

Placebo's invisible brother – a restricted scoping review of biomedical literature on the nocebo effect

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BACKGROUND

Placebos and their positive effects have been well-researched. However, the negative effects associated with placebos get less attention, despite the fact that nocebo effects are undesired and may exacerbate existing problems or cause new symptoms.

AIMS

To carry out a restricted scoping review to examine how the nocebo effect is represented in the biomedical literature and to identify the main trends and gaps in existing knowledge.

METHODS

We searched MEDLINE, CINAHL, Cochrane, and PsychINFO databases from their inception to 23 December 2020 for any publication with the term “nocebo/s” or “negative placebo effect/s” in the title or abstract. We also searched two registries of clinical trials, EUCTR and ClinicalTrials.gov, for current and recently completed trials.

Five reviewers independently screened the titles, abstracts, keywords, and subject headings of the identified articles and extracted the characteristics of each publication and the context in which it mentioned the nocebo effect. Differences between the reviewers were resolved by consensus.

RESULTS

We identified 3903 unique publications. We excluded 164 papers, whose abstracts could not be assessed, and reviewed 1152 publications. Most of the research was in the fields of medicine (68%) and psychology (18%); only a few publications were concerned with ethical aspects of nocebos.

Publications on nocebo effects or negative placebo effects were far less common than those that mentioned placebo (**Fig. 1**). The two main categories of publications were primary research (n = 413), which were mainly interventional studies in healthy volunteers, and general non-systematic reviews (n = 395) (**Fig. 2**).

Until 2017, non-systematic reviews were published at a rate that matched or outnumbered primary research papers. Nocebos were mentioned in relatively few systematic reviews and meta-analyses (n = 85) (**Fig. 3**).

Most papers investigated the nocebo effect in the context of pain, “quality of healthcare”, or “quality of life”, but in the last two years there were increased numbers of publications on treatment efficacy and adverse effects, mainly in the context of biosimilars/generic medications.

Studies in children and older adults were very rare.

Fig. 1

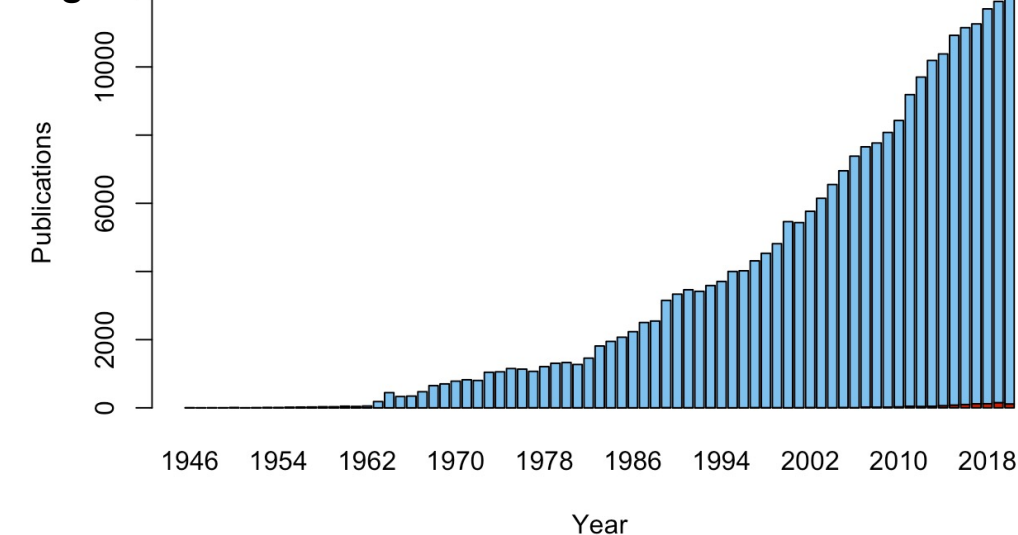
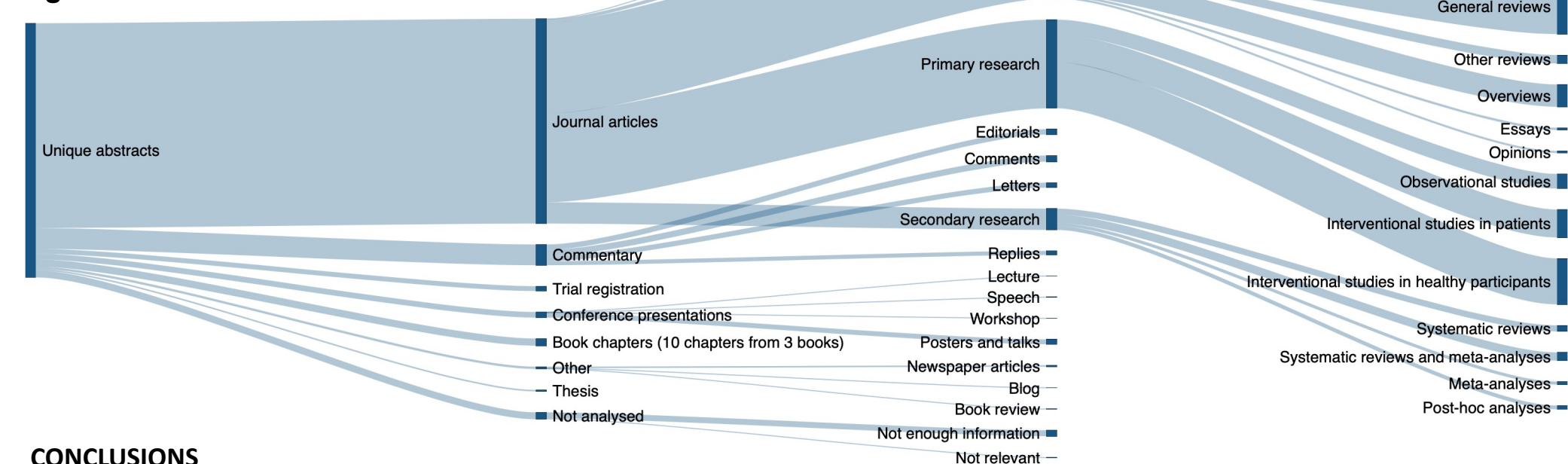


Fig. 2



CONCLUSIONS

Although the numbers of publications concerned with the nocebo effect have increased in the past 20 years, until about three years ago the field was dominated by general reviews based on expert opinion rather than on systematic reviews. More primary research on the nocebo effect is needed in both healthy subjects and patients, including a wide range of clinical conditions, treatment types, and patient groups, followed by high-quality systematic reviews and meta-analyses.

Fig. 3

