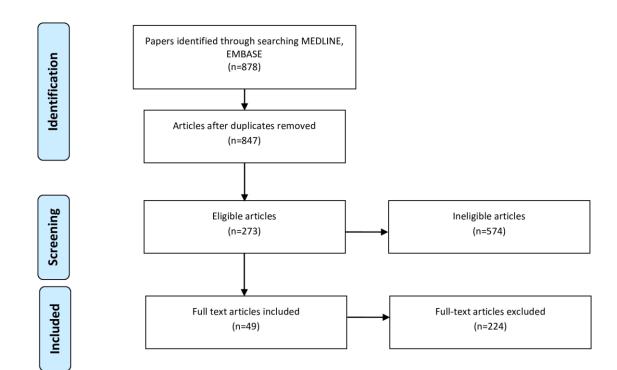**Table 18A.2**. Search terms on Pubmed (June 9, 2014)

Disease		Search Terms
Vascular disease		#1: "Vascular disease*" OR "vascular disorder*" OR "vascular risk*" OR "coronary syndrome" OR " hypertension" OR " cardiovascular disease*" OR "heart disease*" OR diabetes OR diabetic OR stroke OR "cerebrovascular disease" OR obesity OR overweight OR " heart failure" OR "rheumatic heart disease*" OR asthma*" OR "myocardial infarction" OR "Myocardial Infarction"[Mesh]) OR "Acute Coronary Syndrome"[Mesh]) OR "Hypertension"[Mesh]) OR "Diabetes Mellitus"[Mesh]) OR "Stroke"[Mesh]) OR "Obesity"[Mesh]) OR "Heart Failure"[Mesh]) OR "Rheumatic Heart Disease"[Mesh]
Quality improvement intervention	AND	#2: ("Critical Pathways"[Mesh]) OR "Quality of Health Care"[Mesh]) OR "Health Planning Guidelines"[Mesh]) OR "Outcome and Process Assessment (Health Care)"[Mesh]) OR "Healthcare Financing"[Mesh]) OR "Reimbursement, Incentive"[Mesh]) OR "Insurance, Health"[Mesh]) OR "Medication Adherence"[Mesh]) OR "Patient Preference"[Mesh] exp Health Promotion/ OR "Patient Participation" [Mesh] OR " Patient Compliance" [Mesh] OR "clinical pathway*" OR "quality improvement*" OR guideline* OR "task shifting" OR "mobile technology" OR "social franchising" OR "clinical decision support" OR " pay for performance" OR " payment reform*" OR " performance based financing" OR " results based financing " OR "clinical benchmark*" OR " health insurance" OR adherence
Country	AND	#3: exp developing countries/ OR developing countr* OR "low and middle income countries" OR (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brazil or Bulgaria or "Burkina Faso" or "Burkina Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central African Republic" or Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic") OR (Macedonia or Madagascar or "Malagasy Republic" or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or "Marshall Islands" or Mauritania or Mauritius or "Agalega Islands" or Mexico or Micronesia or "Middle East" or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or

		Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or "Netherlands Antilles" or "New Caledonia" or Nicaragua or Niger or Nigeria or "Northern Mariana Islands" or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or "Puerto Rico") OR (Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts" or "St Kitts" or Nevis or "Saint Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or Samoa or "Samoan Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka" or Ceylon or "Solomon Islands" or Somalia or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania or Thailand or Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia)
Type of study	AND	#4: randomized controlled trial OR controlled clinical trial OR randomized controlled trials OR random allocation OR double-blind method OR single-blind method OR clinical trial OR exp clinical trials OR (clinical trial*) OR ((singl* or doubl* or trebl* or tripl*) AND (mask* or blind*)) OR placebos OR placebo* OR random* OR comparative study OR exp evaluation studies OR follow-up studies OR prospective studies OR (control* or prospective* or volunteer*) OR cross-over studies OR systematic review OR meta-analysis OR metaanalysis OR ("meta-analysis as topic"[MeSH Terms]
Search Results		687 hits

Table18A.3. Search terms on EMBASE (June 9, 2014)

Disease		Search Terms
Vascular disease		cardiovascular disease or vascular disease OR vascular disorder* OR "coronary syndrome" or heart muscle ischemia OR hypertension OR ischemic heart disease or stroke or heart disease* OR hypertension OR diabetes or diabetes mellitus OR (obesity or overweight) OR asthma or asthma*
Quality improvement intervention	AND	critical pathways or clinical pathway OR clinical pathway OR quality of health care or health care quality OR health care planning OR (outcome and process assessment) OR health care financing OR health incentives or health insurance OR medication adherence or medication compliance OR task shifting OR mobile phone/ or mobile technology OR clinical benchmark OR pay for performance OR financial incentive*
Country	AND	developing countries or developing country OR low and middle income countries OR LMIC OR (asia or africa or south america or oceania or latin america) OR (asia or africa or (south and america) or oceania or (latin and america)) OR (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brazil or Bulgaria or "Burkina Faso" or "Burkina Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central African Republic" or Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic") OR (Djibouti or "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or "East Timur" or "Timor Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or Eritrea or Estonia or Ethiopia or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or Georgia or Georgian or Ghana or "Gold Coast" or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or "Isle of Man" or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania) OR (Macedonia or Madagascar or

"Malagasy Republic" or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or "Marshall Islands" or Mauritania or Mauritius or "Agalega Islands" or Mexico or Micronesia or "Middle East" or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or "Netherlands Antilles" or "New Caledonia" or Nicaragua or Niger or Nigeria or "Northern Mariana Islands" or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or "Puerto Rico") OR (Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts" or "St Kitts" or Nevis or "Saint Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or Samoa or "Samoan Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka" or Ceylon or "Solomon Islands" or Somalia or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania or Thailand or Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia)

Type of study	randomized controlled trial OR controlled clinical trial or controlled clinical trial OR random allocation or randomization OR double-blind* OR "systematic review" or "systematic review*" OR (metaanalysis or meta-analysis)
Search results	191 hits

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