Citation

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Review question

Research question:

What are the criteria to define rare diseases (RDs) and orphan drugs (ODs) globally?

PICO:

P (Patients) = patients with RDs and taking ODs;

I (Intervention) = international definitions;

C (Comparators) = not applicable;

O (Outcomes) = qualitative / quantitative criteria.

Searches

A systematic literature search will be conducted after identifying the research question, using terms relating to rare diseases and orphan drugs.

The search will be conducted in several Internal Health Technology Assessment organizations.
We will be seeking English language studies and human modules.

The information will be retrieved from different sources: PubMed, MEDLINE, Embase, Scopus, Web of Science (Science and Social Science Citation Index), and the grey literature (regulatory information, theses, abstracts, and conferences).

The searches will be updated before the final analyses and further studies reclaimed for inclusion.

Additional search strategy information can be found in the attached PDF document (link provided below).

Types of study to be included

Inclusion: any study design, opinion pieces, commentaries, letters, and editorials, talking about standards used to define rare diseases, ultra and very ultra rare diseases, and orphan drugs (medications) will be considered. The study will cover seven geographic regions of the world (North America, South America, Asia, Europe, Africa, Oceania, and the Middle East). limited to the English language and human modules.

Exclusion: any study design, opinion pieces, commentaries, letters, and editorials, talking about standards used to define rare cancers, infectious diseases, poisonings, or specific rare disease or orphan drug. and animal studies.

Condition or domain being studied

Rare diseases and orphan drugs, and the criteria used to define them (qualitative or/and quantitative criteria).

Participants/population

Inclusion: patients with rare diseases, ultra and very ultra rare diseases, and treatment with orphan drugs (medications) will be considered. The study will cover seven geographic regions of the world (North America, South America, Asia, Europe, Africa, Oceania, and the Middle East).

Human studies only will be included.

Exclusion: rare cancers, infectious diseases, poisonings, or specific rare disease or orphan drugs and animal studies.

Intervention(s), exposure(s)

The criteria used to define rare diseases and orphan drugs.

Until today, there is no universal definition of a rare disease (RD) or orphan drug (OD). Qualitative criteria and/or quantitative criteria are used to define them. This systematic review will summarize these criteria and discuss them with stakeholders to study their applicability to have a national definition of RDs and ODs in Saudi Arabia.

Comparator(s)/control

Not applicable.

Main outcome(s)

Rare diseases and orphan drugs definition criteria (qualitative and/or quantitative).

Measures of effect

Prevalence threshold, number needed to treat, incremental cost-effectiveness ratio, cost-benefit ratio, quality of life.

Additional outcome(s)

To propose a national definition for rare diseases and orphan drugs in Saudi Arabia.

Data extraction (selection and coding)

Study selection:

Studies will be selected after publications are compiled and duplicates are removed. Then, two independent reviewers will conduct two rounds of screening the titles and abstracts for the initial eligibility of publications based on inclusion and exclusion criteria. The disagreements between individual reviewers will be resolved by the third reviewer (Chief Investigator). All decisions will be documented in an Excel spreadsheet.

Data extraction:

Included articles will be analyzed using a custom-made Excel spreadsheet developed for data extraction. This extracted data will be done by two independent data extractors. For missing, unreported data or additional details, the study investigator (first reviewer) will attempt to contact the study authors. The timeframe for a replay before the article is excluded on the basis of the requested information is three weeks.

Data that will be collected from each study includes author reference; study characteristics (design, country of origin, year of publication); type of rare diseases criteria (qualitative or quantitative); type of orphan drugs criteria (qualitative or quantitative); rare diseases criteria parameters; orphan drugs criteria parameters.

Any discrepancies between the two independent data extractors will be resolved by the chief investigator. This review does not require approval from an ethical research committee, as there is no human involvement.

Risk of bias (quality) assessment

ROBIS will be used for assessing the risk of bias

Strategy for data synthesis

Narrative synthesis from multiple studies will be undertaken to summarize and explain the current state of knowledge in relation to the systematic review question. The initial description of the included study's results will be developed using a preliminary synthesis in form of thematic and content analysis (quantitative and/or qualitative) and presenting data in tabular form.

From each article, the following data will be extracted: author, publication year, journal title, format (summary, journal article), study design, study setting, time range of data collection, results of study quality assessment, definitions of rare disease and their sub-classes, definitions of orphan drugs and their sub-classes, type of rare diseases criteria, type of orphan drugs criteria, the parameter of these criteria, and other results. This framework will be performed by one author and independent data extractor will be involved.

These data will be handled by different statistical approaches from qualitative and quantitative studies to investigate the similarities and differences between studies and explore the relationships within the data aiming to report key elements for defining rare diseases, orphan drugs, and subcategories qualitatively and quantitatively.

Analysis of subgroups or subsets

Data will be categorized into qualitative criteria and quantitative criteria.

Contact details for further information

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Type and method of review

Epidemiologic, Intervention, Systematic review

Anticipated or actual start date

13 June 2021

Anticipated completion date

18 December 2021

Funding sources/sponsors

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Conflicts of interest

Language
English

Country
Northern Ireland, Saudi Arabia

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Cost-Benefit Analysis; Developed Countries; Developing Countries; Drug Therapy; Epidemiology; Global Health; Humans; Numbers Needed to Treat; Orphan Drug Production; Pharmaceutical Preparations; Prevalence; Public Health; Quality of Life; Rare Diseases; Saudi Arabia

Date of registration in PROSPERO
13 August 2021

Date of first submission
30 June 2021

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
13 August 2021