APPENDIX. Detailed search strategy for each database.

There are 3 concepts in our search. Firstly, the exposure measure of non-communicable diseases or chronic diseases. The outcome measure comprises 2 concepts, out-of-pocket expenditure, and medicines.

Search was conducted in Jan 2017, for papers published from 1 Jan 2000 to 31 Dec 2016.

Ovid Medline

Purpose

Ovid Medline was our main database that captured the bulk of articles.

Settings and limits

We used 'Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present' under 'Advanced Search'. Keywords were searched under 'mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]'.

Concept 1: Non-communicable diseases

Medical Subject Heading (MeSH): Chronic disease

There is no MeSH term 'non-communicable disease' in Ovid Medline.

Key words: Chronic adj 2 (disease* OR condition* OR illness*) OR multimorbid OR multimorbidit* OR non-communicable OR noncommunicable OR 'non communicable'

'adj2' was used to capture terms such as 'chronic health', 'chronic medical'. The inverted commas for 'non communicable' were to capture the 2 words in that exact order.

Concept 2: Out-of-pocket expenditure

Medical Subject Heading (MeSH): Health expenditures, Health care costs

There is no MeSH term 'out-of-pocket' in Ovid Medline.

Key words: health adj2 (expenditure* OR spending* OR cost*) OR out-of-pocket OR 'out of pocket' OR financ* OR utilisation OR utilization.

'adj2' was used to capture terms such as 'health care', 'health system'. The inverted commas for 'out of pocket' were to capture the 3 words in that exact order. 'Financ*' was to capture 'financial' (eg. financial burden) and 'finances'.

Concept 3: Medicines

Medical Subject Heading (MeSH): Prescription drugs

Key words: Prescription drug* OR medicine* OR drug* OR pharmac* OR polypharmac*

Concepts 1, 2, and 3, were then combined with the operator 'AND'.

Cochrane Library

Settings and limits

We used 'Advanced Search'. Keywords were searched 'Title, Abstract, Keywords'. We limited the search to only primary articles under 'Trials', excluding reviews, method studies, technology assessments, economic evaluations.

Concept 1: Non-communicable diseases

Medical Subject Heading (MeSH): Chronic disease

There is no MeSH term 'non-communicable disease' in Cochrane Library.

Key words: Chronic NEAR/2 (disease* OR condition* OR illness*) OR multimorbid OR multimorbidit* OR non-communicable OR noncommunicable OR 'non communicable;

'NEAR/2' was used to capture terms such as 'chronic health', 'chronic medical'. The inverted commas for 'non communicable' were to capture the 2 words in that exact order.

Concept 2: Out-of-pocket expenditure

Medical Subject Heading (MeSH): Health expenditures, Health care costs

There is no MeSH term 'out-of-pocket' in Cochrane Library.

Key words: health NEAR/2 (expenditure* OR spending* OR cost*) OR out-of-pocket OR 'out of pocket' OR financ* OR utilisation OR utilization.

'NEAR/2' was used to capture terms such as 'health care', 'health system'. The inverted commas for 'out of pocket' was to capture the 3 words in that exact order. 'Financ*' was to capture 'financial' (eg. financial burden) and 'finances'.

Concept 3: Medicines

Medical Subject Heading (MeSH): Prescription drugs

Key words: Prescription drug* OR medicine* OR drug* OR pharmac* OR polypharmac*

Concepts 1, 2, and 3, were then combined with the operator 'AND'.

Embase

Purpose

Embase, being database for pharmaceutical and biomedical research, was used to focus our search on medicines and drugs, to find articles not in our other databases.

Settings and limits

We used 'Advanced Search'. Keywords were searched under all fields, including 'Free Text in All Fields'.

Concept 1: Non-communicable diseases

Emtree Terms: Chronic disease, Non communicable disease

'Non communicable disease' is an Emtree Term in Embase, unlike Ovid Medline and Cochrane Library whereby it is not a MeSH term.

Key words: Chronic NEAR/2 (disease* OR condition* OR illness*) OR multimorbid OR multimorbidity OR noncommunicable OR 'non communicable'

'NEAR/2' was used to capture terms such as 'chronic health', 'chronic medical'. The inverted commas for 'non communicable' were to capture the 2 words in that exact order.

Concept 2: Out-of-pocket expenditure

Emtree Term: Drug cost

As mentioned, with Embase being a database to focus on medicines, we did not search for similar MeSH Terms used in Ovid Medline and Cochrane, like 'health care costs' or 'health expenditures', to focus on drugs and pharmaceuticals.

Key words: out-of-pocket OR expenditure* OR spending*

Concept 3: Medicines

Emtree Term: Prescription drug

Key words: medicine* OR pharmaceutical*

Concepts 1, 2, and 3, were then combined with the operator 'AND'.

EconLit

Settings and limits

We used 'Advanced Search'. Keywords were searched under 'mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]'.

Concept 1: Non-communicable diseases

Key words: Chronic adj2 (disease* OR condition* OR illness*) OR multimorbid OR multimorbidit* OR non-communicable OR noncommunicable OR 'non communicable'

'adj2' was used to capture terms such as 'chronic health', 'chronic medical'. The inverted commas for 'non communicable' were to capture the 2 words in that exact order.

Concept 2: Out-of-pocket expenditure

Key words: health adj2 (expenditure* OR spending* OR cost*) OR out-of-pocket OR "out of pocket" OR financ* OR utilisation OR utilization.

'adj2' was used to capture terms such as 'health care', 'health system'. The inverted commas for 'out of pocket' was to capture the 3 words in that exact order. 'Financ*' was to capture 'financial' (eg. financial burden) and 'finances'.

Concept 3: Medicines

Key words: Prescription drug* OR medicine* OR drug* OR pharmac* OR polypharmac*

Concepts 1, 2, and 3 were then combined with the operator 'AND'

WHO Global Health Library

Purpose

To search 'grey literature' for relevant articles not captured from our other databases.

Settings and limits

We used 'Advanced Search'. Keywords were searched under 'Title, Abstract, Subject'.

Concept 1: Non-communicable diseases

Key words: Chronic disease* OR chronic condition* OR chronic illness* OR noncommunicable

Concept 2: Out-of-pocket expenditure

Key words: out-of-pocket

Concept 3: Medicines

Key words: Drug* OR medicine*

Concepts 1, 2, and 3 were then combined with the operator ‘AND’

APPENDIX. Newcastle Ottawa Scale Quality Assessment Scale for Observational Studies.

A study can be awarded a maximum of one point for each numbered item under 'Selection', 'Comparability' and 'Outcome' categories.

A. Selection

1. Is the source population appropriate and representative of the population of interests?
    a. Yes, the sample studied was nationally representative. (1 Point)
    b. No, the sample studied was unlikely to be nationally representative, given the information provided in the article. (0 Points)
    c. No, the sample was definitely not nationally representative, given the information provided in the article. (0 Points)

2. Is ascertainment of non-communicable diseases adequate?
    a. No, ascertainment was only via self-report by patients and was not be verified by any other means. (0 Points)
    b. Yes, ascertainment was done via self-report and in addition, a panel of physicians reviewed if NCDs reported by subjects met ICD-9/ICD-10 codes of chronic condition definitions. (1 Point)

3. How varied is the study of multimorbidity?
    a. Varied. Multimorbidity was studied as different categories of number of NCDs (eg. 5 categories: 0 NCDs, 1 NCD, 2-3 NCDs, 3-5 NCDs ≥6 NCDs) (1 Point)
    b. Not varied. Multimorbidty was studied as only a limited number of NCDs (eg. 2 categories: 1 NCDs, ≥2 NCDs), or only compared between presence and absence of NCDs (eg. 2 categories: 0 NCDs, ≥2 NCDs) (0 Points)

4. Comparison with reference group
    a. Definition of a reference group was clear and appropriate
    b. Results was compared with a representative reference from the sample (ie. there was comparison with a group with 0 NCDs)
    c. Comparison with general population, or the same individuals before and after they had multimorbidity.

B. Comparability

1. Comparability of results on the basis of design and analysis
   a. Results were described in age and/or sex subgroups
   b. Results adjusted for/described in different socioeconomic factors or disease related confounders
   c. Statistical adjustment for potential cofounders was not adequate

C. Outcome

1. Is ascertainment of medicine out-of-pocket expenditure adequate?
   a. Yes, ascertainment was from administrative data. (1 Point)
   b. Yes, ascertainment was from self-reported OOPE, with verification from other sources. (1 Point)
   c. No, OOPE was self-reported only. (0 Points)

APPENDIX. Quality assessment scoring

	Crystal et al, 2000.	Hwang et al, 2001.	Sambamoorthi et al, 2003.	Gellad et al, 2006.	Ruger et al, 2007.	Paez et al, 2009.	Kemp et al, 2013	Campbell et al, 2014	Park et al, 2014.	Pati et al, 2014.	Park et al, 2015.	Thorpe et al, 2015.	Hennessy et al, 2016.	Jung et al, 2016.
A. Selection														
Is the source population appropriate and representative of the population of interests?	1	1	1	1	1	1	0	0	1	1	1	1	0	1
Is ascertainment of non-communicable diseases adequate?	0	1	0	0	0	1	0	0	0	1	0	0	0	0
How varied is the study of multimorbidity?	1	1	1	1	1	1	0	0	1	1	1	1	0	1
Comparison with reference group (i.e. a group with 0 NCDs).	1	1	1	1	1	1	0	0	1	1	0	0	0	0
B. Comparability														
Comparability of results on the basis of design and analysis	1	1	1	1	1	1	1	1	1	1	1	1	1	1
C. Outcome														
Is ascertainment of medicine out-of-pocket expenditure adequate?	1	0	1	0	0	0	0	0	0	0	0	0	0	0
Total **Max=6 points**	5	5	5	3	4	4	1	1	4	5	3	3	1	3
Quality	High	High	High	Moderate	High	High	Satis-factory	Satisfactory	High	High	Moderate	Moderate	Satisfactory	Moderate

Appendix. Secondary Outcomes

Ref	Study Design, Data, Population, Settings	Secondary Outcomes			Quality Assessment
		Medicine Utilisation for multimorbidity	Coping strategies for OOPE on medicines	OOPE for other healthcare services	
Crystal et al, 2000.[21] USA	Cross-sectional. **Data:** 1995 Medicare Current Beneficiary Survey (MCBS). **No. of subjects:** 7,886 **Age:** ≥65	Not studied.	Not studied.	Medicines was largest proportion of OOPE (33.9%), followed by medical provider costs (35.1%), dental (18.3%), outpatient (6%), inpatient (4.1%), and home health (2.1%). Impact of multimorbidity on OOPE was most noticeable for medicines, OOPE decreased for dental health, and OOPE remained stable for medical provider costs.	High
Hwang et al, 2001.[22] USA	Cross-sectional. **Data:** 1996 Medical Expenditure Panel Survey (MEPS). **No. of subjects:** 22,326 individuals and 8,605 families. **Age:** All	For those aged below 65 years, percentage utilisation of drugs increased with more NCDs (user rates of drugs were 63%, 85%, 84%, 99% for 0, 1, 2, ≥3 NCDs, respectively). For those aged 65 years and above, user rates of drugs also increased with more NCDs (user rates of drugs were 69%, 93%, 97%, 99% for 0, 1, 2, ≥3 NCDs, respectively).	Not studied.	For those aged 65 years and above, mean OOPE was highest for drugs, followed by office dental services. For those aged less than 65 years, mean OOPE was highest for physician visits, and spending increased with more NCDs except dental services and vision aids.	High
Sambamoorthi et al, 2003.[23] USA	Cross-sectional. **Data:** Medicare beneficiaries from 1997 Medicare Current Beneficiary Survey (MCBS) Cost and Use files. **No. of subjects:** 8, 814 individuals. **Age:** ≥65	Not studied.	Not studied.	Not studied.	High
Gellad et al, 2006.[24] USA	Cross-sectional. **Data:** 1996-2000 Medical Expenditure Panel Survey Household Component (MEPS-HC). **No. of subjects:** 5,996	Not studied.	Not studied.	Not studied.	Moderate

	individuals **Age:** ≥65				
Ruger et al, 2007.[25] Korea	Cross-sectional. **Data:** 1998 Korean National Health and Nutrition Survey (KHNS). **No. of subjects:** 13,523 households and 39,060 household members. **Age:** All	Even though OOPE burden ratio increased with more NCDs for all income quintiles, pharmacy user rates increased with more NCDs only for the lowest income quintile 1, but decreased with more NCDs, for quintiles 2, 3, 4, and 5.	Not studied.	OOPE burden spread unevenly among income groups. For the lowest income quintile, OOPE burden ration was highest for oriental clinics, followed by professional hospitals, and lowest at public health centers. Burden ratio for oriental clinics and hospital facilities was about 6 times that of highest quintile.	High
Paez et al, 2009.[26] USA	Cross-sectional + Longitudinal. Cross-sectional Data: 2005 Medical Expenditure Panel Survey (MEPS). Longitudinal Data: 1996 and 2005 MEPS. No. of subjects: Unspecified, weighted to represent 292 million civilian non-institutionalised US population. Age: All.	For those aged less than 65 years, percentage utilisation of drugs increased with more NCDs (user rates of drugs were 52%, 91%, 98%, 100% for 0, 1, 2, ≥3 NCDs, respectively.) For those aged more than 65 years, percentage utilisation of drugs also increased with more NCDs (user rates of drugs were 64%, 93%, 100%, 100% for 0, 1, 2, ≥3 NCDs, respectively).	Not studied.	After drugs, dental care followed drugs for highest OOPE, but was less likely than other categories to be directly associated with multimorbidity. OOPE on drugs was less than 5 times that of office visits.	High
Kemp et al, 2013.[27] Australia	Cross-sectional. **Data:** 2 Australian Bureau of Statistics' (ABS) surveys: the Household Expenditure Survey and Survey of Income and Expenditure 2009-2010. **No. of subjects:** 9,774 households and 17,995 individuals. **Age:** ≥15	Not studied.	Not studied.	Not studied.	Satisfactory
Campbell et al, 2014.[28] Canada	Cross-sectional. **Data:** Survey designed by the interdisciplinary Chronic Disease Collaboration-	Not studied.	**Non-adherence:** Of those that reported financial barriers to medications, 37.7% stopped taking prescribed medications.	Not studied.	Satisfactory

	Barriers to Care for People with Chronic Health Conditions (BCPCHC), Feb 1-March 31, 2012. **No. of subjects:** 1,849 individuals. **Age:** ≥40				
Park et al, 2014.[29] Korea	Cross-sectional. **Data:** 2008 Korea Health Panel Survey (KHPS). **No. of subjects:** 2,342 individuals. **Age:** ≥65	Not studied.	Not studied.	OOPE for all medical services (hospital stays, outpatient services, emergency room visits, outpatient prescriptions) increased with more NCDs.	High
Pati et al, 2014.[30] India.	Cross-sectional. **Data:** WHO study on Global Ageing and Adult Health (SAGE) wave 1 survey of India, 2007. **Subjects:** 12,198 individuals. **Age:** ≥18	Not studied.	Not studied.	OOPE for medicines constituted the largest proportion for medical services. OOPE during last outpatient visit increased compared with 0 NCDs and ≥2 NCDs, but there was no increase for inpatient OOPE with more NCDs. There was a non-trivial proportion of OOPE on transport (outpatient 8.3%, inpatient 11.8%) and medical tests (outpatient 4.4%, inpatient 10.5%)	High
Park et al, 2015.[31] Korea	Cross-sectional (from 3 waves) **Data:** 2008 1st-wave survey, 2008 2nd-wave survey, 2009 3rd-wave survey from Korea Health Panel Survey. **No. of subjects:** 5,640 individuals **Age:** ≥20	Not studied.	Not studied.	Not studied.	Moderate
Thorpe et al, 2015.[32] USA	Cross-sectional. **Data**: Medical Expenditue Panel Survey (MEPS) 2012, and Health Insurance	Not studied.	Not studied.	Not studied.	Moderate

	Exchange Compare dataset 2014. **No. of subjects:** Unspecified **Age:** 18-64 years				
Hennessy et al, 2016.[33] Canada	Cross-sectional. **Data:** Survey designed by the Interdisciplinary Chronic Disease Collaboration-Barriers to Care for People with Chronic Health Conditions (BCPCHC), Feb 1-March 31, 2012. **No. of subjects:** 1,849 individuals **Age:** ≥40	As OOPE for drugs/pharmaceutical (as percentage of household income) increased from 0 to 0-5% to >5%, mean no. of medications increased from 4.0 to 3.9 to 6.9.	**Non-adherence:** Those with OOPE on drugs/pharmaceuticals as 0-5% of income had 5.2% prevalence of non-adherence, while OOPE as 5% or more of income had 21.5% prevalence of non-adherence.	Not studied.	Satisfactory
Jung et al, 2016.[34] Korea	Cross-sectional. **Data:** 2008 Korea Health Panel Survey (KHPS). **No. of subjects**: 8,103 individuals. **Age:** ≥20	Prevalence of receiving any prescriptions is high for all levels of NCDs and increases slightly from 87.02% to 95.01% to 98.01%, for 1, 2 and ≥3 NCDs, respectively.	Not studied.	Not studied.	Moderate

Appendix. Outcome measures

Reference	Primary Outcomes					Secondary Outcomes		
	Absolute amounts of OOPE on medicines	Cost ratios or odd ratios for financial burden from OOPE on medicines	OOPE on medicines as a proportion of total healthcare/medical services expenditure by patients	Comparison of OOPE on medicines between income groups	Comparison of OOPE on medicines between age groups	Medicine utilisation for multimorbidity	Coping strategies for OOPE on medicines	OOPE for other healthcare services
Crystal et al, 2000.[21] USA	√		√					√
Hwang et al, 2001.[22] USA	√		√		√	√		√
Sambamoorthi et al, 2003.[23] USA	√							
Gellad et al, 2006.[24] USA	√							
Ruger et al, 2007.[25] Korea				√		√		√
Paez et al, 2009.[26] USA	√		√		√	√		√

Kemp et al, 2013.[27] Australia	√							
Campbell et al, 2014.[28] Canada	√				√		√	
Park et al, 2014.[29] Korea		√						√
Pati et al, 2014.[30] India.	√		√					√
Park et al, 2015.[31] Korea		√						
Thorpe et al, 2015.[32] USA	√							
Hennessy et al, 2016.[33] Canada	√					√	√	
Jung et al, 2016.[34] Korea	√					√		