

The economic burden of non-communicable diseases (NCDs) in low- and middle-income countries (LMICs): a systematic review

Study protocol version 2.3

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December 2013

Table of contents

1. Background	3
2. Objectives.....	4
3. Methods	5
3.1. Definitions.....	5
3.2. Study eligibility	6
3.3. Data sources.....	6
3.4. Search strategy	7
3.5. Study selection	7
3.6. Data extraction	8
3.7. Quality appraisal	8
3.8. Presentation and synthesis of results	9
4. References	10
Appendix 1. The World Bank list of low- and middle-income countries	11
Appendix 2. Search strategies for the included databases.....	12
Appendix 3. Proposed quality assessment tool for the studies included in the systematic review.....	36
Appendix 4. Shell tables for presenting the economic findings	38

1. Background

The Global Burden of Disease Study 2010 estimated that non-communicable diseases (NCDs) account for 54% of disability-adjusted life years (DALYs) worldwide [1]. This confirmed the trends identified in previous updates of the study which suggested a shift in global disease burden from communicable diseases to NCDs [2]. Ischemic heart disease is currently the major cause of disability worldwide; stroke, low back pain and chronic obstructive pulmonary disease (COPD) are also in top 10 [1].

Evidence suggests that NCDs have a substantial global impact both on years of life lost (YLL) and on years of life lived with disability (YLDs). Eight of the ten major causes of YLDs are NCDs, with low back pain and depression particularly prominent [3]. Furthermore, ischemic heart disease and stroke are the first and third, respectively, global causes of YLLs [4].

Available data indicate a disproportionately larger impact of NCDs in low- and middle-income countries (LMICs) compared to high-income countries (HICs) [5]. For example, the age-standardised death rates due to NCDs are much higher in LMICs than in HICs [6]. Furthermore, in Sub-Saharan Africa half of cardiovascular deaths occur in the 30-69 age group, at least ten years earlier than in HICs [7].

Disability caused by NCDs has economic consequences at multiple levels: individual, household, economic agents, public institutions, government and the society as a whole. It has been estimated that the global economic burden of NCDs in the 2010-2030 interval amounts to 75% of the global GDP in 2010 [8]. Not only is this burden expected to increase throughout this time horizon, but LMICs will have an increasing share of this burden due to population growth, ageing and globalization. In addition, the economic consequences of NCDs on households, health systems and national incomes in developing countries may jeopardise the ongoing poverty reduction initiatives [9].

Several economic modelling studies provided approximate estimates on the economic burden of NCDs in LMICs [10, 11]. However, these studies were informed by selective literature reviews. It has also been pointed out that substantial research effort and funding must be directed towards generating evidence on the burden of NCDs in LMICs, as the existing data appears to be insufficient and of questionable quality [12]. To our knowledge, no comprehensive review on the topic is available.

These facts point towards the necessity of systematically reviewing the existing evidence on the economic impact of NCDs in LMICs. Its findings would inform the formulation of policy and research objectives in this field and would also provide robust data for future economic modelling exercises.

2. Objectives

The aim of this systematic review is to synthesize the available information on the economic impact of major NCDs in low- and middle-income countries (LMICs).

The specific objectives are as follows:

1. Identify and summarize the findings of existing studies which provide monetary estimates of the household and societal impact of NCDs in LMICs.
2. Describe the array of methodological approaches which have been used to measure the economic burden of NCDs in LMICs.
3. Assess the methodological quality and policy relevance of existing studies.
4. Identify knowledge gaps in the existing body of literature and formulate directions for future research.
5. Inform future policy initiatives, research programs and funding for NCDs.

3. Methods

3.1. Definitions

The following definitions were used to operationalise the objectives of the review:

- **Economic burden:** the economic burden of disease refers to the economic consequences that the presence of disease and its outcomes exert on individuals and society as a whole. Cost-of-illness studies provide an assessment of economic burden by measuring and valuing the resources foregone in relation to the diseases under scrutiny. The cost-of-illness methodology has been described in detail elsewhere [13, 14].

Cost-of-illness studies measure direct and indirect costs:

- Direct costs refer to the opportunity cost of resources deployed for the prevention, detection and treatment of the disease; these include medical and non-medical costs.
- Indirect costs refer to the value of resources lost due to the presence of disease; they usually include valuations of lost productivity due to morbidity and mortality.

The WHO guidance on assessing the economic impact of disease and injury expanded the cost-of-illness framework and distinguished between microeconomic and macroeconomic studies based on the level at which economic information is aggregated[15]. The microeconomic approach measures consequences of ill-health at a particular level in the society e.g. individual, households, firms or the government and focus on evaluating variations in metrics such as consumption, productivity or expenditure. On the other hand, macroeconomic approaches measure the impact on society as a whole and focus on metrics such as growth rate and social welfare.

- **Non-communicable diseases:** for the purpose of the 2008 Global Burden of Disease update study, WHO identified NCDs as 'Group II' diseases which include the following conditions/causes of death: neoplasms, diabetes mellitus, endocrine disorders, neuropsychiatric disorders, sense organ disorders (glaucoma, cataract, refractive errors, hearing loss, macular degeneration and others), cardiovascular diseases, respiratory diseases (COPD, asthma and others), digestive diseases (peptic ulcer, cirrhosis of the liver, appendicitis and others), genitourinary diseases, skin diseases, musculoskeletal diseases, congenital anomalies and oral conditions (dental caries, periodontal disease and others) [2].

- Low- and middle-income countries: 139 LMICs were identified based on the World Bank income classification of countries: 36 low-income, 48 lower-middle-income and 55 upper-middle-income countries (Appendix 1).

In light of these conceptual delimitations, this systematic review aims to identify cost-of-illness studies which are relevant to LMICs and focus on the seven NCD categories associated with the largest global burden according to the 2010 Global Burden of Disease study (%DALYs): cardiovascular diseases (11.8% DALYs), neoplasms (7.6% DALYs), mental disorders (7.4% DALYs), musculoskeletal diseases (6.8% DALYs), chronic respiratory diseases (4.7% DALYs), neurologic disorders (3% DALYs) and diabetes mellitus (1.9% DALYs) [1].

3.2. Study eligibility

Inclusion criteria:

- original studies using primary or secondary data to produce economic estimates of the impact of NCDs;
- study designs: observational (e.g. cohort studies) with a cost collection component; cost-of-illness; economic modelling.
- studies published after 1990 (inclusive);
- population: all population categories;
- outcome: any economic outcome;
- setting: one or more LMICs as defined above. Multi-country studies referring to a mix of LMICs and high-income countries will be included only subject to providing explicit and detailed economic estimates for the considered LMICs.

The elements of the research question are presented in PICOS format below:

Population – all population categories;

Intervention – exposure to NCDs as defined in section 3.1 above;

Comparator – not applicable;

Outcomes – any economic outcome related to the prevention, diagnosis, management and consequences of NCDs;

Setting – one or more LMICs as defined in section 3.1 above.

3.3. Data sources

The following electronic databases will be searched: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations (Ovid); EMBASE; NHS Economic Evaluation Database (NHSEED); EconLit; Cochrane Central Register of Controlled Trials (CENTRAL); Cochrane Database of Abstracts of Reviews of Effects (DARE); PsycInfo (Ovid); Latin American and Caribbean Health Sciences Literature database (LILACS); MedCarib; Africa-Wide Information; Global Health; Index Medicus for the South-East Region (IMSER); Index Medicus for the

Eastern Mediterranean Region (IMSEAR); Western Pacific Region Index Medicus (WPRIM); Open Grey (INIST); New York Academy of Medicine Grey Literature Report.

All databases will be searched from 1990 to present day.

In addition, the websites of relevant public and private organisations will be searched for publications in connection with the review's objectives. The list of such organisations includes, but is not limited to: World Health Organization; The World Bank; World Economic Forum; and NCD Alliance.

3.4. Search strategy

The generic search strategy will combine three groups of search terms, pertaining to the following conceptual areas: 1) NCDs; 2) LMICs; and 3) economic burden.

1) The search terms will include the seven individual disease categories (cardiovascular disease, neoplasms, mental health, musculoskeletal disease, respiratory disease, neurologic disease and diabetes), adapted to each database.

2) The LMIC names will be entered individually together with generic terms such as 'low-income' and 'middle-income'.

3) Relevant search terms for economic burden were identified by reviewing previously published systematic review of cost of illness studies. The following generic search terms were identified: burden of illness; cost of illness; health expenditure; costs and cost analysis; absenteeism; productivity loss; poverty; income; economic modelling; economic burden; resource utilization; employment; labour.

There are indications that the search terms "costs", "cost analysis" and "health expenditures" yield a large number of records which are not cost-of-illness studies [16].

The detailed search strategies for each database are presented in Appendix 2. Language filters will not be applied. Commentaries, editorials and letters will be excluded where the online databases allow it.

3.5. Study selection

Study selection will follow a three-stage process:

1. In Stage 1, two independent reviewers will perform title & abstract screening and exclude the irrelevant studies. Disagreements will be discussed and resolved consensually. If necessary, the opinion of a third reviewer will be elicited.
2. In Stage 2, two independent reviewers will screen the full-text articles against the inclusion/exclusion criteria and exclude them appropriately while documenting the rationale for exclusion. The reviewers' agreement will be assessed using Cohen's kappa.

Disagreements will be discussed and resolved consensually. If necessary, the opinion of a third reviewer will be elicited.

3. In Stage 3, forward and backward reference list searches will be performed on the remaining studies to identify any other relevant publications.

The remaining studies at the end of Stage 2 and any studies identified in Stage 3 will be included in the review.

3.6. Data extraction

The following minimum information will be extracted from the included studies: year; authors; title; country(ies); setting and any relevant contextual information; scope (institutional; regional; national; international); disease area(s); perspective (microeconomic/macro-economic); type of study design; population characteristics; study design characteristics; study duration/time horizon; type(s) of economic estimates reported; actual economic estimates, by cost component; data sources; confounding factors; and risk of bias assessment (see section **3.6 Quality appraisal** below).

A data extraction template will be developed and piloted on a randomly selected sample of four included studies; feedback from the piloting exercise will inform the final version of the data extraction tool. Two independent reviewers will perform data extraction and compare their outputs. Disagreements will be resolved by consensus. If necessary, the opinion of a third reviewer will be elicited.

All cost data reported as US\$ will be converted to US\$ 2012 using the appropriate consumer price index. If the costing reference year is not reported in the publication, it will be assumed to be the year before publication year. All cost data reported in any other currency than US\$ will first be converted to 2012 values using the local consumer price index; then converted to US\$2012 using the appropriate 2012 average purchasing power parity index (World Bank).

When available, economic outcomes reported as a relative measure e.g. % of GDP, will also be extracted. No adjustments will be made to such outcomes.

3.7. Quality appraisal

The quality appraisal of the included studies will focus on two aspects: the design of the economic study; and, if applicable, the design of the clinical study alongside which the economic study was conducted.

We have no knowledge of a methodological quality checklist for cost-of-illness studies. Nevertheless, previous reviews adapted checklists for economic evaluation studies such as the one proposed by Drummond and Jefferson[17]. The most recently published economic evaluation checklist is the CHEERS (Consolidated Health Economic Evaluation Reporting Standards) Statement[18].

A quality assessment tool has been developed for the purpose of this study (Appendix 3). The tool will be piloted on a sample of ten included studies after Stage 2 of Study selection and adjusted accordingly.

3.8. Presentation and synthesis of results

The following information will be abstracted, aggregated (where appropriate) and tabulated:

- Characteristics of the included studies;
- Economic burden estimates, by cost component, disease category, perspective (microeconomic/macroeconomic) and geographical location (where appropriate). Ranges (minimum-maximum) will be presented subject to data availability. An example of such a table is presented in Appendix 4.

Due to the expected heterogeneity of the included studies in terms of design, population, setting, methodological choices, perspective and other characteristics, a quantitative synthesis of the cost data is unlikely to be appropriate. The results will be interpreted qualitatively in a narrative synthesis which will focus on the following aspects: the overall economic burden of NCDs on health systems and populations; the contribution of various cost components to the economic burden of NCDs; the available evidence on factors that explain the variation in economic burden estimates; comparative assessments of economic burden across geographical locations and diseases; and current research gaps. A comparison will be made between the seven NCDs in terms of the evidence available and the estimated economic burden. If the appropriate information is available, time-dependent relationships will also be explored.

4. References

References

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8. Bloom, D.E., et al., *The Global Economic Burden of Noncommunicable Diseases*, 2011, World Economic Forum: Geneva.
9. World Health Organization, *Global status report on noncommunicable diseases 2010*, 2011, WHO: Geneva.
10. Suhrcke, M., et al., *Chronic Disease: An Economic Perspective*, 2006, Oxford Health Alliance: London.
11. Nikolic, I.A., A.E. Stanciole, and M. Zaydman, *Chronic Emergency: Why NCDs Matter*, 2011, World Bank: Washington.
12. Ebrahim, S., et al., *Tackling Non-Communicable Diseases In Low- and Middle-Income Countries: Is the Evidence from High-Income Countries All We Need?* PLoS Med, 2013. **10**(1): p. e1001377.
13. Rice, D.P., *Estimating the cost of illness*. American Journal of Public Health and the Nations Health, 1967. **57**(3): p. 424-440.
14. Segel, J.E., *Cost-of-Illness Studies-A Primer*, 2006, RTI International,.
15. World Health Organization, *WHO guide to identifying the economic consequences of disease and injury*, 2009, WHO,.
16. Clabaugh, G. and M.M. Ward, *Cost-of-Illness Studies in the United States: A Systematic Review of Methodologies Used for Direct Cost*. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, 2008. **11**(1): p. 13-21.
17. Drummond, M.F. and T.O. Jefferson, *Guidelines For Authors And Peer Reviewers Of Economic Submissions To The BMJ*. BMJ: British Medical Journal, 1996. **313**(7052): p. 275-283.
18. Husereau, D., et al., *Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement*. BMJ, 2013. **346**.

Appendix 1. The World Bank list of low- and middle-income countries

Low-income economies (\$1,035 or less) [36 countries]: Afghanistan, Gambia, Myanmar, Bangladesh, Guinea, Nepal, Benin, Guinea-Bissau, Niger, Burkina Faso, Haiti, Rwanda, Burundi, Kenya, Sierra Leone, Cambodia, Korea, Dem Rep., Somalia, Central African Republic, Kyrgyz Republic, South Sudan, Chad, Liberia, Tajikistan, Comoros, Madagascar, Tanzania, Congo, Malawi, Togo, Eritrea, Mali, Uganda, Ethiopia, Mozambique, Zimbabwe.

Lower-middle-income economies (\$1,036 to \$4,085) [48 countries]: Armenia, India, Samoa, Bhutan, Kiribati, São Tomé and Príncipe, Bolivia, Kosovo, Senegal, Cameroon, Lao PDR, Solomon Islands, Cape Verde, Lesotho, Sri Lanka, Congo, Mauritania, Sudan, Côte d'Ivoire, Micronesia, Swaziland, Djibouti, Moldova, Syrian Arab Republic, Egypt, Mongolia, Timor-Leste, El Salvador, Morocco, Ukraine, Georgia, Nicaragua, Uzbekistan, Ghana, Nigeria, Vanuatu, Guatemala, Pakistan, Vietnam, Guyana, Papua New Guinea, West Bank and Gaza, Honduras, Paraguay, Yemen, Indonesia, Philippines, Zambia.

Upper-middle-income economies (\$4,086 to \$12,615) [55 countries]: Angola, Fiji, Palau, Albania, Gabon, Panama, Algeria, Grenada, Peru, American Samoa, Hungary, Romania, Argentina, Iran, Serbia, Azerbaijan, Iraq, Seychelles, Belarus, Jamaica, South Africa, Belize, Jordan, St. Lucia, Bosnia and Herzegovina, Kazakhstan, St. Vincent and the Grenadines, Botswana, Lebanon, Suriname, Brazil, Libya, Thailand, Bulgaria, Macedonia FYR, Tonga, China, Malaysia, Tunisia, Colombia, Maldives, Turkey, Costa Rica, Marshall Islands, Turkmenistan, Cuba, Mauritius, Tuvalu, Dominica, Mexico, Venezuela, Dominican Republic, Montenegro, Ecuador, Namibia.

Appendix 2. Search strategies for the included databases

Database: Africa-Wide Information (EBSCO)

#	Search terms	Records
S1	TI (economic N2 (model* or forecast* or simulat* or predict* or estimat*)) OR AB (economic N2 (model* or forecast* or simulat* or predict* or estimat*))	1,595
S2	TI (earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labo#r or workforce or productiv* or absenteeism or employment or employab*) OR AB (earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labo#r or workforce or productiv* or absenteeism or employment or employab*)	108,322
S3	TI ((cost* OR burden OR impact OR consequence*) N3 (disease* OR disorder* OR NCD* OR illness OR economic)) OR AB ((cost* OR burden OR impact OR consequence*) N3 (disease* OR disorder* OR NCD* OR illness OR economic))	10,531
S4	TI (gross domestic product OR national income OR economic growth) OR AB (gross domestic product OR national income OR economic growth)	11,852
S5	TI cost-of-illness OR AB cost-of-illness	89
S6	S1 OR S2 OR S3 OR S4 OR S5	122,558
S7	TI ((Heart or vascular or blood or cardio-vascular or cardiovascular or cerebro-vascular or cerebrovascular or coronary) N2 (disease* or disorder* or affect* or syndrome)) OR AB ((Heart or vascular or blood or cardio-vascular or cardiovascular or cerebro-vascular or cerebrovascular or coronary) N2 (disease* or disorder* or affect* or syndrome))	9,338
S8	TI (((atrial or ventricular) N2 (fibrillat* or flutter)) or isch#em* or aneurysm* or stroke or angina or myocard* infarct* or embolism or thrombo* or hypertensi* or anti-hypertensi* or antihypertensi* or blood pressure) OR AB (((atrial or ventricular) N2 (fibrillat* or flutter)) or isch#em* or aneurysm* or stroke or angina or myocard* infarct* or embolism or thrombo* or hypertensi* or anti-hypertensi* or antihypertensi* or blood pressure)	36,451
S9	TI (asthm* or COPD or (chronic obstructive N1 (pulmonary or lung))) OR AB (asthm* or COPD or (chronic obstructive N1 (pulmonary or	6,748

lung)))

S10	TI (Neoplasm* or cancer* or lymphom* or myelom* or leuk#em* or malignan* or melanom* or tumo#r* or neoplas*) OR AB (Neoplasm* or cancer* or lymphom* or myelom* or leuk#em* or malignan* or melanom* or tumo#r* or neoplas*)	72,605
S11	TI (Diabet* or (insulin* N2 (defic* or resistan*)) or (glucose N2 (toleran* or intoleran*)) or insulindepend* or insulin-depend* or noninsulin-depend*) OR AB (Diabet* or (insulin* N2 (defic* or resistan*)) or (glucose N2 (toleran* or intoleran*)) or insulindepend* or insulin-depend* or noninsulin-depend*)	19,632
S12	TI (musculoskeletal or (((arthrit* or osteoarthritis* or gout or rheumat*) N2 arthrit*) or back pain or neck pain)) OR AB (musculoskeletal or (((arthrit* or osteoarthritis* or gout or rheumat*) N2 arthrit*) or back pain or neck pain))	5,254
S13	TI (depression or ((depressive or affective or bipolar or unipolar) N2 disorder*)) OR AB (depression or ((depressive or affective or bipolar or unipolar) N2 disorder*))	9,050
S14	TI (schizophren* or (personality N3 disorder) or epileps* or epilept* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* N2 disorder*) or agoraphobia or phobi* or obsessive-compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) N2 sclerosis)) OR AB (schizophren* or (personality N3 disorder) or epileps* or epilept* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* N2 disorder*) or agoraphobia or phobi* or obsessive-compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) N2 sclerosis))	19,213
S15	TI (insomni* or (sleep N2 (depriv* or disorder*)) or migrain* or headache* or head ache) OR AB (insomni* or (sleep N2 (depriv* or disorder*)) or migrain* or headache* or head ache)	4,942
S16	TI ((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) N3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstinen*)) OR AB ((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) N3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstinen*))	6,350
S17	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	169,774
S18	S6 AND S17	5,831

#	Search terms	Records
1	((Heart or vascular or blood or cardiovascular or cerebrovascular or coronary) adj2 (disease* or disorder* or affect* or syndrome)).ti,ab.	360
2	((atrial or ventricular) adj2 (fibrillat* or flutter)) or isch?em* or aneurysm* or stroke or angina or (myocard* adj2 infarct*) or embolism or thrombo* or hypertensi* or anti-hypertensi* or (blood adj pressure)).ti,ab.	545
3	1 or 2	817
4	(Asthm* or COPD or (chronic obstructive adj (pulmonary or lung))).ti,ab.	26
5	((arthrit* or osteoarthritis* or gout or rheumat*) adj2 arthrit*) or low back pain or neck pain).ti,ab.	79
6	(Neoplasm* or cancer* or lymphom* or myelom* or leuk?em* or malignan* or melanom* or tumo?r* or neoplas*).ti,ab.	1053
7	(Diabet* or (insulin* adj2 (defic* or resistanc*))) or (glucose adj2 (toleran* or intoleranc*)) or non?insulin?depend* or insulin?depend* or noninsulin-depend*).ti,ab.	311
8	(depression or ((depressive or affective or bipolar or unipolar) adj2 disorder*)).ti,ab.	3142
9	(schizophren* or (personality adj3 disorder) or epilep* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* adj2 disorder*) or agoraphobia or phobi* or obsessive?compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) adj2 sclerosis)).ti,ab.	876
10	(insomni* or (sleep adj2 (depriv* or disorder*)) or migrain* or headache* or head ache)).ti,ab.	65
11	((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) adj3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstinen*)).ti,ab.	509
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11	6476
13	(Afghanistan or Gambia or Myanmar or Bangladesh or Guinea or Nepal or Benin or Bissau or Niger or Burkina or Haiti or Rwanda or Burundi or Kenya or Leone or Cambodia or Korea or Somalia or "Central African Republic" or Kyrgyz or Sudan or Chad or Liberia or Tajikistan or Comoros or Madagascar or Tanzania or Congo or Malawi or Togo or Eritrea or Mali or Uganda or Ethiopia or Mozambique or Zimbabwe).ti,ab.	19631
14	(Armenia or India or Samoa or Bhutan or Kiribati or Tome or Bolivia or Kosovo or Senegal or Cameroon or Lao* or Solomon or "Cape	39656

	Verde" or Lesotho or "Sri Lanka" or Congo or Mauritania or Sudan or "Côte d'Ivoire" or Ivory Coast or Micronesia or Swaziland or Djibouti or Moldova or Syria* or Egypt or Mongolia or Timor or "El Salvador" or Morocco or Ukraine or Georgia or Nicaragua or Uzbekistan or Ghana or Nigeria or Vanuatu or Guatemala or Pakistan or Vietnam or Guyana or Papua or "West Bank" or Gaza or Honduras or Paraguay or Yemen or Indonesia or Philippines or Zambia).ti,ab.	
15	(Angola or Fiji or Palau or Albania or Gabon or Panama or Algeria or Grenada or Peru or Samoa or Hungary or Romania or Argentina or Iran or Serbia or Azerbaijan or Iraq or Seychelles or Belarus or Jamaica or "South Africa" or Belize or Jordan or "St. Lucia" or Saint Lucia or Bosnia or Kazakhstan or "St. Vincent" or Saint Vincent or Botswana or Lebanon or Suriname or Brazil or Libya or Thailand or Bulgaria or Macedonia or Tonga or China or Malaysia or Tunisia or Colombia or Maldives or Turkey or "Costa Rica" or "Marshall Islands" or Turkmenistan or Cuba or Mauritius or Tuvalu or Dominica* or Mexico or Venezuela or Montenegro or Ecuador or Namibia).ti,ab.	66665
16	(((low or medium or middle or mid) adj income) or developing) adj countr*).ab,ti.	24168
17	(Africa or ((Latin or South or Central) adj1 America) or Asia or Pacific or (East* adj1 Europe)).ti,ab.	38601
18	13 or 14 or 15 or 16 or 17	154364
19	12 and 18	553
20	limit 19 to yr="1990 -Current"	504

Database: EMBASE Classic + EMBASE (Ovid)

#	Search terms	Records
1	exp Cardiovascular Diseases/	3106549
2	((Heart or vascular or blood or cardiovascular or cerebrovascular or coronary) adj2 (disease* or disorder* or affect* or syndrome)).ab,ti.	478639
3	((atrial or ventricular) adj2 (fibrillat* or flutter)) or isch?em* or aneurysm* or stroke or angina or (myocard* adj infarct*) or embolism or thrombo* or hypertensi* or anti?hypertensi* or (blood adj pressure)).ab,ti.	1700638
4	1 or 2 or 3	3563988
5	(Asthm* or COPD or (chronic obstructive adj (pulmonary or lung))).ab,ti.	210174
6	exp Pulmonary Disease, Chronic Obstructive/	69861
7	exp Asthma/	193457
8	5 or 6 or 7	255853
9	exp *back pain/ or exp *neck pain/	31349
10	exp Musculoskeletal Diseases/	1684507
11	((arthrit* or osteoarthrit* or gout or rheumat*) adj2 arthrit*) or back pain or neck pain).ab,ti.	224167
12	9 or 10 or 11	1734832
13	exp Neoplasms/	3553571
14	(Neoplasm* or cancer* or lymphom* or myelom* or leuk?em* or malignan* or melanom* or tumo?r* or neoplas*).ab,ti.	3013568
15	13 or 14	4129437
16	exp Diabetes Mellitus, Type 1/ or exp Diabetes Mellitus, Type 2/ or exp Diabetes Mellitus/	595925
17	(Diabet* or (insulin* adj2 (defic* or resistanc*)) or (glucose adj2 (toleran* or intoleranc*)) or insulindepend* or insulin-depend* or noninsulin-depend*).ti,ab.	614953
18	16 or 17	739680
19	exp *Mental Disorders/	1086296
20	exp *Mental Health/	27581
21	exp *Neurology/	18755
22	exp neurodegenerative diseases/ or exp neuromuscular diseases/ or exp sleep disorders/	620413
23	(depression or ((depressive or affective or bipolar or unipolar) adj2	322734

	disorder*)).ab,ti.	
24	(schizophren* or (personality adj3 disorder) or epileps* or epilept* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* adj2 disorder*) or agoraphobia or phobi* or obsessive?compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) adj2 sclerosis)).ab,ti.	771389
25	(insomni* or (sleep adj2 (depriv* or disorder*)) or migrain* or headache* or head ache*).ab,ti.	145269
26	((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) adj3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstin*))).ab,ti.	122256
27	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	2231163
28	2 or 3 or 5 or 11 or 14 or 17 or 23 or 24 or 25 or 26	6679202
29	4 or 8 or 12 or 15 or 18 or 27	10646567
30	(Afghanistan or Gambia or Myanmar or Bangladesh or Guinea or Nepal or Benin or Bissau or Niger or Burkina or Haiti or Rwanda or Burundi or Kenya or Leone or Cambodia or Korea or Somalia or "Central African Republic" or Kyrgyz* or Sudan or Chad or Liberia or Tajikistan or Comoros or Madagascar or Tanzania or Congo or Malawi or Togo or Eritrea or Mali or Uganda or Ethiopia or Mozambique or Zimbabwe).ab,ti.	273152
31	(Armenia or India or Samoa or Bhutan or Kiribati or Tome or Bolivia or Kosovo or Senegal or Cameroon or Lao* or Solomon or "Cape Verde" or Lesotho or "Sri Lanka" or Congo or Mauritania or Sudan or "Côte d'Ivoire" or "Ivory Coast" or Micronesia or Swaziland or Djibouti or Moldova or Syria* or Egypt or Mongolia or Timor or "El Salvador" or Morocco or Ukraine or Georgia or Nicaragua or Uzbekistan or Ghana or Nigeria or Vanuatu or Guatemala or Pakistan or Vietnam or Guyana or Papua or "West Bank" or Gaza or Honduras or Paraguay or Yemen or Indonesia or Philippines or Zambia).ab,ti.	220327
32	(Angola or Fiji or Palau or Albania or Gabon or Panama or Algeria or Grenada or Peru or Samoa or Hungary or Romania or Argentina or Iran or Serbia or Azerbaijan or Iraq or Seychelles or Belarus or Jamaica or "South Africa" or Belize or Jordan or "St. Lucia" or "Saint Lucia" or Bosnia or Kazakhstan or "St. Vincent" or "Saint Vincent" or Botswana or Lebanon or Suriname or Brazil or Libya or Thailand or Bulgaria or Macedonia or Tonga or China or Malaysia or Tunisia or Colombia or Maldives or Turkey or "Costa Rica" or "Marshall Islands" or Turkmenistan or Cuba or Mauritius or Tuvalu or Dominica* or Mexico or Venezuela or Montenegro or Ecuador or Namibia).ab,ti.	355509
33	exp africa/ or exp caribbean region/ or exp central america/ or exp	1198063

	latin america/ or exp mexico/ or exp south america/ or exp asia/ or exp europe, eastern/ or exp transcaucasia/ or exp pacific islands/	
34	exp Developing Countries/	76740
35	(((((low or medium or middle or mid) adj income) or developing) adj countr*).ab,ti.	50941
36	30 or 31 or 32 or 33 or 34 or 35	1573928
37	exp Economics/	228726
38	exp "cost of illness"/	14424
39	exp Models, Economic/	107612
40	exp Efficiency/	24029
41	exp Income/	61768
42	exp Poverty/	29939
43	exp Employment/	52828
44	(economic adj2 (model* or forecast* or simulat* or predict* or estimat*)).ab,ti.	4343
45	(earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labo?r or workforce or productiv* or absenteeism or employment or employab*).ti,ab.	354042
46	((cost* or burden or impact or consequence*) adj3 (disease* or disorder* or NCD* or illness or economic)).ab,ti.	63553
47	(gross domestic product or national income or economic growth).ab,ti.	3531
48	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47	783730
49	29 and 36 and 48	25382
50	limit 49 to yr="1990 -Current"	24206
51	(animal not (human and animal)).sh.	1401802
52	(rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*).ti.	2031946
53	51 or 52	3025172
54	50 not 53	24084
55	(comment or editorial or letter).pt.	1279288
56	54 not 55	23600

Database: MEDLINE (Ovid)

#	Search terms	Records
1	exp Cardiovascular Diseases/	1850910
2	((Heart or vascular or blood or cardiovascular or cerebrovascular or coronary) adj2 (disease* or disorder* or affect* or syndrome)).ab,ti.	330631
3	((atrial or ventricular) adj2 (fibrillat* or flutter)) or isch?em* or aneurysm* or stroke or angina or (myocard* adj2 infarct*) or embolism or thrombo* or hypertensi* or anti-hypertensi* or (blood adj pressure)).ab,ti.	1163371
4	1 or 2 or 3	2285933
5	(Asthm* or COPD or ((chronic obstructive) adj (pulmonary or lung)).ab,ti.	148200
6	exp Pulmonary Disease, Chronic Obstructive/	23637
7	exp Asthma/	108051
8	5 or 6 or 7	142447
9	exp *back pain/ or exp *neck pain/	22921
10	exp Musculoskeletal Diseases/	826246
11	((arthrit* or osteoarthritis* or gout or rheumat*) adj2 arthrit*) or back pain or neck pain).ab,ti.	153969
12	9 or 10 or 11	873747
13	exp Neoplasms/	2566969
14	(Neoplasm* or cancer* or lymphom* or myelom* or leuk?em* or malignan* or melanom* or tumo?r* or neoplas*).ab,ti.	2213699
15	13 or 14	3007737
16	exp Diabetes Mellitus, Type 1/ or exp Diabetes Mellitus, Type 2/ or exp Diabetes Mellitus/	312800
17	(Diabet* or (insulin* adj2 (defic* or resistanc*)) or (glucose adj2 (toleran* or intoleranc*)) or insulindepend* or insulin-depend* or noninsulin-depend*)ti,ab.	421462
18	16 or 17	470650
19	exp Mental Disorders/	942927
20	exp Mental Health/	21239
21	exp Neurology/	14179
22	exp neurodegenerative diseases/ or exp neuromuscular diseases/ or exp sleep disorders/	475354
23	(depression or ((depressive or affective or bipolar or unipolar) adj2	226374

	disorder*)).ab,ti.	
24	(schizophren* or (personality adj3 disorder) or epilep* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* adj2 disorder*) or agoraphobia or phobi* or obsessive?compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) adj2 sclerosis)).ab,ti.	538714
25	(insomni* or (sleep adj2 (depriv* or disorder*)) or migrain* or headache* or head ache).ab,ti.	92381
26	((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) adj3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstin*))).ab,ti.	90428
27	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	1738899
28	2 or 3 or 5 or 11 or 14 or 17 or 23 or 24 or 25 or 26	4775765
29	4 or 8 or 12 or 15 or 18 or 27	7457197
30	(Afghanistan or Gambia or Myanmar or Bangladesh or Guinea or Nepal or Benin or Bissau or Niger or Burkina or Haiti or Rwanda or Burundi or Kenya or Leone or Cambodia or Korea or Somalia or "Central African Republic" or Kyrgyz* or Sudan or Chad or Liberia or Tajikistan or Comoros or Madagascar or Tanzania or Congo or Malawi or Togo or Eritrea or Mali or Uganda or Ethiopia or Mozambique or Zimbabwe).ab,ti.	198144
31	(Armenia or India or Samoa or Bhutan or Kiribati or Tome or Bolivia or Kosovo or Senegal or Cameroon or Lao* or Solomon or "Cape Verde" or Lesotho or "Sri Lanka" or Congo or Mauritania or Sudan or "Côte d'Ivoire" or "Ivory Coast" or Micronesia or Swaziland or Djibouti or Moldova or Syria* or Egypt or Mongolia or Timor or "El Salvador" or Morocco or Ukraine or Georgia or Nicaragua or Uzbekistan or Ghana or Nigeria or Vanuatu or Guatemala or Pakistan or Vietnam or Guyana or Papua or "West Bank" or Gaza or Honduras or Paraguay or Yemen or Indonesia or Philippines or Zambia).ab,ti.	163716
32	(Angola or Fiji or Palau or Albania or Gabon or Panama or Algeria or Grenada or Peru or Samoa or Hungary or Romania or Argentina or Iran or Serbia or Azerbaijan or Iraq or Seychelles or Belarus or Jamaica or "South Africa" or Belize or Jordan or "St. Lucia" or "Saint Lucia" or Bosnia or Kazakhstan or "St. Vincent" or "Saint Vincent" or Botswana or Lebanon or Suriname or Brazil or Libya or Thailand or Bulgaria or Macedonia or Tonga or China or Malaysia or Tunisia or Colombia or Maldives or Turkey or "Costa Rica" or "Marshall Islands" or Turkmenistan or Cuba or Mauritius or Tuvalu or Dominica* or Mexico or Venezuela or Montenegro or Ecuador or Namibia).ab,ti.	260724
33	exp africa/ or exp caribbean region/ or exp central america/ or exp latin america/ or exp mexico/ or exp south america/ or exp asia/ or exp europe, eastern/ or exp transcaucasia/ or exp pacific islands/	1010689

34	exp Developing Countries/	62487
35	(((((low or medium or middle or mid) adj income) or developing) adj countr*).ab,ti.	40592
36	30 or 31 or 32 or 33 or 34 or 35	1266949
37	exp Economics/	487986
38	exp "cost of illness"/	17502
39	exp Models, Economic/	10102
40	exp Efficiency/	11511
41	exp Income/	49725
42	exp Poverty/	31092
43	exp Employment/	53483
44	(economic adj2 (model* or forecast* or simulat* or predict* or estimat*)).ab,ti.	3101
45	(earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labor or workforce or productiv* or absenteeism or employment or employab*).ti,ab.	273426
46	((cost* or burden or impact or consequence*) adj3 (disease* or disorder* or NCD* or illness or economic)).ab,ti.	44626
47	(gross domestic product or national income or economic growth).ab,ti.	3245
48	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47	796623
49	29 and 36 and 48	19635
50	limit 49 to yr="1990 -Current"	18307
51	(animals not (humans and animals)).sh.	3912617
52	(rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*).ti.	1622323
53	51 or 52	4142726
54	50 not 53	18194
55	(comment or editorial or letter).pt.	1222570
56	54 not 55	17606

#	Search terms	Records
1	MeSH descriptor: [Cardiovascular Diseases] explode all trees	69182
2	((Heart or vascular or blood or cardiovascular or cerebrovascular or coronary) near/2 (disease* or disorder* or affect* or syndrome))	41032
3	((atrial or ventricular) near/2 (fibrillat* or flutter)) or isch?em* or aneurysm* or stroke or angina or (myocard* near/1 infarct*) or embolism or thrombo* or hypertensi* or anti?hypertensi* or (blood near/1 pressure))	115501
4	#1 or #2 or #3	147155
5	MeSH descriptor: [Diabetes Mellitus] explode all trees	14655
6	(Diabet* or (insulin* near/2 (defic* or resist*))) or (glucose near/2 (toleran* or intoleran*)) or insulin-depend* or insulindepend* or noninsulin-depend*)	33067
7	#5 or #6	33050
8	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	2026
9	MeSH descriptor: [Asthma] 3 tree(s) exploded	8969
10	(Asthm* or COPD or ((chronic obstructive) near/1 (pulmonary or lung)))	28985
11	#8 or #9 or #10	29358
12	MeSH descriptor: [Musculoskeletal Diseases] explode all trees	21803
13	MeSH descriptor: [Back Pain] explode all trees	2587
14	MeSH descriptor: [Neck Pain] explode all trees	515
15	((arthrit* or osteoarthrit* or gout or rheumat*) near/2 arthrit*) or back pain or neck pain)	17109
16	#12 or #13 or #14 or #15	32214
17	MeSH descriptor: [Neoplasms] explode all trees	46935
18	(Neoplasm* or cancer* or lymphom* or myelom* or leuk?em* or malignan* or melanom* or tumo?* or neoplas*)	83102
19	#17 or #18	85111
20	MeSH descriptor: [Mental Disorders] explode all trees	39477
21	MeSH descriptor: [Mental Health] explode all trees	538
22	MeSH descriptor: [Neurodegenerative Diseases] explode all trees	5029
23	MeSH descriptor: [Neuromuscular Diseases] explode all trees	4762
24	MeSH descriptor: [Sleep Disorders] explode all trees	3951
25	(depression or ((depressive or affective or bipolar or unipolar) near/2 disorder*))	33704
26	(schizophren* or (personality near/3 disorder) or epileps* or epilept* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* near/2 disorder*) or agoraphobia or phobi* or obsessive?compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) near/2 sclerosis))	48843
27	(insomni* or (sleep near/2 (depriv* or disorder*)) or migraine* or headache* or head ache)	17472
28	((alcohol* or drug or amphetamine* or cocaine or marijuana or	31257

	opioid* or tobacco or substance) near/3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstinen*))	
29	#20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28	114942
30	#4 or #7 or #11 or #16 or #19 or #29	375595
31	MeSH descriptor: [Africa] explode all trees	3831
32	MeSH descriptor: [Caribbean Region] explode all trees	281
33	MeSH descriptor: [Central America] explode all trees	180
34	MeSH descriptor: [Latin America] explode all trees	74
35	MeSH descriptor: [South America] explode all trees	1253
36	MeSH descriptor: [Europe, Eastern] explode all trees	906
37	MeSH descriptor: [Transcaucasia] explode all trees	17
38	MeSH descriptor: [Pacific Islands] explode all trees	123
39	MeSH descriptor: [Developing Countries] explode all trees	693
40	(Afghanistan or Gambia or Myanmar or Bangladesh or Guinea or Nepal or Benin or Bissau or Niger or Burkina or Haiti or Rwanda or Burundi or Kenya or Leone or Cambodia or Korea or Somalia or "Central African Republic" or Kyrgyz* or Sudan or Chad or Liberia or Tajikistan or Comoros or Madagascar or Tanzania or Congo or Malawi or Togo or Eritrea or Mali or Uganda or Ethiopia or Mozambique or Zimbabwe)	9461
41	(Armenia or India or Samoa or Bhutan or Kiribati or Tome or Bolivia or Kosovo or Senegal or Cameroon or Lao* or Solomon or "Cape Verde" or Lesotho or "Sri Lanka" or Congo or Mauritania or Sudan or "Côte d'Ivoire" or "Ivory Coast" or Micronesia or Swaziland or Djibouti or Moldova or Syria* or Egypt or Mongolia or Timor or "El Salvador" or Morocco or Ukraine or Georgia or Nicaragua or Uzbekistan or Ghana or Nigeria or Vanuatu or Guatemala or Pakistan or Vietnam or Guyana or Papua or "West Bank" or Gaza or Honduras or Paraguay or Yemen or Indonesia or Philippines or Zambia)	17368
42	(Angola or Fiji or Palau or Albania or Gabon or Panama or Algeria or Grenada or Peru or Samoa or Hungary or Romania or Argentina or Iran or Serbia or Azerbaijan or Iraq or Seychelles or Belarus or Jamaica or South Africa or Belize or Jordan or St. Lucia or Saint Lucia or Bosnia or Kazakhstan or St. Vincent or Saint Vincent or Botswana or Lebanon or Suriname or Brazil or Libya or Thailand or Bulgaria or Macedonia or Tonga or China or Malaysia or Tunisia or Colombia or Maldives or Turkey or Costa Rica or Marshall Islands or Turkmenistan or Cuba or Mauritius or Tuvalu or Dominica* or Mexico or Venezuela or Montenegro or Ecuador or Namibia)	40982
43	(((((low or medium or middle or mid) near/1 income) or developing) near/1 countr*))	3742
44	#31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43	66336
45	MeSH descriptor: [Economics] explode all trees	21743
46	MeSH descriptor: [Cost of Illness] explode all trees	1045
47	MeSH descriptor: [Models, Economic] explode all trees	1713
48	MeSH descriptor: [Efficiency] explode all trees	257

49	MeSH descriptor: [Income] explode all trees	634
50	MeSH descriptor: [Poverty] explode all trees	891
51	MeSH descriptor: [Employment] explode all trees	1032
52	(economic near/2 (model* or forecast* or simulat* or predict* or estimat*))	8036
53	(earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labor or workforce or productiv* or absenteeism or employment or employab*)	18001
54	((cost* or burden or impact or consequence*) near/3 (disease* or disorder* or NCD* or illness or economic))	14051
55	(gross domestic product or national income or economic growth)	2095
56	#45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55	39014
57	#30 and #44 and #56	3252

#	Search terms	Records
1	exp Cardiovascular Disorders/	39701
2	((Heart or vascular or blood or cardiovascular or cerebrovascular or coronary) adj2 (disease* or disorder* or affect* or syndrome)).ab,ti.	18013
3	((atrial or ventricular) adj2 (fibrillat* or flutter)) or isch?em* or aneurysm* or stroke or angina or (myocard* adj2 infarct*) or embolism or thrombo* or hypertensi* or anti?hypertensi* or (blood adj pressure)).ab,ti.	48366
4	1 or 2 or 3	68643
5	(Asthm* or COPD or (chronic obstructive adj (pulmonary or lung))).ab,ti.	1257
6	exp Chronic Obstructive Pulmonary Disease/	681
7	exp Asthma/	3490
8	5 or 6 or 7	4796
9	exp *back pain/ or exp *neck pain/	2335
10	exp Musculoskeletal Disorders/	11569
11	((arthrit* or osteoarthrit* or gout or rheumat*) adj2 arthrit*) or back pain or neck pain).ab,ti.	7662
12	9 or 10 or 11	16771
13	exp Neoplasms/	31808
14	(Neoplasm* or cancer* or lymphom* or myelom* or leuk?em* or malignan* or melanom* or tumo?r* or neoplas*).ab,ti.	48076
15	13 or 14	50048
16	exp Diabetes Mellitus, Type 1/ or exp Diabetes Mellitus, Type 2/ or exp Diabetes Mellitus/	3484
17	(Diabet* or (insulin* adj2 (defic* or resistanc*)) or (glucose adj2 (toleran* or intoleranc*)) or insulin-depend* or insulin*depend* or noninsulin-depend*).ti,ab.	18502
18	16 or 17	18554
19	exp Mental Disorders/	414025
20	exp Mental Health/	37299
21	exp Neurology/	14089
22	exp neurodegenerative diseases/ or exp neuromuscular diseases/ or exp sleep disorders/	55758
23	(depression or ((depressive or affective or bipolar or unipolar) adj2	183481

	disorder*)).ab,ti.	
24	(schizophren* or (personality adj3 disorder) or epilep* or seizure* or Alzheimer* or dementia* or anorex* or bulim* or (eat* adj2 disorder*) or agoraphobia or phobi* or obsessive?compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) adj2 sclerosis)).ab,ti.	352959
25	(insomni* or (sleep adj2 (depriv* or disorder*)) or migrain* or headache* or head ache).ab,ti.	25017
26	((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) adj3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstinen*)).ab,ti.	70917
27	19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	716614
28	2 or 3 or 5 or 11 or 14 or 17 or 23 or 24 or 25 or 26	627759
29	4 or 8 or 12 or 15 or 18 or 27	818414
30	(Afghanistan or Gambia or Myanmar or Bangladesh or Guinea or Nepal or Benin or Bissau or Niger or Burkina or Haiti or Rwanda or Burundi or Kenya or Leone or Cambodia or Korea or Somalia or "Central African Republic" or Kyrgyz* or Sudan or Chad or Liberia or Tajikistan or Comoros or Madagascar or Tanzania or Congo or Malawi or Togo or Eritrea or Mali or Uganda or Ethiopia or Mozambique or Zimbabwe).ab,ti.	19362
31	(Armenia or India or Samoa or Bhutan or Kiribati or Tome or Bolivia or Kosovo or Senegal or Cameroon or Lao* or Solomon or "Cape Verde" or Lesotho or "Sri Lanka" or Congo or Mauritania or Sudan or "Côte d'Ivoire" or "Ivory Coast" or Micronesia or Swaziland or Djibouti or Moldova or Syria* or Egypt or Mongolia or Timor or "El Salvador" or Morocco or Ukraine or Georgia or Nicaragua or Uzbekistan or Ghana or Nigeria or Vanuatu or Guatemala or Pakistan or Vietnam or Guyana or Papua or "West Bank" or Gaza or Honduras or Paraguay or Yemen or Indonesia or Philippines or Zambia).ab,ti.	32458
32	(Angola or Fiji or Palau or Albania or Gabon or Panama or Algeria or Grenada or Peru or Samoa or Hungary or Romania or Argentina or Iran or Serbia or Azerbaijan or Iraq or Seychelles or Belarus or Jamaica or "South Africa" or Belize or Jordan or "St. Lucia" or "Saint Lucia" or Bosnia or Kazakhstan or "St. Vincent" or "Saint Vincent" or Botswana or Lebanon or Suriname or Brazil or Libya or Thailand or Bulgaria or Macedonia or Tonga or China or Malaysia or Tunisia or Colombia or Maldives or Turkey or "Costa Rica" or "Marshall Islands" or Turkmenistan or Cuba or Mauritius or Tuvalu or Dominica* or Mexico or Venezuela or Montenegro or Ecuador or Namibia).ab,ti.	53923
33	exp Developing Countries/	3502

34	(((((low or medium or middle or mid) adj income) or developing) adj countr*).ab,ti.	6143
35	30 or 31 or 32 or 33 or 34	101777
36	exp Economics/	15302
37	exp Efficiency/	493
38	exp Poverty/	5551
39	exp Employment/	13499
40	(economic adj2 (model* or forecast* or simulat* or predict* or estimat*)).ab,ti.	1259
41	(earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labo?r or workforce or productiv* or absenteeism or employment or employab*).ti,ab.	131823
42	((cost* or burden or impact or consequence*) adj3 (disease* or disorder* or NCD* or illness or economic)).ab,ti.	10796
43	(gross domestic product or national income or economic growth).ab,ti.	1466
44	36 or 37 or 38 or 39 or 40 or 41 or 42 or 43	157447
45	29 and 35 and 44	2318
46	(animals not (humans and animals)).sh.	5619
47	(rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*).ti.	106537
48	46 or 47	111843
49	45 not 48	2317

#	Search terms	Records
1	exp cardiovascular diseases/	76123
2	((Heart or vascular or blood or cardiovascular or cerebrovascular or coronary) adj2 (disease* or disorder* or affect* or syndrome)).ab,ti.	53572
3	((atrial or ventricular) adj2 (fibrillat* or flutter)) or isch?em* or aneurysm* or stroke or angina or (myocard* adj2 infarct*) or embolism or thrombo* or hypertensi* or anti?hypertensi* or (blood adj pressure)).ab,ti.	84164
4	1 or 2 or 3	140544
5	(Asthm* or COPD or ((chronic obstructive) adj (pulmonary or lung))).ab,ti.	22697
6	exp asthma/	14595
7	exp chronic obstructive pulmonary disease/	2702
8	5 or 6 or 7	18058
9	((arthrit* or osteoarthrit* or gout or rheumat*) adj2 arthrit*) or back pain or neck pain).ab,ti.	13377
10	exp neoplasms/	136669
11	(Neoplasm* or cancer* or lymphom* or myelom* or leuk?em* or malignan* or melanom* or tumo\$* or neoplas*).ab,ti.	159100
12	10 or 11	185859
13	(Diabet* or (insulin* adj2 (defic* or resistanc*)) or (glucose adj2 (toleran* or intoleranc*)) or insulindepend* or insulin-depend* or noninsulin-depend*).ab,ti.	86948
14	exp type 1 diabetes/ or exp diabetes mellitus/ or exp type 2 diabetes/	30018
15	13 or 14	87363
16	exp mental disorders/	34039
17	exp mental health/	7737
18	exp neurology/	516
19	exp neuromuscular diseases/	436
20	(depression or ((depressive or affective or bipolar or unipolar) adj2 disorder*)).ab,ti.	20323
21	(schizophren* or (personality adj3 disorder) or epileps* or epilept* or seizure* or Alzheimer* or dementia* anorex* or bulim* or (eat* adj2 disorder*) or agoraphobia or phobi* or obsessive?compulsive or obsessive or compulsive or anxiety or Parkinson* or ((multiple or lateral) adj2 sclerosis)).ab,ti.	35772

22	(insomni* or (sleep adj2 (depriv* or disorder*)) or migrain* or headache* or head ache).ab,ti.	14704
23	((alcohol* or drug or amphetamine* or cocaine or marijuana or opioid* or tobacco or substance) adj3 (syndrome* or addict* or withdraw* or disorder* or abus* or abstinen*)).ab,ti.	12208
24	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23	91579
25	4 or 8 or 9 or 12 or 15 or 24	471020
26	(Afghanistan or Gambia or Myanmar or Bangladesh or Guinea or Nepal or Benin or Bissau or Niger or Burkina or Haiti or Rwanda or Burundi or Kenya or Leone or Cambodia or Korea or Somalia or "Central African Republic" or Kyrgyz* or Sudan or Chad or Liberia or Tajikistan or Comoros or Madagascar or Tanzania or Congo or Malawi or Togo or Eritrea or Mali or Uganda or Ethiopia or Mozambique or Zimbabwe).ti,ab.	109400
27	(Armenia or India or Samoa or Bhutan or Kiribati or Tome or Bolivia or Kosovo or Senegal or Cameroon or Lao* or Solomon or "Cape Verde" or Lesotho or "Sri Lanka" or Congo or Mauritania or Sudan or "Côte d'Ivoire" or Ivory Coast or Micronesia or Swaziland or Djibouti or Moldova or Syria* or Egypt or Mongolia or Timor or "El Salvador" or Morocco or Ukraine or Georgia or Nicaragua or Uzbekistan or Ghana or Nigeria or Vanuatu or Guatemala or Pakistan or Vietnam or Guyana or Papua or "West Bank" or Gaza or Honduras or Paraguay or Yemen or Indonesia or Philippines or Zambia).ab,ti.	158303
28	(Angola or Fiji or Palau or Albania or Gabon or Panama or Algeria or Grenada or Peru or Samoa or Hungary or Romania or Argentina or Iran or Serbia or Azerbaijan or Iraq or Seychelles or Belarus or Jamaica or "South Africa" or Belize or Jordan or "St. Lucia" or Saint Lucia or Bosnia or Kazakhstan or "St. Vincent" or Saint Vincent or Botswana or Lebanon or Suriname or Brazil or Libya or Thailand or Bulgaria or Macedonia or Tonga or China or Malaysia or Tunisia or Colombia or Maldives or Turkey or "Costa Rica" or "Marshall Islands" or Turkmenistan or Cuba or Mauritius or Tuvalu or Dominica* or Mexico or Venezuela or Montenegro or Ecuador or Namibia).ab,ti.	221886
29	(((((low or medium or middle or mid) adj income) or developing) adj countr*).ab,ti.	24926
30	(Africa or ((Latin or South or Central) adj1 America) or Asia or Pacific or (East* adj1 Europe)).ti,ab.	78974
31	exp Developing Countries/	588170
32	26 or 27 or 28 or 29 or 30 or 31	689497
33	exp economics/	15118
34	utilization/ or exp health care utilization/	14744

35	exp income/	7276
36	exp poverty/	6851
37	exp employment/	2016
38	exp efficiency/	1244
39	(economic adj2 (model* or forecast* or simulat* or predict* or estimat*)).ab,ti.	768
40	(earning* or income or poverty or expense* or out-of-pocket or OOP or payment* or expenditure* or labor or workforce or productiv* or absenteeism or employment or employab*).ti,ab.	79374
41	((cost* or burden or impact or consequence*) adj3 (disease* or disorder* or NCD* or illness or economic)).ab,ti.	13607
42	(gross domestic product or national income or economic growth).ab,ti.	1636
43	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42	118276
44	25 and 32 and 43	6504
45	limit 44 to yr="1990 -Current"	5728
46	(correspondence or editorial).pt.	39908
47	45 not 46	5702
48	(rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*).ti.	247158
49	47 not 48	5676

Database: LILACS

#	Search term	Results
1	earning\$ or income or poverty or expense\$ or out-of-pocket or OOP or payment\$ or expenditure\$ or labor or labour or workforce or productiv\$ or absenteeism or employment or employab\$ or gross domestic product or national income or economic growth or cost of illness or cost-of-illness or burden of illness or burden-of-illness or economic burden or economic consequences or economic model [Words]	26584
2	"CARDIOVASCULAR DISEASES/" or "ASTHMA" or "CHRONIC OBSTRUCTIVE PULMONARY DISEASE/" or "NEOPLASM" or "DIABETES" or "MUSCULOSKELETAL DISEASES/" or "MENTAL DISORDERS" or "MENTAL HEALTH" or "NEUROLOGY/" or "NEUROMUSCULAR DISEASES/" or "BACK PAIN/" or "NECK PAIN/" [Words]	29105
3	heart or vascular or blood or cardiovascular or cerebrovascular or coronary or atrial or ventricular or fibrillat\$ or myocard\$ or hypertensi\$ or stroke or angina or aneurysm or asthm\$ or COPD or chronic obstructive or arthrit\$ or gout\$ or rheumat\$ or diabet\$ or depressi\$ or bipolar or unipolar or schizophren\$ or epilep\$ or seizure or dementia or Parkinson\$ or anorex\$ or bulim\$ or obsessive or compulsive or anxiety or multiple sclerosis or insomni\$ or migrain\$ or headache or head ache or addict\$ or withdraw\$ or abstinen\$ or non-communicable or noncommunicable or NCD\$ [Words]	118027
4	2 or 3	128694
5	1 and 4	3171

Database: MedCarib

#	Search term	Results
1	earning\$ or income or poverty or expense\$ or out-of-pocket or OOP or payment\$ or expenditure\$ or labor or labour or workforce or productiv\$ or absenteeism or employment or employab\$ or gross domestic product or national income or economic growth or cost of illness or cost-of-illness or burden of illness or burden-of-illness or economic burden or economic consequences or economic model [Words]	782
2	"CARDIOVASCULAR DISEASES/" or "ASTHMA" or "CHRONIC OBSTRUCTIVE PULMONARY DISEASE/" or "NEOPLASM" or "DIABETES" or "MUSCULOSKELETAL DISEASES/" or "MENTAL DISORDERS" or "MENTAL HEALTH" or "NEUROLOGY/" or "NEUROMUSCULAR DISEASES/" or "BACK PAIN/" or "NECK PAIN/" [Words]	1302
3	heart or vascular or blood or cardiovascular or cerebrovascular or coronary or atrial or ventricular or fibrillat\$ or myocard\$ or hypertensi\$ or stroke or angina or aneurysm or asthm\$ or COPD or chronic obstructive or arthrit\$ or gout\$ or rheumat\$ or diabet\$ or depressi\$ or bipolar or unipolar or schizophren\$ or epilep\$ or seizure or dementia or Parkinson\$ or anorex\$ or bulim\$ or obsessive or compulsive or anxiety or multiple sclerosis or insomni\$ or migrain\$ or headache or head ache or addict\$ or withdraw\$ or abstinen\$ or non-communicable or noncommunicable or NCD\$ [Words]	4033
4	2 or 3	4215
5	1 and 4	189

#	Search term	Results
1	heart OR vascular OR blood OR cardiovascular OR cerebrovascular OR coronary OR atrial OR ventricular OR fibrillat* OR myocard* OR hypertensi* OR stroke OR angina OR aneurysm OR asthm* OR COPD OR chronic obstructive OR arthrit* OR gout* OR rheumat* OR diabet* OR depressi* OR bipolar OR unipolar OR schizophren* OR epilep* OR seizure OR dementia OR Parkinson* OR anorex* OR bulim* OR obsessive OR compulsive OR anxiety OR multiple sclerosis OR insomni* OR migrain* OR headache OR head ache OR addict* OR withdraw* OR abstinen* OR non-communicable OR noncommunicable OR NCD*	52033
2	earning* OR income OR poverty OR expense* OR out-of-pocket OR OOP OR payment* OR expenditure* OR labor OR labour OR workforce OR productiv* OR absenteeism OR employment OR employab* OR gross domestic product OR national income OR economic growth OR cost of illness OR cost-of-illness OR burden of illness OR burden-of-illness OR economic burden OR economic consequences OR economic model	224
3	1 and 2	182

Database: IMEMR

#	Search term	Results
1	"CARDIOVASCULAR DISEASES/" or "ASTHMA" or "CHRONIC OBSTRUCTIVE PULMONARY DISEASE/" or "NEOPLASM" or "DIABETES" or "MUSCULOSKELETAL DISEASES/" or "MENTAL DISORDERS" or "MENTAL HEALTH" or "NEUROLOGY/" or "NEUROMUSCULAR DISEASES/" or "BACK PAIN/" or "NECK PAIN/" [Words]	8590
2	heart or vascular or blood or cardiovascular or cerebrovascular or coronary or atrial or ventricular or fibrillat\$ or myocard\$ or hypertensi\$ or stroke or angina or aneurysm or asthm\$ or COPD or chronic obstructive or arthrit\$ or gout\$ or rheumat\$ or diabet\$ or depressi\$ or bipolar or unipolar or schizophren\$ or epilep\$ or seizure or dementia or Parkinson\$ or anorex\$ or bulim\$ or obsessive or compulsive or anxiety or multiple sclerosis or insomni\$ or migrain\$ or headache or head ache or addict\$ or withdraw\$ or abstinens\$ or non-communicable or noncommunicable or NCD\$	39645
3	1 or 2	40809
4	earning\$ or income or poverty or expense\$ or out-of-pocket or OOP or payment\$ or expenditure\$ or labor or labour or workforce or productiv\$ or absenteeism or employment or employab\$ or gross domestic product or national income or economic growth or cost of illness or cost-of-illness or burden of illness or burden-of-illness or economic burden or economic consequences or economic model [Words]	3272
5	3 and 4	947

Database: WPRIM

#	Search term	Results
1	"CARDIOVASCULAR DISEASES/" or "ASTHMA" or "CHRONIC OBSTRUCTIVE PULMONARY DISEASE/" or "NEOPLASM" or "DIABETES" or "MUSCULOSKELETAL DISEASES/" or "MENTAL DISORDERS" or "MENTAL HEALTH" or "NEUROLOGY/" or "NEUROMUSCULAR DISEASES/" or "BACK PAIN/" or "NECK PAIN/"	22866
2	heart or vascular or blood or cardiovascular or cerebrovascular or coronary or atrial or ventricular or fibrillat\$ or myocard\$ or hypertensi\$ or stroke or angina or aneurysm or asthm\$ or COPD or chronic obstructive or arthrit\$ or gout\$ or rheumat\$ or diabet\$ or depressi\$ or bipolar or unipolar or schizophren\$ or epilep\$ or seizure or dementia or Parkinson\$ or anorex\$ or bulim\$ or obsessive or compulsive or anxiety or multiple sclerosis or insomni\$ or migrain\$ or headache or head ache or addict\$ or withdraw\$ or abstinen\$ or non-communicable or noncommunicable or NCD\$	105804
3	1 or 2	125324
4	earning\$ or income or poverty or expense\$ or out-of-pocket or OOP or payment\$ or expenditure\$ or labor or labour or workforce or productiv\$ or absenteeism or employment or employab\$ or gross domestic product or national income or economic growth or cost of illness or cost-of-illness or burden of illness or burden-of-illness or economic burden or economic consequences or economic model	4826
5	3 and 4	

Appendix 3. Proposed quality assessment tool for the studies included in the systematic review

1. Economic component

Question	Assessment
1. Was the methodology appropriate for the study aims and transparently presented?	Yes/No/Partially
2. Were data sources for expenditure, resource use and unit costs clearly explained?	Yes/No/Partially/NA
3. Were cost and/or expenditure data transparently presented?	Yes/No/Partially/NA
4. Have productivity costs been included?	Yes/No/Partially/NA
5. If productivity costs were included, were results presented with and without these?	Yes/No/Partially/NA
6. Did the analysis address uncertainty and/or heterogeneity? E.g. sensitivity analysis, subgroup analysis	Yes/No

Note: Most studies in the review are cost-of-illness studies. The NA ('Not applicable') category will apply to studies which did not estimate costs, but evaluated outcomes such as % GDP reduction, % subjects reporting catastrophic expenditure or % reduction in workforce reinsertion rate attributable to NCDs.

2. Epidemiologic component (if applicable)

The following checklist was adapted from *Shamliyan et al. (2013) Development and Implementation of the Standards for Evaluating and Reporting Epidemiologic Studies on Chronic Disease Incidence or Prevalence. American Journal of Public Health Research, 1(7): 183-190.*

Question	Assessment
1. Is the patient sampling method appropriate for the study objectives?	Yes/No/Unclear
2. Does the source of incidence/prevalence data contribute to the study's internal validity?	Yes/No/Unclear
3. Were the outcomes (i.e. presence of chronic disease) explicitly defined according to a recognized/internationally accepted definition?	Yes/No/Unclear

Appendix 4. Shell tables for presenting the economic findings

Microeconomic studies of cardiovascular disease impact

Study (year)	Country	Type of NCD	Unit of assessment (e.g. individual, household, firm)	Cost per unit of assessment per year US\$			
				Direct costs		Indirect costs	
				Medical costs	Non-medical costs	Morbidity costs	Mortality costs

Macroeconomic studies of cardiovascular disease impact

Study (year)	Country	Type of NCD	Time horizon (years)	Type of societal indicator (e.g. GDP, growth rate)	Impact on indicator (%)