

## Evidence for biological markers in tinnitus: A systematic review

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**Introduction:** Biological markers are an emerging field in the area of Otolaryngology. Once identified, they may provide a means of determining the time-course or most effective treatment for an individual with tinnitus, presbycusis or any other otologic disease or impairment. Potential tinnitus biomarkers include mutations in mitochondrial DNA, chromosomal mutations, proteins, hormones, immunoglobulin, cytokine, interleukin, vitamins.

**Purpose:** To evaluate what biological factors are predictive of subjective tinnitus and tinnitus severity. The protocol is registered at PROSPERO: CRD42017070998.

**Methods:** We conducted a systematic search employing CINAHL, PsychINFO, EMBASE, ASSIA, PubMed, Web of Science, Science Direct, and EBSCO Host, using the search terms: tinnitus\* AND gene\* OR protein OR hormone OR immunoglobulin OR enzyme OR cytokine OR interleukin OR lipid OR vitamin OR marker. The initial search was complemented by scanning reference lists from relevant systematic reviews and the included primary studies; citation searching of the included primary studies using Web of Science; and hand searching the last six months of key otology journals.

**Inclusion criteria:** Human subjects with subjective tinnitus. Searches were limited to articles in the English language, published in peer reviewed journals.

**Exclusion criteria:** Animal studies, objective tinnitus, Ménière's disease, Otosclerosis, Chronic otitis media, history of oncology and chemotherapy, ototoxic drugs intake, autoimmune diseases, neurodegenerative or demyelinating disease.

**Results:** All stages of the study were carried out by at least two members of the review team. The titles and abstracts of the studies identified through the initial search has yielded 3801 records, after removal of duplicates and exclusion based on defined criteria 79 records were selected and the full text articles was requested.

Data were extracted using a data extraction form which was developed for purpose and piloted prior to its use. Any disagreements were resolved through discussion or consultation with the third member of the review team. Extracted data included participant information (demographics, baseline characteristics, sample size), country, control, study design, research question, tinnitus characteristics (type of sound, constancy, severity [measure used]), genes and/or biological factor assessed, and key data and findings, conclusions.

Pooled estimates (or narrative synthesis) of the association between biological factors and presence or severity of tinnitus from individual studies will be presented.

**Key words:** Tinnitus, biomarker, hearing loss, genetic

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