

## Utilisation of real-world data from heart failure registries in OECD countries - A systematic review☆



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### ABSTRACT

**Background:** Heart failure represents a major public health issue that impacts 26 million people globally. Currently, real-world data represents a key instrument for providing the verification of both internal and external validity, yet there is still a lack of understanding regarding its scope in complementing evidence of treatments for heart failure. This study aims to increase understanding of the utilisation of real-world data from heart failure registries in Organisation for Economic Co-operation and Development (OECD) countries.

**Method:** This was a systematic review of existing observational studies from heart failure registries in 35 OECD member countries. Studies from 2000 to March 2017 were identified through electronic databases (MEDLINE (Ovid), EMBASE, Web of Science Core Collection, CINAHL (Ebsco), Cochrane CENTRAL) and appraised according to eligibility criteria.

**Results:** Two-hundred and two studies met the inclusion criteria, in which the majority were published from 2013 to 2016. All 202 studies were observational, among which 98% were cohort studies (198). The median sample size of all studies was 5152 (2417 to 32,890) and median study period 55 months (33.0 to 72.0). Swedish heart failure registry had the most publications (24, 12%).

**Conclusion:** Since 2000 there has been an upward trend in the number of published observational studies on heart failure registries in OECD countries with increasingly diverse outcomes and advanced statistical methods to improve their validity and reliability. This indicates that the utilisation of real-world data has experienced a significant upsurge in complementing the findings of clinical trials for improved research of heart failure treatments.

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### 1. Introduction

Heart failure (HF) represents a major public health issue that impacts as many as 26 million people globally [1,2]. Treatments for HF are various, including lifestyle modification, medication and medical device implantation. Thus, it is important to investigate different treatment options and their impacts on patients' health. Randomised clinical trials (RCTs) deliver the highest level of evidence on the subject of safety and efficacy of HF treatments [3]. Importantly, randomization is the only reliable method

to control for confounding factors when comparing treatment groups. However, RCTs are often associated with increasingly prohibitive costs of conducting adequately powered studies with sufficient follow period, and RCTs only involve selected patients who are treated according to protocols that might not represent real-world practice [3–5]. In contrast, studies based on real-world data such as observational studies based on quality registry or Registry-based randomised clinical trials (RRCT) [6] may also include patients that are not typically included in RCTs, and the follow-up periods are usually sufficiently long to assess delayed risks and long-term benefits of a treatment.

Real-world data (RWD) currently represent an instrument for providing the verification of both efficacy and effectiveness of investigated treatments, including those for HF. This particular type of evidence is widely acknowledged to be extracted from sources that cannot be incorporated in RCTs, for example patient HF registries that provide detailed information about treatment, drug compliance, clinical outcomes, adherence and costs, presenting the main source of evidence for various stakeholders in healthcare [7,8]. Relative to RCTs, they are cheaper and

**Abbreviations:** CONSORT, consolidated standards of reporting trials; HF, heart failure; OECD, Organisation for Economic Co-operation and Development; PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analysis; PROMS, patient reported outcome measures; RCT, randomised controlled trial; RRCT, registry-based randomised clinical trials; RWD, real-world data.

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enable analysis on a large group of indicators e.g. resource utilisation, provider characteristics and patient socio-economic status [9]. Despite the acknowledged value of RWD there is still a lack of understanding of its scope in generating evidence for treatments in addition to RCTs. To our knowledge current usage of RWD for HF has not yet been systematically evaluated [10–12]. Organisation for Economic Co-operation and Development (OECD) member countries have the world's highest level of adherence to evidence-based chronic HF therapies, primarily in North America, Western Europe, and Japan [13] and are pioneering access and implementation of RWD for decision-makers and various stakeholders in healthcare [14]. Therefore, the aim of this study was to increase understanding of the utilisation of RWD from HF registries in OECD countries.

## 2. Methods

This systematic review was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and followed the systematic review PRISMA (Preferred Reporting Items for Systematic review and Meta-Analysis) 2009 checklist for the reporting of the study [15–17].

### 2.1. Systematic search

A literature search was performed to identify studies based on HF registries in OECD countries in the following electronic databases: Medline (OVID), Embase.com, CINAHL (Ebsco), Web of Science Core Collection and Cochrane Library (Wiley). The MeSH-terms identified for searching Medline (OVID) were adapted in accordance to corresponding vocabularies in Embase and Cinahl. Each search concept was also complemented with relevant free-text terms: HF, cardiac failure, registry, database. The free-text terms were, if appropriate, truncated and/or combined with proximity operators. No language restriction was applied. Databases were searched from inception to March 2017. The searches were supported by two librarians at the Karolinska Institutet University Library in March 2017. Articles were also identified from additional sources, such as reference lists and HF registries website. The search strategies are available in [Appendix A](#).

### 2.2. Inclusion & exclusion criteria

Inclusion criteria for studies were as follows: 1. registry-based only; 2. observational study or pragmatic clinical trial (RRCT); 3. abstract available for review; 4. conducted in any of the 35 OECD member-countries listed as of March 2017 (<http://www.oecd.org/about/membersandpartners/list-oecd-member-countries.htm>); 5. no time limitation. Exclusion criteria for studies were: 1. surveys; 2. abstracts from conferences, editorials or commentaries; 3. articles providing descriptive registry information; 4. study sample size less than 1000; 5. no medical outcomes; 6. no full-text available (no full-text online or paid ones). Furthermore, observational studies based on international HF registries were included in the analysis if they matched the specified inclusion criteria and were based on an international HF registry that had an OECD member country as one of the participatory centers.

### 2.3. Data extraction

The abstracts and full-texts of identified studies were reviewed by the two authors (XD, and AK) independently. A study flow chart adapted from Prisma was applied to record the reviewing process [15]. The following categories of data from each identified study were collected and extracted in a standardized form in Excel by the two authors (XD, and AK) independently: 1. general information, which included unique identifier number, author, year of publication, disease type, aim and main findings; 2. study population; 3. study design; 4. statistical analysis; 5. quality assessment; 6. limitations. Abstract review

was undertaken using the Rayyan software for screening and coding of studies through use of tagging and filtering to code and organize a large amount of references efficiently [18].

### 2.4. Statistical analysis

Descriptive analyses were performed with a total of 87 baseline variables. Categorical variables were summarized using count and percentage (n, %). Continuous variables were summarized using the median with interquartile intervals. Analyses were undertaken in R studio version 1.0.136 (R foundation for Statistical Computing, Vienna, Austria) [19].

## 3. Results

The total number of records in the five electronic databases was 6706. After excluding all duplicates and including 10 records identified through reference lists and HF registry website, the number of hits retrieved was 4393. Based on title and abstraction, after applying the inclusion criteria, 4110 records were excluded. Of the remaining 283 documents identified, 81 were excluded after full text review; 11 excluded due to a sample size of less than 1000 and 2 because full text versions were not available and no response from the first author. Two-hundred and two records met the criteria; 193 in English and 9 non-English articles (these were analysed with assistance from native speakers) (see [Fig. 1](#)).

Within the 15-year period the majority of the studies were published between 2013 and 2016 ([Fig. 2](#)), showing an upward trend in the use of RWD. The Swedish heart failure registry (SwedeHF) had the most publications (n = 24) among all studies identified; this was followed by the Acute Decompensated Heart Failure National Registry (ADHERE) and Get With The Guidelines-HF Quality Improvement Registry (GWTG-HF), with 23 and 19 studies respectively.

Among the 202 included studies the median sample size was 5152 (2417, 32,890). The median study period was 55 months (33.0, 72.0). No pragmatic clinical trials were found. The majority were observational cohort studies (98%) while 4 studies were economic studies. One-hundred and sixty-nine (84%) studies stratified patient groups by age, sex, race or other variables. Over 90% studies did subgroup/sensitivity analysis to control for confounders. Some studies included multiple primary outcomes; most (91%) studies used mortality, followed by hospital admission (17%) and length of stay (15%). One fifth of the studies mentioned secondary outcomes as well, mostly mortality (8%), followed by hospital admission and survival ([Table 1](#)). Cost were reported by four economic studies from ARNO registry, ADHERE, and Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure registry. Seventy (35%) studies involved evaluation of interventions of drugs surgeries, or devices.

### 3.1. Patient characteristics

Age, sex, comorbidities and baseline health status, as patient baseline characteristics were documented in most studies ([Table 1](#)). Socio-economic status was input in 66 (33%) studies, in which 17 studies were based on GWTG-HF, 15 from SwedeHF and 13 studies from ADHERE. Life style factors were recorded in 91 (45%) studies, containing 16 studies from GWTG-HF, 16 studies from ADHERE, 15 studies from SwedeHF, 10 studies from Norwegian Heart Failure Registry, and 9 studies from Japanese Cardiac Registry of Heart Failure in Cardiology.

### 3.2. Statistical method

The Kaplan Meier survival curve was applied in 107 (53%) studies; the most common statistical test was the chi-test (155; 77%). Generalized linear models were performed in 191 (95%) studies (see [Table 2](#)). Multi-level model, mainly generalized estimating equation was used

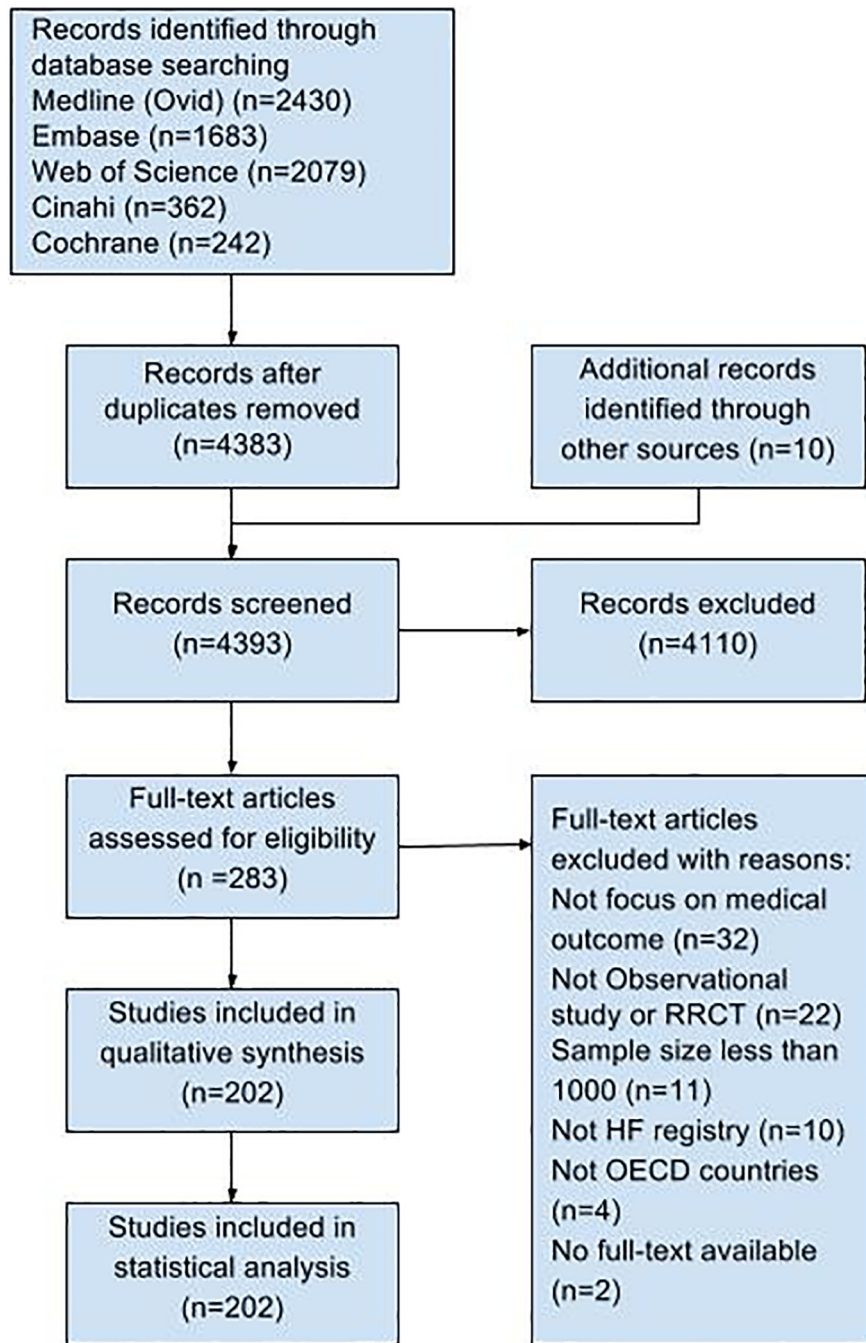


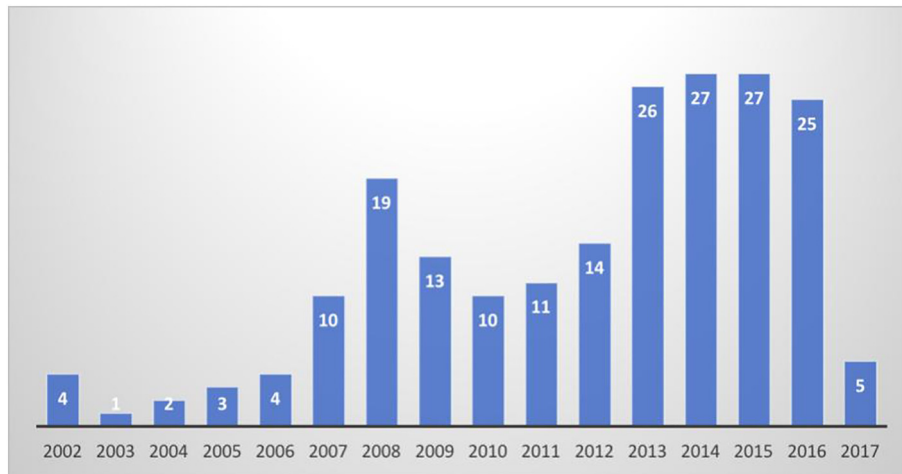
Fig. 1. PRISMA flow diagram showing study identification, selection, eligibility, and inclusion.

in 30 (15%) studies. Forty-nine (24%) studies applied a propensity score method complementary to regression models. Advanced machine learning was used in 8 (4%) studies from the USA and Japan. Only 4 studies (2%) mentioned quality assessment but 186 studies (92%) discussed study limitations (Table 2).

#### 4. Discussion

This systematic review has shown an increase in the volume of identified studies over time, suggesting that the utilisation of RWD from HF registries has been gradually increasing since the 2000s, as well as the growth pattern of the number of published observational studies and the number of established HF registries. These findings are similar to those of a study by Moen F. et al. on the value of cancer treatments from RWD and a systematic review by Oyinlola J. et al. on RWD

influencing practice across a number of disease areas, such as diabetes, obesity and mental illness [13,14]. The results of these studies illustrate an increasing, yet relatively small utilisation of RWD in healthcare research compared with the amount of available RWD sources since their inception at the end of the 20th century. Despite the increasing awareness of the importance of studies based on RWD, this type of research is often neglected or initiated late. This happens due to the fact that the proper utilisation of RWD requires a close cooperation between healthcare, industry, patients and authorities. Currently, with the growing demand for RWD, questions regarding the sustainability of patient registries and databases are being raised more frequently [20–22]. In addition, as the stratification of disease areas and treatments continues to expand, larger cohorts of patients are needed to provide more generalizable and sufficient data sets. For many complicated diseases, including HF, as well as for smaller countries, this will demand international collaboration.



**Fig. 2.** Number of published observational studies based on HF registries in 35 OECD countries per year\*. \*2002 was the first year observational studies on HR were published and met the inclusion criteria and 2017 includes only January to March.

This review also showed that the variability of the design of identified observational studies is low, with cohort studies accounting for 98% of all analysed studies based on the HF registries. Also, despite the growing application of in clinical and scientific communities, this systematic review identified no publications of RRCT according to inclusion criteria. The most prevalent main outcome of identified observational studies proved to be mortality. Survival, length of stay, admission, and cost were also defined to be among either primary or secondary outcomes. Furthermore, the findings of the present review showed that the existing observational studies from HF registries in OECD countries apply a number of advanced statistical methods to enable the minimization of bias and limitations of RWD, which in turn improve their validity

and reliability. The findings of the present review have also demonstrated that RWD from HF registries has been employed primarily with the same purpose as RWD for cancer and rare diseases, which is to evaluate new treatments outside the defined protocol of clinical trials [23,24]. As such, the results of this review are generalizable to other studies based on RWD applications in the evaluation of treatments and health outcomes in other disease areas. However, the value of a particular HF treatment has not yet been done in a definitive way even with the application of RWD, since the value of the investigated treatment must be assessed in contrast with other treatment therapy that could have been employed instead. Such an estimate of the treatment value is required to support healthcare decision making and evaluate the cost and benefits of novel treatments, as has been shown with cancer treatment studies [25].

**Table 1**  
Summary characteristics of the observational studies.

	N = 202	%
Study type		
Cohort	198	98,0
Case-control	1	0,5
Cross-sectional	3	1,5
Primary outcome		
Mortality	184	91,0
Survival	26	13,0
PROMS	0	0,0
Cost	4	2,0
Hospital admission	35	17,0
Length of stay	31	15,0
Secondary outcome	40	20,0
Mortality	16	8,0
Survival	10	5,0
PROMS	0	0,0
Cost	0	0,0
Hospital admission	13	6,0
Length of stay	7	3,0
Intervention	70	35,0
Comparator	46	23,0
Stratification	169	84,0
Controlling confounder	193	96,0
Patient baseline characteristics		
Age	201	99,0
Sex	200	99,0
Socio-economic	66	33,0
Life style factors	91	45,0
Comorbidities	198	98,0
Baseline health status	197	98,0
Median		IQR
Sample size	5152	2471,32,890
Study period (month)*	55	33,0, 72,0

\*53 studies had missing data for study period.

**Table 2**  
Statistical analysis and quality check of observational studies.

	N = 202	%
Descriptive analysis	202	100,0
Mean/median, SD/IQR, Min, Max	196	97,0
Percentage	201	99,0
Count	136	67,0
Kaplan Meier survival curve	107	53,0
Statistical tests	182	90,0
t-test	76	38,0
Wilcoxon rank test/Mann-Whitney U test	72	36,0
ANOVA	46	24,0
Kruskal-Wallis test	42	23,0
Chi-test	155	77,0
Fisher's exact test	25	12,0
Log-Rank test	56	28,0
Regression models	191	95,0
General linear regression	12	6,0
Generalized linear models	191	95,0
Logistic	95	47,0
Logit	0	0,0
Probit	0	0,0
Tobit	0	0,0
Quantile regression	0	0,0
Count regression	10	5,0
Survival models (time-to-event)	137	68,0
Multi-level model	30	15,0
Propensity score	49	24,0
Machine learning	8	4,0
Quality check		
Quality assessment performed	4	2,0
Compliance with results from RCTs	128	63,0
Limitations addressed	186	92,0

Moreover, this review has illustrated that the strength of registry-based studies in the field of HF lies not only in rapid collection of data in a large number of patients. Registry-based studies also prove applicability in population-based healthcare improvement by allowing hypothesis generation in estimation of mortality, morbidity and resource utilisation, which can serve as the basis for a clinical trial [26,27]. In addition, as the present findings indicate, such studies allow for the comparison of the disease management between several different countries. Yet, the limitations of HF registry-based studies include long-term data collection, high set-up and running costs as well as quality control enablement [28].

There are a number of strengths to this review. First, it was conducted with the application of the PRISMA methodology for performing systematic reviews [13] to ensure completeness in the reporting of results. Moreover, a comprehensive search of multiple bibliographic databases was applied using five different databases. The review also focused on identifying studies based on the HF registries of all 35 OECD member-countries, thus providing a cross-border comparison of the utilisation of RWD in the OECD region. In addition, the review employed no language or time restriction, thus enabling a broader coverage of pertinent observational studies. Also, the search strategies were supported by librarians at the Karolinska Institutet University Library and the researchers also sought help from experts in the cardiology field to ensure a proper clinical understanding of HF conditions for the purpose of the present review.

However, a number of limitations to this review should also be noted. Because the value of particular HF treatments has not yet been assessed using RWD at this time, it is not possible to currently assess how the studies have influenced the indications and recommendations in HF guidelines. Also, since the research question was relatively broad, various study design types were included which made comparisons between studies challenging. Therefore, no risk of bias was performed for each single study or across studies. Furthermore, it was not possible to do a meta-analysis for this review due to the absence of correlation of mutual exposures and outcomes of identified studies. Future research on the utilisation of RWD should include a more specific assessment of the quality of the published studies based on RWD, evaluation of risk of bias and the effect of research results on HF recommendation guidelines.

## 5. Conclusion

Since 2000 there has been an upward trend in the number of published observational studies on HF registries in OECD countries with increasingly diverse outcomes and advanced statistical methods to improve their validity and reliability. This indicates that the utilisation of RWD from HF registries has experienced a significant upsurge in complementing the findings of clinical trials for improved research of HF treatments.

## Acknowledgements

The authors thank Synergus AB, and the Karolinska Institutet Library Support office, in particular Klas Moberg and Carl Gornitzki, for helping us with producing quality level research strategies for this systematic review and providing us with an extended number of search databases.

## Conflicts of interest

None.

## Appendix A. Search strategies

### Databases:

1. Medline (Ovid)
2. Embase ([embase.com](http://embase.com))

3. Web of Science Core Collection
4. Cinahl (Ebsco)
5. Cochrane (Wiley)

### Total number of hits:

- Before deduplication: 6706
- After deduplication: 4383

## 1. Medline (Ovid)

Date of Search: 2017-03-30

Number of hits: 2,340

Comments:

Field labels:

- .ti,ab. = titel & abstract
- .kf. = keywords
- .au,fa. = authors
- / = MeSH
- exp/ = MeSH, exploded
- adjx = adjacent within x words

1. exp Heart Failure/  
2. ((heart\* or cardia\* or myocard\*) adj3 (fail\* or decompensat\* or edema\* or incompetence or insufficiency)).ti,ab,kf.  
3. or/1-z

4. Registries/  
5. Databases, Factual/  
6. Databases as Topic/  
7. (registry or registries or register or registers).ti,ab,kf,au,fa.  
8. database\*.ti.  
9. or/4-8

10. exp Australia/  
11. Austria/  
12. Belgium/  
13. exp Canada/  
14. Chile/  
15. Czech Republic/  
16. exp "Scandinavian and Nordic Countries"/  
17. Estonia/  
18. exp France/  
19. exp Germany/  
20. Greece/  
21. Hungary/  
22. Iceland/  
23. Ireland/  
24. Israel/  
25. exp Italy/  
26. exp Japan/  
27. exp Republic of Korea/  
28. Latvia/  
29. Luxembourg/  
30. Mexico/  
31. Netherlands/  
32. New Zealand/  
33. Poland/  
34. Portugal/  
35. Slovakia/  
36. Slovenia/  
37. Spain/  
38. Switzerland/  
39. Turkey/  
40. exp United Kingdom/  
41. exp United States/  
42. "Organisation for Economic Co-Operation and Development"/  
43. (oecd or australia\* or austria\* or belgium or belgian or canada or canadian or chile\* or czech\* or denmark or danish or estonia\* or finland or finnish or france or french or german\* or greece or greek or hungar\* or iceland\* or ireland or irish or israel\* or italy or italian or japan\* or korea\* or latvia\* or luxembourg\* or mexico or mexican or netherlands or dutch or holland\* or new zealand or norway or norwegian or poland or polish or portugal or portuguese or slovak\* or slovenia\* or spain or spanish or sweden or swedish or switzerland or swiss or turkey or turkish or united kingdom or great britain or wales or england or scotland or united states or uk or us or usa or america\*).ti,ab,kf.  
44. or/10-43  
45. exp Clinical Trial/

46. Observational Study/  
 47. Observational Studies as Topic/  
 48. exp Case-Control Studies/  
 49. exp Cohort Studies/  
 50. Cross-Over Studies/  
 51. Cross-Sectional Studies/  
 52. Multicenter Study/  
 53. Matched-Pair Analysis/  
 54. Epidemiologic Studies/  
 55. Pragmatic Clinical Trial/  
 56. Pragmatic Clinical Trials as Topic/  
 57. (case control\* or cohort\* or cross over or cross sectional or follow up or followed or longitudinal or pragmatic or practical or random\* or real world or clinical trial\*).ti,ab,kf.  
 58. or/45-57

59. 3 and 9 and 44 and 58  
 60. remove duplicates from 59  
 61. limit 60 to (comment or editorial or letter)  
 62. 60 not 61

## 2. Embase (embase.com)

Date of Search: 2017-03-30      Field labels:  
 Number of hits: 1,683  
 Comments:

- ab, ti = titel & abstract
- au = authors
- /exp = Emtree, exploded
- /de = Emtree, not exploded
- NEAR/x = adjacent within x words

'heart failure'/exp OR ((heart\* OR cardia\* OR myocard\*) NEAR/3 (fail\* OR decompensat\* OR edema\* OR incompetence OR insufficiency)):ti,ab AND  
 'register'/de OR 'disease registry'/de OR 'factual database'/exp OR registry:ti,ab,au OR registries:ti,ab,au OR register:ti,ab,au OR registers:ti,ab,au OR database\*:ti AND  
 'australia'/exp OR 'austria'/de OR 'belgium'/exp OR 'canada'/exp OR 'chile'/de OR 'czech republic'/de OR 'scandinavia'/exp OR 'estonia'/de OR 'france'/exp OR 'germany'/exp OR 'greece'/de OR 'hungary'/de OR 'iceland'/de OR 'ireland'/de OR 'israel'/de OR 'italy'/exp OR 'south korea'/de OR 'latvia'/de OR 'luxembourg'/de OR 'mexico'/exp OR 'netherlands'/de OR 'new zealand'/de OR 'poland'/de OR 'portugal'/exp OR 'slovakia'/de OR 'slovenia'/de OR 'spain'/exp OR 'switzerland'/de OR 'turkey (republic)'/de OR 'united kingdom'/exp OR 'united states'/exp OR 'organisation for economic co-operation and development'/de OR oecd:ti,ab OR australia\*:ti,ab OR austria\*:ti,ab OR belgium:ti,ab OR belgian:ti,ab OR canada:ti,ab OR canadian:ti,ab OR chile\*:ti,ab OR czech\*:ti,ab OR denmark:ti,ab OR danish:ti,ab OR estonia\*:ti,ab OR finland:ti,ab OR french:ti,ab OR france:ti,ab OR french:ti,ab OR german\*:ti,ab OR greece:ti,ab OR greek:ti,ab OR hungar\*:ti,ab OR iceland\*:ti,ab OR ireland:ti,ab OR irish:ti,ab OR israel\*:ti,ab OR italy:ti,ab OR italian:ti,ab OR japan\*:ti,ab OR korea\*:ti,ab OR latvia\*:ti,ab OR luxembourg\*:ti,ab OR mexico:ti,ab OR mexican:ti,ab OR netherlands:ti,ab OR dutch:ti,ab OR holland\*:ti,ab OR 'new zealand':ti,ab OR norway:ti,ab OR norwegian:ti,ab OR poland:ti,ab OR polish:ti,ab OR portugal:ti,ab OR portuguese:ti,ab OR slovak\*:ti,ab OR slovenia\*:ti,ab OR spain:ti,ab OR spanish:ti,ab OR sweden:ti,ab OR swedish:ti,ab OR switzerland:ti,ab OR swiss:ti,ab OR turkey:ti,ab OR turkish:ti,ab OR united:ti,ab AND kingdom:ti,ab OR 'great britain':ti,ab OR wales:ti,ab OR england:ti,ab OR scotland:ti,ab OR 'united states':ti,ab OR uk:ti,ab OR us:ti,ab OR usa:ti,ab OR america\*:ti,ab AND  
 'clinical trial'/exp OR 'observational study'/de OR 'case control study'/exp OR 'cohort analysis'/de OR 'crossover procedure'/de OR 'cross-sectional study'/de OR 'case control\*':ti,ab OR cohort\*:ti,ab OR 'cross over':ti,ab OR 'cross sectional':ti,ab OR 'follow up':ti,ab OR followed:ti,ab OR longitudinal:ti,ab OR pragmatic:ti,ab OR practical:ti,ab OR random\*:ti,ab OR 'real world':ti,ab OR 'clinical trial\*':ti,ab AND  
 ('article'/it OR 'article in press'/it OR 'conference paper'/it OR 'review'/it)

## 3. Web of Science Core Collection

Date of Search: 2017-03-30      Field labels:  
 Number of hits: 2,079  
 Comments:

- TS = Topic = title, abstract & keyword
- NEAR/x = adjacent within x words

#6 #4 AND #3 AND #2 AND #1  
 Refined by: [excluding]: DOCUMENT TYPES: (EDITORIAL MATERIAL OR LETTER OR NOTE OR MEETING ABSTRACT OR BOOK CHAPTER)  
 DocType=All document types; Language=All languages;

#5 #4 AND #3 AND #2 AND #1  
 DocType=All document types; Language=All languages;

#4 TOPIC: ("case control\*" OR cohort\* OR "cross over" OR "cross sectional" OR "follow up" OR followed OR longitudinal OR pragmatic OR practical OR random\* OR "real world" OR "clinical trial\*")  
 DocType=All document types; Language=All languages;

#3 TOPIC: ((oecd OR australia\* OR austria\* OR belgium OR belgian OR canada OR canadian OR chile\* OR czech\* OR denmark OR danish OR estonia\* OR finland OR finnish OR france OR french OR german\* OR greece OR greek OR hungar\* OR iceland\* OR ireland OR irish OR israel\* OR italy OR italian OR japan\* OR korea\* OR latvia\* OR luxembourg\* OR mexico OR mexican OR netherlands OR dutch OR holland\* OR "new zealand" OR norway OR norwegian OR poland OR polish OR portugal OR portuguese OR slovak\* OR slovenia\* OR spain OR spanish OR sweden OR swedish OR switzerland OR swiss OR turkey OR turkish OR "united kingdom" OR "great britain" OR wales OR england OR scotland OR "united states" OR uk OR us OR usa OR america\*))  
 DocType=All document types; Language=All languages;

#2 TOPIC: (registry OR registries OR register OR registers) OR AUTHOR: (registry OR registries OR register OR registers) OR TITLE: (database\*)  
 DocType=All document types; Language=All languages;

#1 TOPIC: ((heart\* OR cardia\* OR myocard\*) NEAR/3 (fail\* OR decompensat\* OR edema\* OR incompetence OR insufficiency))  
 DocType=All document types; Language=All languages;

## 4. Cinahl (Ebsco)

Date of Search: 2017-03-30      Field labels:  
 Number of hits: 362  
 Comments:

- TI, AB = titel & abstract
- AU = authors
- MH = Cinahl Heading
- + = Exploded Cinahl Heading

Nx = adjacent within x words  
 (MH "Heart Failure+")  
 S1 TI ((heart\* or cardia\* or myocard\*) N3 (fail\* or decompensat\* or edema\* or incompetence or insufficiency)) OR AB ((heart\* or cardia\* or myocard\*) N3 (fail\* or decompensat\* or edema\* or incompetence or insufficiency))  
 S2 S1 OR S2  
 S3 (MH "Registries, Disease")  
 S4 (MH "Resource Databases")  
 S5 TI (registry or registries or register or registers) OR AB (registry or registries or register or registers) OR AU (registry or registries or register or registers)  
 S6 TI database\*  
 S7 S4 OR S5 OR S6 OR S7  
 S8 (MH "Australia+")  
 S9 (MH "Austria")  
 S10 (MH "Belgium")  
 S11 (MH "Canada+")  
 S12 (MH "Chile")  
 S13 (MH "Czech Republic")  
 S14 (MH "Scandinavia+")  
 S15 (MH "Estonia")  
 S16 (MH "France")  
 S17 (MH "Germany+")  
 S18 (MH "Greece")  
 S19 (MH "Hungary")  
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 S21 (MH "Ireland")  
 S22 (MH "Israel")  
 S23 (MH "Italy")  
 S24 (MH "Japan")  
 S25 (MH "South Korea")  
 S26 (MH "Latvia")  
 S27 (MH "Luxembourg")  
 S28 (MH "Mexico")  
 S29 (MH "Netherlands")  
 S30 (MH "New Zealand")  
 S31 (MH "Poland")  
 S32 (MH "Portugal")  
 S33 (MH "Slovakia")  
 S34

(continued on next page)

S35 (MH "Slovenia")  
 S36 (MH "Spain")  
 S37 (MH "Switzerland")  
 S38 (MH "Turkey")  
 S39 (MH "United Kingdom+")  
 S40 (MH "United States+")  
 S41 (MH "Organisation for Economic Co-Operation and Development")  
 S42 TI (oecd or australia\* or austria\* or belgium or belgian or canada or canadian or chile\* or czech\* or denmark or danish or estonia\* or finland or finnish or france or french or german\* or greece or greek or hungar\* or iceland\* or ireland or irish or israel\* or italy or italian or japan\* or korea\* or latvia\* or luxembourg\* or mexico or mexican or netherlands or dutch or holland\* or "new zealand" or norway or norwegian or poland or polish or portugal or portuguese or slovak\* or slovenia\* or spain or spanish or sweden or swedish or switzerland or swiss or turkey or turkish or "united kingdom" or "great britain" or wales or england or scotland or "united states" or uk or us or usa or america\*) OR AB (oecd or australia\* or austria\* or belgium or belgian or canada or canadian or chile\* or czech\* or denmark or danish or estonia\* or finland or finnish or france or french or german\* or greece or greek or hungar\* or iceland\* or ireland or irish or israel\* or italy or italian or japan\* or korea\* or latvia\* or luxembourg\* or mexico or mexican or netherlands or dutch or holland\* or new zealand or norway or norwegian or poland or polish or portugal or portuguese or slovak\* or slovenia\* or spain or spanish or sweden or swedish or switzerland or swiss or turkey or turkish or "united kingdom" or "great britain" or wales or england or scotland or "united states" or uk or us or usa or america\*)  
 S43 S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42  
 S44 (MH "Clinical Trials+")  
 S45 (MH "Nonexperimental Studies")  
 S46 (MH "Case Control Studies+")  
 S47 (MH "Prospective Studies+")  
 S48 (MH "Crossover Design")  
 S49 (MH "Cross Sectional Studies")  
 S50 (MH "Retrospective Design")  
 S51 (MH "Multicenter Studies")  
 S52 (MH "Matched-Pair Analysis")  
 S53 (MH "Epidemiological Research")  
 S54 TI ("case control" or cohort\* or "cross over" or "cross sectional" or "follow up" or followed or longitudinal or pragmatic or practical or random\* or "real world" or "clinical trial") OR AB ("case control" or cohort\* or "cross over" or "cross sectional" or "follow up" or followed or longitudinal or pragmatic or practical or random\* or "real world" or "clinical trial")  
 S55 S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54  
 S56 S3 AND S8 AND S43 AND S55

## 5. Cochrane (Wiley)

Date of Search: 2017-03-30	Field labels:
Number of hits: 242	
Comments:	<ul style="list-style-type: none"> <li>ti,ab = titel &amp; abstract</li> <li>au = authors</li> <li>near/x = adjacent within x words</li> </ul>
#1 ((heart* or cardia* or myocard*) near/3 (fail* or decompensat* or edema* or incompetence or insufficiency)):ti,ab	
#2 (registry or registries or register or registers):ti,ab,au	
#3 (oecd or australia* or austria* or belgium or belgian or canada or canadian or chile* or czech* or denmark or danish or estonia* or finland or finnish or france or french or german* or greece or greek or hungar* or iceland* or ireland or irish or israel* or italy or italian or japan* or korea* or latvia* or luxembourg* or mexico or mexican or netherlands or dutch or holland* or "new zealand" or norway or norwegian or poland or polish or portugal or portuguese or slovak* or slovenia* or spain or spanish or sweden or swedish or switzerland or swiss or turkey or turkish or "united kingdom" or "great britain" or wales or england or scotland or "united states" or uk or us or usa or america*):ti,ab	
#4 #1 and #2 and #3	

## References

- P. Ponikowski, S.D. Anker, K.F. Alhabib, et al., Heart failure: preventing disease and death worldwide, *Eur. Soc. Cardiol.* 373 (9667) (2014) 941–955.
- M. Christ, S. Störk, M. Dörr, H.J. Heppner, C. Müller, R. Wachter, et al., Heart failure epidemiology 2000–2013: insights from the German Federal health monitoring system for the trend HF Germany project, *Eur. J. Heart Fail.* 18 (2016) 1009–1018 Available from <http://onlinelibrary.wiley.com/store/10.1002/ehf.567/asset/ehf567.pdf?v=1&t=j2du2b4z&s=16a03f8bd9b5e07ec4c34414dc54520390d25f78> (cited 2017 May 7).
- K.C. Wollert, G.P. Meyer, J. Lotz, S. Ringes Lichtenberg, P. Lippolt, C. Breidenbach, et al., Intracoronary autologous bone-marrow cell transfer after myocardial infarction: the BOOST randomised controlled clinical trial, *Lancet* 364 (9429) (2004) 141–148 Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0140673604166269> (Jul [cited 2017 Mar 7]).
- R. Agha, D. Cooper, G. Muir, The reporting quality of randomised controlled trials in surgery: a systematic review, *Int. J. Surg.* 5 (6) (2007) 413–422 Available from <http://www.ncbi.nlm.nih.gov/pubmed/18029237> (Dec [Cited 2017 May 7]).
- R. Bolli, A.R. Chugh, D. D'Amario, J.H. Loughran, M.F. Stoddard, S. Ikram, et al., Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial, *Lancet* 378 (9806) (2011) 1847–1857 Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0140673611615900> (Nov [cited 2017 Mar 7]).
- L.H. Lund, J. Oldgren, S. James, Registry-based pragmatic trials in heart failure: current experience and future directions, *Curr. Heart Fail. Rep.* 1–12 (2017) Available from: <http://link.springer.com/10.1007/s11897-017-0325-0> (Feb 28 [cited 2017 Mar 4]).
- K.J. Rothman, *Real world data*, *Value Heal.* 10 (2007) 322–323.
- D. Filippatos, V. Farmakis, V. Bistola, A. Karavidas, A. Mebazaa, A.P. Maggioni, Temporal trends in epidemiology, clinical presentation and management of acute heart failure: results from the Greek cohorts of the Acute Heart Failure Global Registry of Standard Treatment and the European Society of Cardiology-Heart Failure pilot survey [Internet] *Eur. Hear J. Acute Cardiovasc Care*, 2014, 2048872614527012. Available from: <https://doi.org/10.1177/2048872614527012> (Mar 4 [cited 2017 Mar 30]).
- J.O. Oyinlola, J. Campbell, A.A. Kousoulis, Is real world evidence influencing practice? A systematic review of CPRD research in NICE guidances, *BMC Health Serv. Res.* 16 (2016) 299 Available from <http://www.ncbi.nlm.nih.gov/pubmed/27456701> (Jul 26 [cited 2017 Apr 23]).
- J.C. Trullàs, Ò. Miró, F. Formiga, F.J. Martín-Sánchez, M. Montero-Pérez-Barquero, J. Jacob, et al., The utility of heart failure registries: a descriptive and comparative study of two heart failure registries, *Postgrad. Med. J.* 92 (1087) (2016) 260–266 Available from <http://www.ncbi.nlm.nih.gov/pubmed/26739849> (May [cited 2017 Mar 2]).
- European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT), 1-year follow-up outcomes and differences across regions, *Eur. J. Heart Fail.* 19 (3) (2017) 438 Available from <http://www.ncbi.nlm.nih.gov/pubmed/28251778> (Mar [cited 2017 Mar 4]).
- C.-Y. Hu, Y. Xing, J.N. Cormier, G.J. Chang, Assessing the utility of cancer-registry-processed cause of death in calculating cancer-specific survival, *Cancer* 119 (10) (2013) 1900–1907 Available from: <http://doi.wiley.com/10.1002/cncr.27968> (May 15 [cited 2017 Mar 2]).
- A.P. Maggioni, K. Van Gool, N. Biondi, R. Urso, N. Klazinga, R. Ferrari, et al., Appropriateness of prescriptions of recommended treatments in organisation for economic co-operation and development health systems: findings based on the long-term registry of the European society of cardiology on heart failure, *Value Health* 18 (8) (2015) 1098–1104 Available from: <https://doi.org/10.1016/j.jval.2015.08.005>.
- M. Montero-Perez-Barquero, L. Manzano, F. Formiga, M. Roughton, A. Coats, F. Rodríguez-Artalejo, et al., Utility of the SENIORS elderly heart failure risk model applied to the RICA registry of acute heart failure. On behalf of the RICA investigators, *Int. J. Cardiol.* 182 (2015) 449–453.
- A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gøtzsche, J.P.A. Ioannidis, et al., The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration, *PLoS Med.* 6 (7) (2009) e1000100 Available from: <https://doi.org/10.1371/journal.pmed.1000100> (Jul 21 [cited 2017 May 7]).
- D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the prisma statement, *PLoS Med.* 6 (7) (2009) e1000097 Available from: <https://doi.org/10.1371/journal.pmed.1000097> (Jul 21 [cited 2017 May 7]).
- J.P. Higgins, S. Green, *Cochrane Handbook for Systematic Reviews of Interventions* Cochrane Book Series THE COCHRANE COLLABORATION @Available from: <https://dhost.files.wordpress.com/2011/12/cochrane-handbook-for-systematic-reviews-of-interventions.pdf> ([cited 2017 May 7]).
- Mourad Ouzzani, Hossam Hammady, Zbys Fedorowicz, Ahmed Elmagarmid, Rayyan - a web and mobile app for systematic reviews, *Syst. Rev.* 5 (2016) 210, <https://doi.org/10.1186/s13643-016-0384-4> Available from <https://rayyan.qcri.org/> (cited 2017 May 7).
- R Core Team, R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria, 2015 Available from <https://www.R-project.org/>.
- C.D. Mullins, Using Real World Data for Coverage and Payment Decisions: The ISPOR Real World Data Tast Force Report Available from: [https://www.ispor.org/workpaper/RWD\\_TF/RWTFManuscript.pdf](https://www.ispor.org/workpaper/RWD_TF/RWTFManuscript.pdf) (cited 2017 Mar 4).
- R. Mahajan, *Real world data: additional source for making clinical decisions*, *Int. J. Appl. Basic Med. Res.* 5 (2) (2015) 82 Available from <http://www.ncbi.nlm.nih.gov/pubmed/26097811> (cited 2017 Feb 27).
- M.L. Berger, C. Lipset, A. Gutteridge, K. Axelsen, P. Subedi, D. Madigan, Optimizing the leveraging of real-world data to improve the development and use of medicines, *Value Health* 18 (1) (2015) 127–130.

- [23] L. Hartling, M. Hamm, A. Milne, B. Vandermeer, P.L. Santaguida, M. Ansari, et al., Validity and Inter-Rater Reliability Testing of Quality Assessment Instruments [Internet]. Validity and Inter-Rater Reliability Testing of Quality Assessment Instruments, Agency for Healthcare Research and Quality (US), 2012 Available from <http://www.ncbi.nlm.nih.gov/pubmed/22536612> (cited 2017 May 8).
- [24] J.A. Sterne, M.A. Hernán, B.C. Reeves, J. Savović, N.D. Berkman, M. Viswanathan, et al., ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions, *BMJ* 355 (2016) Available from: <http://www.bmj.com/content/355/bmj.i4919> (cited 2017 May 8).
- [25] F. Moen, J. Svensson, K. Steen Carlsson, Assessing the value of cancer treatments from real world data—issues, empirical examples and lessons learnt, *J. Cancer Policy* 11 (2017) 32–37 Available from: <http://linkinghub.elsevier.com/retrieve/pii/S221353831630039X> (Mar [cited 2017 May 7]).
- [26] Graeme L. Hickey, Stuart W. Grant, Rebecca Cosgriff, Ioannis Dimarakis, Domenico Pagano, Arie P. Kappetein, Ben Bridgewater, Clinical registries: governance, management, analysis and applications, *Eur. J. Cardiothorac. Surg.* 44 (4) (2013) 605–614 Available from <https://doi.org/10.1093/ejcts/ezt018>.
- [27] L.H. Lund, J. Oldgren, S. James, Registry-based pragmatic trials in heart failure: current experience and future directions, *Curr. Heart Fail. Rep.* 14 (2) (2017) 59–70 Available from <https://doi.org/10.1007/s11897-017-0325-0> (cited 2018 Feb 10).
- [28] D.M.E. Hoque, V. Kumari, M. Hoque, R. Ruseckaite, L. Romero, S.M. Evans, Impact of clinical registries on quality of patient care and clinical outcomes: a systematic review, *PLoS ONE* 12 (9) (2017) e0183667 Available from <https://doi.org/10.1371/journal.pone.0183667> (cited 2018 Feb 10).