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Selective searching for high quality health-related evidence syntheses – more bias or time gained?

Global Evidence Summit, 13-16 September 2017, Cape Town, South Africa

Background and objectives

Cochrane and other evidence synthesis organisations advocate using a comprehensive search approach consisting of sensitive search strategies conducted in multiple databases. This results in time-consuming search and screening processes. Recent findings suggest that further exploration of the current recommendation is warranted. We aimed to reproduce and complement these findings by investigating a third dataset of Cochrane Reviews regarding the impact of non PubMed-indexed studies on the overall results.

Previous findings

Recently two publications examined different sets of Cochrane Reviews (CR) and retrospectively analysed from which databases the included studies of these reviews originated [1,2]. They investigated whether the exclusion of specific studies had an effect on the meta-analyses (MA) by removing studies that could not be identified via Pubmed [1] or a combination of two databases [2].

Both publications showed that the majority of included studies could be identified either via PubMed or a combination of two databases.

1. Halladay CW, Trikalinos TA, Schmid IT, Schmid CH, Dahabreh IJ. [Using data sources beyond PubMed has a modest impact on the results of systematic reviews of therapeutic interventions](#). J Clin Epidemiol. 2015 Sep;68(9):1076-84.

2. Hartling L, Featherstone R, Nuspl M, Shave K, Dryden DM, Vandermeer B. [The contribution of databases to the results of systematic reviews: a cross-sectional study](#). BMC Med Res Methodol. 2016 Sep 26;16(1):127.

Halladay et al. 2015

Data set:

- Sample: **50 randomly chosen CR** which:
 1. used PubMed/Medline and Embase in their search
 2. included **at least 1 MA with 10 studies**
- Topics: CR of **therapeutic interventions**
- Not specified: which Cochrane groups the selected CR came from and which study designs they included

Results:

- **84% of all publications of included studies were indexed in PubMed**
- **1 out of 50 MA came to a different conclusion after exclusion of non-PubMed-indexed studies**

Hartling et al. 2016

Data set:

- Sample: **129 CR** with at least 1 MA relevant to „**Child Health**”
- Topics: from 3 Cochrane Review groups
 - **Acute Respiratory Infections** (ARI, n = 57)
 - **Infectious Diseases** (ID, n = 38)
 - **Developmental, Psychosocial and Learning Problems** (DPLP, n = 34)
- Study design: CR which only considered **RCT**
- Not specified: type of intervention of included CR

Results:

- Studies included in MA of important outcomes and indexed in **Medline: ARI 85%, ID 92%, DPLP 75%**
- **Change of significance in 6/55 (ARI) und 2/37 (ID) MA when excluding studies not indexed in Medline** (no data available for DPLP)

Our methodes and results

We examined all **47 CR published by the Metabolic and Endocrine Disorders Group** between 01/2011 and 05/2016 which included randomised controlled trials (RCT) or controlled clinical trials (CCT). The reviews were classified by condition and type of intervention. We did not only assess the publications from „included studies“, but also those from studies „awaiting assesement" and "ongoing". We analysed whether the restriction to publications indexed in PubMed resulted in relevant changes to the effect estimates.

Searched sources

All **47 CR** used **MEDLINE, Embase** and the **Cochrane Library**. In addition they used:

- 49% **ClinicalTrials.gov**
- 38% **CINAHL**
- 36% **WHO ICTRP**
- 28% **Web of Science**
- 26% **LILACS**
- 23% **PsycINFO**

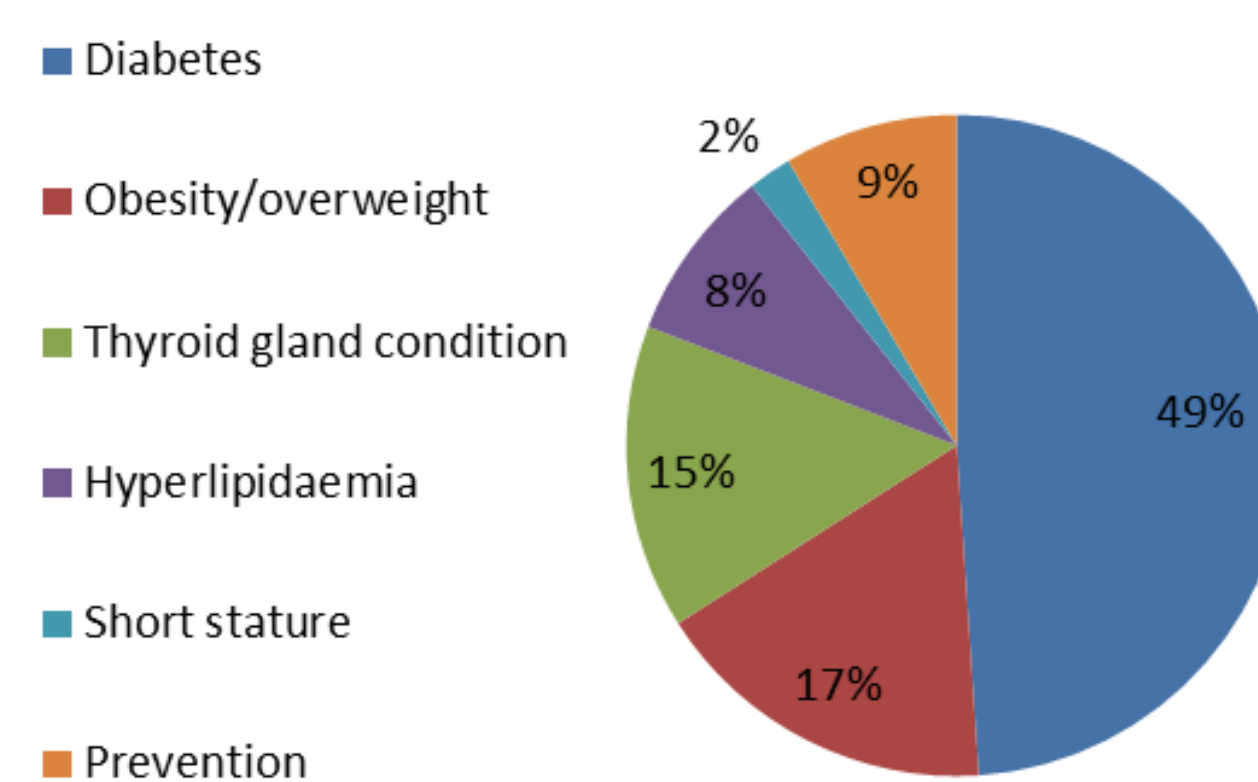
Retrospective identification of included publications (n = 1037)

All included publications → in Pubmed 89%

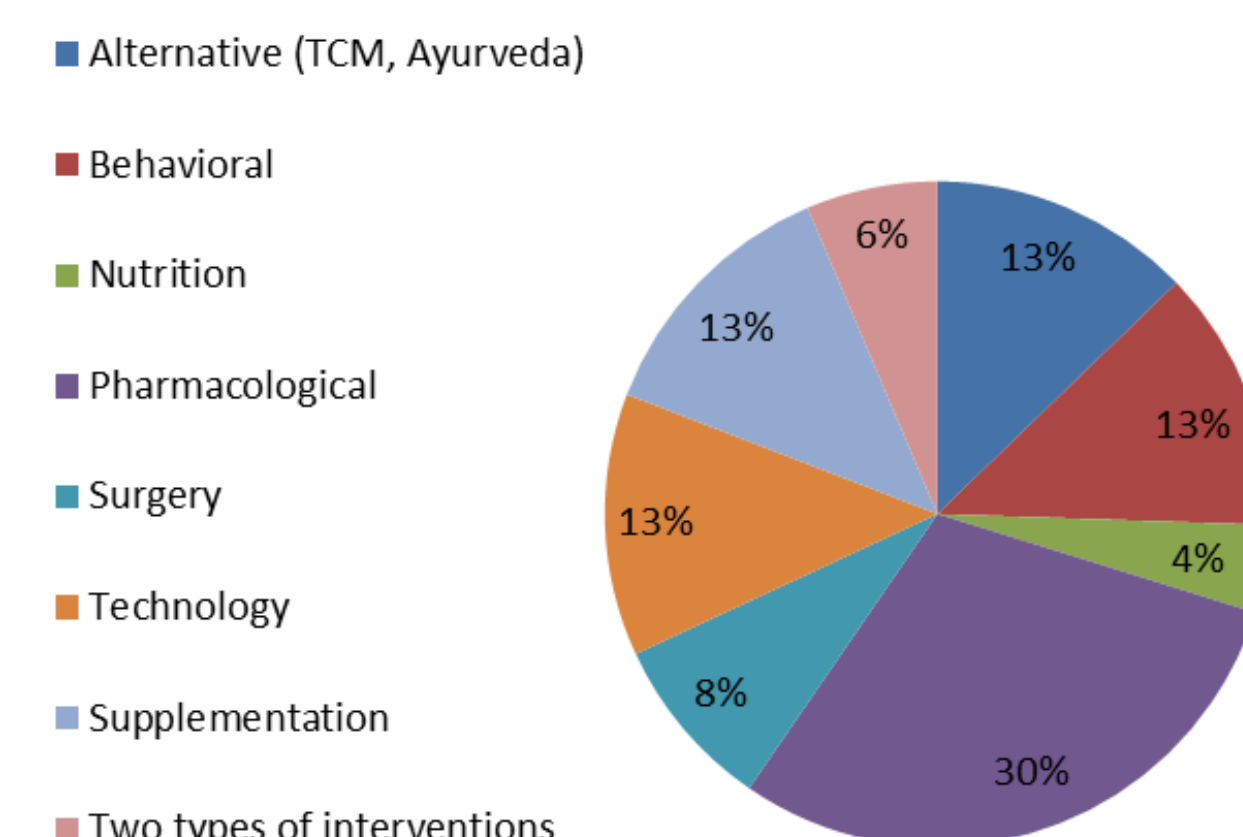
- included studies → in PubMed 90%
- studies awaiting assessment → in PubMed 45%
- ongoing studies → in PubMed 92%

Most non-PubMed-indexed publications (n = 113) were identified in **Embase 36%** and **CENTRAL 25%**

Condition



Type of intervention



Effects on meta-analyses

15 out of 47 CR included trials that were not indexed in PubMed*. **Excluding trials which were not identifiable in PubMed did not have a substantial impact on meta-analyses of these CR**, because the trials did not contribute enough data to alter the effect estimates.

However, evaluation of separate meta-analyses of non-PubMed indexed trials versus trials indexed in PubMed for the same outcome measure showed a trend of greater effect sizes favouring the intervention of the non-PubMed-indexed trials.

* We only analysed trials which were not identifiable in PubMed at all (i.e. no publication on the trial was available in PubMed). We did not analyse trials if publications were partly available in PubMed.

Topic analyses

An analysis of those CR including more than 1/3 of non-PubMed-indexed publications (7 out of 47) showed that these were reviews on **complementary and alternative medicine** (ayurveda, traditional chinese medicine) and **dietary supplements**.

After excluding all 12 CR on both of these topics from our set, the remaining CR's percentage of **included publications available in PubMed increased to 92%**.

Interpretation of current evidence

Existing literature and our data suggest that **a solely PubMed/Medline-based but sensitivity maximising literature search:**

- **has hardly an effect on the results of a MA** when the expected number of included studies is over 10 (Halladay et al. 2015).
- **leads to a negligible risk of bias regarding many types of interventions** (Halladay et al. 2015, Hartling et al. 2016, our data).
- **might not be sufficient in specific contexts**, e.g. topics like development, psychosocial and learning problems (Hartling et al. 2016), complementary and alternative medicine and dietary supplementation (our data), and when searching for study types other than RCT and CCT.

Hence, for some review questions it seems viable to abstain from searching multiple databases. Restricting the search to PubMed/Medline favours identifying studies that are larger and published in higher quality peer reviewed journals [3] and which probably are of better overall quality. More research is needed to confirm under which circumstances (topics and types of interventions) a selective literature search is (not) warranted.

3. Booth A. Over 85% of included studies in systematic reviews are on MEDLINE. J Clin Epidemiol. 2016 Nov;79:165-6.

We thank Philipp Simons for his contribution to the data extraction.