Systematic review of prospective studies assessing risk factors to predict the onset of anorexia nervosa

CITATION

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BACKGROUND

Anorexia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED) are the most common eating disorders (ED) (APA, 2013). AN is a developmental disorder, which occurs most often in the peri-pubertal period. Depending on the study, AN incidence varies from 4.2 to 8.3 per 100000 person years (Hoek, 2006). Incidence rates for AN are significantly highest for females aged 15–19 years; approximately 40% of all identified cases. The average point prevalence rate is about 0.29% in young females (Hoek & van Hoeken, 2003). Its lifetime prevalence is estimated from 0.3 to 0.9 for the women and 0.3% for the men (Hudson & al., 2007; Keski-Rahkonen & Mustelin, 2016; Mangweth-Matzek & Hoek, 2017; Raevuori & al., 2009; Smink & al., 2012; Swanson & al., 2011). It is a psychiatric disorder associated with significant morbidity and several recent studies confirm its high mortality rate (Birmingham & al., 2005; Fichter & al., 2006; Millar & al., 2005 in Hoek, 2006).

Although the AN syndrome is recognized for several centuries (Dell'Osso & al., 2016; Habermas, 2015), very few longitudinal population studies tend to identify the risk factors and / or prediction of the onset of this eating disorder.

MATERIALS AND METHODS

This study is a systematic review conducted in order to find original articles, written in English, outlining the results of prospective studies on the association between risk factors / predictors and the onset of AN. The aim is to answer the following questions:

- What are the risk factors, the potential reliable predictors, of the development of anorexia nervosa identified by prospective studies in populations that were initially non-syndromic?

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- Ultimately, what predictors identified by prospective studies make it possible to distinguish subjects who eventually develop anorexia nervosa from those who do not?

The purpose here is to identify: the multiple risk factors, taken as a whole (psychological, family, other) and potentially identified as reliable predictors, to which subjects are exposed and resulting in the development of AN.

Search strategy

The research protocol is built by cooperation with the medical team (endocrinologists and psychiatrists), experts of the health laboratory TAPE (eating disorders and extreme weight) and of the Eating Disorders Center of the Loire department. It is established with reference to the critical appraisal tool ARMSTAR 2. This tool was evaluated and validated by Shea et al (2017). Its reliability has been enhanced (Lorenz et al., 2020). This guideline leads the researcher through a succession of sixteen questions to which the answers are: yes, no, partial yes. The Research strategy summary, according to the AMSTAR check list is included in a table below.

The research question is established using the PICO method (Population, Intervention, Comparator, Outcome). After several preliminary tests, and according to our prior knowledge of the subject, key words are included in order to perceive more broadly the potential studies which would have used expressions synonymous with prospective study (e.g., longitudinal study). Finally, to see all the results of potential studies that would have investigated certain aspects of anorexia, new terms can be included (e.g., alexithymia). A saturation threshold can be obtained when the addition of new terms in the equation does not modify the numerical results obtained. All of these steps are developed and validated by consensus by the authors of this systematic review.

The following databases will be investigated: Pubmed, PsychInfo and Cochrane. Preliminary research on databases found that no systematic review of the previous literature had been carried out on the same subject. The research protocol is registered on the International prospective register of systematic reviews, PROSPERO.

The following search equation will be used to identify publications about risk factors / predictors of anorexia nervosa with a prospective design (these search terms can be adapted for each database as necessary):

Exposure ((risk factors) OR (predictors) OR (predicting) OR (risky eating) OR (High risks) OR (risky eating behaviors) OR (dieting) OR (dieters) OR (dieters) OR (dieting behaviors) OR (eating disturbances) OR (dietary restriction) OR (perfectionism) OR (disordered eating) OR (eating attitudes) OR (alexithymia) OR (performance) OR (SCOFF) OR (EAQ) OR (Q-EDD) OR (Eating Attitudes Questionnaire) OR (body

weight) OR (eating problems) OR (food restriction) OR (restricting) OR (restrictive) OR (pursuit of thinness) OR (body dissatisfaction) OR (self-esteem) OR (body image) OR (teasing) OR (guilt) OR (personality) OR (cognition) OR (cognitive) OR (cognitive restriction) OR (compensatory behaviors) OR (development) OR (emotions) OR (emotional distress) OR (psychometric characteristics))

Outcome ((anorexia nervosa) AND (onset))

Design ((longitudinal study) OR (prospective study) OR (community based study))

Limits ((autism) OR (schizophrenia) OR (diabetes) OR (pregnant) OR (case control) OR (cross sectional) OR (mortality) OR (outcourse) OR (Covid))To complement the database searches, we will review all the references of the selected articles. Moreover, to go around the question, we will search for grey literature.

Inclusion and exclusion criteria

We will include prospective study researching and analyzing risk factors / predictors, specific for anorexia nervosa. These studies may be conducted in non-clinical population, only in general population with subjects identified as not affected by an eating disorder at the start of the study.

The inclusion criteria are as follows:

- The study is an original study published in a journal with an editorial board and peer review.
- The study is a prospective study researching and analyzing risk factors / predictors, specific for anorexia nervosa.
- The subjects of the study were recruited from the general female population and should not be a diagnosed clinical population at T1. The subjects were identified as not affected by an eating disorder at the start of the study.
- The subjects were recruited as female adolescents or pre-adolescents at T1. Moreover, the duration of the reported study was greater than 12 months.

We exclude studies of diagnosed clinical population at T1. More broadly, the studies that are not correspond to all of the inclusion criteria.

We will make comparison between:

- Subjects who, at the end of the study, develop anorexia nervosa in its clinical or subclinical forms.
- And subjects who do not develop anorexia nervosa at the end of the study.

Outcome

Main outcome:

Accuracy of psychological or somatic markers to predict the onset of clinical or sub-clinical anorexia nervosa identified from the current DSM diagnostic criteria, at the end and also on the duration of a prospective study.

The measures of effect will be based on: specificity, sensibility, ROC curves, risk difference.

Additional outcome:

Relationship between potential risk factors and the onset of the clinical and sub-clinical forms of anorexia nervosa measured at the end and also on the duration of a prospective study.

The measures of effect will be based on: relative risks, odds ratios.

Selection and extraction of the articles

Two of the authors of the systematic review will use the following three standard steps to perform the selection of the studies independently:

1. analyzing the articles' titles
2. reading the titles and abstracts
3. reading the full texts

Data will be extracted independently. Researchers will be blind to the decisions of others. At each step there will be systematically a confrontation of point of views between them.
At each step, if there are divergences, a third author will be asked to judge. A fourth expert from the eating disorders referential center may also be called upon to assist in the decision-making process. Consensus or majority will make the final decision, after discussion during a research meeting in the health research laboratory TAPE. Finally, all cumulative data will be verified, one more time, by the three principal investigators.

Only articles that met all the established criteria will be included. After selection of the studies, the relevant data will be registered in a standardized spreadsheet (Excel). The data will be extracted and summarized according to the following standard aspects:

- Principal author
- Publication date
- Sample size
- Age of study subjects
- Duration of the study

- Duration of follow-up and control periods
- Tools and method used by the study at each control period
- Proportion of lost to follow-up subjects at the last control period
- Sub-populations and criteria to define them
- Main outcomes (AN threshold, AN sub-threshold, eventually AN traits)
- Prevalence of the different clinical forms at the end of the study
- Results of Risk factors reviewed and assessed
- Statistical methods used
- Assessment of the reliability of each predictive marker (Yes or No)
- Methodology used for the assessment of the reliability of predictive markers

Evaluating the methodological quality of the studies

In order to assess the quality of the articles selected and their possible biases, the validated checklist for non-randomized studies, pre-established by Downs and Black (1998) will be used. This checklist is based on twenty-seven items that assess the risk of biases in five areas:

- Study quality
- External validity
- Study biases
- Confounding and selection biases
- Power of the study

Each section includes specific instructions and a quotation system. A final overall rating is proposed.

Strategy for data synthesis.

The results will be presented in tables according to the nature of the risk factor assessed. The main characteristics of the selected studies (authors, year of publication, country, cohort name, follow-up period, measuring instruments, completeness measurement, and outcome measurement = development or not of a disorder) will be presented in alphabetical order of the last names of the first authors. The risk factors identified will be put into order according to their type and subtype. Finally, the tables will describe the final samples, the dependent variable (consequence studied = development of a disorder), the main non-significant results and the control variables used in the analyzes.

Analysis of subgroups.

Ultimately, subgroups could be defined by age group according to the cohorts studied by the targeted studies. Indeed, depending on the data classification method used by the authors of the various prospective studies, subgroups could be defined: family history, traumatic experience, etc.

At this stage of our work, we can assume the existence of a variety of subgroups (in particular by referring to the case-control studies which propose different subgroups). But, in the current state of our knowledge on prospective studies, it is not possible to systematize these subgroups.

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