**ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ**

**«ΜΕΘΟΔΟΛΟΓΙΑ ΒΙΟΪΑΤΡΙΚΗΣ ΕΡΕΥΝΑΣ, ΒΙΟΣΤΑΤΙΣΤΙΚΗ ΚΑΙ ΚΛΙΝΙΚΗ ΒΙΟΠΛΗΡΟΦΟΡΙΚΗ»**

ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ

ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ:

# *"Assess the quality of reporting of observational studies in celiac disease published from 2018 to 2022 using the STROBE statement"*

# *«Εκτίμηση της ποιότητας παρουσίασης μελετών παρατήρησης για τη νόσο της κοιλιοκάκης που δημοσιεύτηκαν την περίοδο 2018-2022 χρησιμοποιώντας τις οδηγίες STROBE»*

Ακαδημαϊκό Έτος : 2021-2022

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## ABSTRACT

### Introduction

Observational studies comprise the main body of research on celiac disease. STROBE guidance has been inadequately implemented on observational studies since its introduction.

### Aim

We attempted to explore the quality of reporting of observational studies on celiac disease using the STROBE guidance in years 2018-2022.

### Methods

We searched PubMed and extracted observational studies themselves and through systematic reviews and meta-analyses and associated their characteristics and the corresponding journals' characteristics with the most inadequately reported items of the STROBE checklist using logistic regression. We also investigated the association between the journals' impact factor and the reporting of STROBE sub-items using the chi-square test.

### Results

The reporting of the STROBE checklist items in the 101 included studies was especially insufficient in certain items, such as bias, sample size determination, statistical methods, generalizability, participants and descriptive data. The journal's impact factor was the only factor that correlated positively with the reporting of some STROBE items. High and lower ranked Journals were different in reporting of a considerable number of STROBE sub-items.

### Conclusion

The adherence to certain aspects of the STROBE guidance was insufficient in the included observational studies. A joint effort to efficiently incorporate the whole STROBE checklist in the process of study reporting could improve the quality of observational studies.

**Key Words:** Observational studies, STROBE, quality, reporting, celiac disease, impact factor



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**ΠΕΡΙΛΗΨΗ**

**Εισαγωγή**

Οι μελέτες παρατήρησης απαρτίζουν το κύριο τμήμα της έρευνας στη νόσο της κοιλιοκάκης. Οι οδηγίες της λίστας STROBE δεν έχουν εφαρμοστεί επιτυχώς στις μελέτες παρατήρησης από την εισαγωγή της μέχρι σήμερα.

**Σκοπός**

Επιχειρήσαμε να διερευνήσουμε την ποιότητα της παρουσίασης των μελετών παρατήρησης στην κοιλιοκάκη σύμφωνα με τις οδηγίες της λίστας STROBE για την περίοδο 2018-2022.

**Μέθοδοι**

Ερευνήσαμε στη βάση δεδομένων PubMed και εξήγαμε αυτούσιες μελέτες παρατήρησης, και επιπλέον μέσω συστηματικών ανασκοπήσεων και μετα-αναλύσεων, και συσχετίσαμε τα χαρακτηριστικά τους και εκείνα των αντίστοιχων επιστημονικών περιοδικών με τα ελλιπέστερα αναφερόμενα αντικείμενα της λίστας STROBE, χρησιμοποιώντας λογαριθμική παλινδρόμηση. Επιπλέον, διερευνήσαμε τη συσχέτιση μεταξύ του συντελεστή απήχησης του εκάστοτε περιοδικού και της παρουσίασης όλων των υποκατηγοριών των αντικειμένων στη λίστα STROBE, χρησιμοποιώντας το $\chi^2$ τεστ.

**Αποτελέσματα**

Η παρουσίαση των αντικειμένων της λίστας STROBE στις 101 συμπεριλαμβανόμενες μελέτες ήταν ιδιαίτερα ανεπαρκής σε συγκεκριμένα αντικείμενα όπως η μεροληψία, ο καθορισμός του μεγέθους δείγματος, οι στατιστικές μέθοδοι, η γενίκευση, οι συμμετέχοντες και τα περιγραφικά δεδομένα. Ο συντελεστής απήχησης των περιοδικών ήταν ο μόνος παράγοντας που συσχετίζονταν θετικά με την επαρκή αναφοράορισμένων αντικειμένων της λίστας STROBE. Τα υψηλά στη βαθμολόγηση επιστημονικά περιοδικά διέφεραν στην παρουσίαση σημαντικού αριθμού υποκατηγοριών των αντικειμένων στη λίστα STROBE σε σχέση με τα αντίστοιχα χαμηλά στη βαθμολόγηση.



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**Συμπεράσματα**

Η συμμόρφωση με συγκεκριμένες παραμέτρους της οδηγίας STROBE ήταν ανεπαρκής στις συμπεριλαμβανόμενες μελέτες παρατήρησης. Μία συντονισμένη προσπάθεια για να ενσωματώσουμε ουσιαστικά ολόκληρη τη λίστα STROBE στη διαδικασία παρουσίασης των μελετών θα βελτίωνε την ποιότητα των μελετών παρατήρησης.

**Λέξεις- κλειδιά**: μελέτες παρατήρησης, STROBE, ποιότητα, κοιλιοκάκη, συντελεστής απήχησης



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## INTRODUCTION

The vast majority of research papers published in clinical journals are observational studies [1,2]. Although interventional trials are traditionally supposed to provide more solid and valid evidence in the clinical field, observational studies contribute to a considerable extent to the clinical and public health knowledge [3].

Initially the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement was published in order to standardize the reporting of observational studies and provide a checklist of items to be addressed ensuring their quality [4]. This need arose as the reporting of observational research was not adequate enough as demonstrated in previous studies [5,6]. Moreover there are weaknesses inherent to the nature of study designs used in observational studies, that cannot be easily overcome. For instance selection bias, attrition bias and residual confounding are limitations of the longitudinal studies.

The compliance to the STROBE guidance differs per journal. Some journals require the submission of the STROBE checklist, whereas other journals only recommend the use of the STROBE statement in their instructions for authors or do not require the compliance to any reporting statement at all.

Several studies have attempted to relate the reporting quality with certain features of the journals such as publication type [7,8], journal's impact factor (IF)[9] and STROBE checklist endorsement policy [10].

Celiac disease as an immune mediated enteropathy triggered by gluten is a quite common medical condition. It affects around 1 % of the population and its incidence has increased rapidly over the last decades. Celiac disease remains a challenging diagnosis and its features pose challenges on both its pathogenesis, diagnosis and its management. Gaps that remain to be solved are the different phenotypes of the disease, the inconsistency between histology, serology and clinical presentation, and the identification of high risk populations and markers of preclinical disease [11]. As an autoimmune and heterogeneous disorder linked with other clinical disorders both laboratory and clinical research have contributed tothe understanding of its many aspects [12]. Studies on celiac disease are



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mainly observational and the quality of their reporting has rarely been addressed [12,13].

Our study attempts to evaluate the quality of reporting of 101 observational studies in celiac disease published in 2018-2022 according to the STROBE checklist and statement. Eligible studies were retrieved from PubMed and their features as well as journal characteristics were analyzed and associated with the reporting of the STROBE list items. We also evaluated the association of the journals' IF to the reporting quality of the STROBE list sub-items.

## METHODS

We searched in PubMed for "celiac" or "coeliac" disease as termsappearing in the title or abstract. The search itself was limited to the following criteria: systematic review (SR) or meta-analysis or observational study as article type. We limited our search to the timeperiod 2018-2022. We then went through the reference list of the SRs and meta-analyses in order to trace observational studies that were included in them, either case control, cohort or cross sectional studies. We evaluated the full text of all initially eligible studies and included in our review only observational studies on celiac disease published in 2018- 2022.

Studies that were not full papers or observational in nature (e.g. case series, literature reviews, expert reviews) were excluded. Moreover some of the studies were excluded as their full text could not be accessed, they were not in English, or they had other than celiac disease study objective, in spite of including among others celiac disease participants, as shown in the flowchart in figure 1.

We extracted data from the selected papers (research question, sample size, design type, study population, continent of study) and information on the characteristics of the journals (journal reporting recommendation, IF, affiliation with a medical society) using an Excel form. We traced the following categories of the research question: extraintestinal manifestations of celiac disease and associated diseases, such as microscopic colitis, etiology and pathogenesis incorporated in a



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multifactorial model including genetics, screening and diagnosis that include both clinical and laboratory/interventional (endoscopic) procedures, follow up of the patients and therapy, that is gluten free diet. With regards to the type of design, studies were categorized as follows: cohort including birth cohort studies, case-control including nested case-control studies, cross-sectional, retrospective chart reviews and population- based cohort studies.

Journals were divided into high-ranked (IF=6 or greater) and lower ranked (IF < 6) according to their impact factor. We arbitrarily used thecut -off value of 6 for IF, as journals with IF = 6 or greater represent the top 5% of the highest ranked journals.

We first presented the distribution (proportions) of the papers according to study and journal characteristics using graphs (figure 2). In table 1 the proportion of the included papers that reported adequately each item and sub-item is shown. We considered an item adequately reported only when all its sub-items were appropriately addressed. When the reporting of a sub-item was considered optional, it did not contribute to the evaluation ofthe involved item.

Some of the items of the STROBE list are not addressed in all studies as they are not relevant due to the specific study design. For example the sensitivity analyses, the loss to follow up and the matching of cases and controls are not applicable in all published studies. In this case they were not taken into account in the total score of STROBE list. This observation along with the variable significance of sub-items have prevented us from using the total STROBE score to point out statistical associations. In this regard we explored the proportion of reporting of all sub-items in the STROBE checklist in all included studies, where they should appear according to the study design and separately in low and higher ranked journals. We compared with a chi square test the proportion of addressed sub-items in the STROBE checklist among high ranked and lower ranked journals and defined statistical significance at p=0.05 (table 2).

Logistic regression was utilized to explore associations between journal and study's features and the six most inadequately reported items (we only included items and not sub-items) from the STROBE checklist (table 3). Again we did not evaluate sub-items that are only suggested and thus are considered optional e.g. presentation of a flow diagram or a sensitivity analysis. The poorly reported items and their proportion of reporting in



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the whole sample of studies were the following: item 9 (bias) in 29%, item 10 (size) in 29% , item 12 (statistics) in 14% , item 13(participants) in 58% , item 14 (descriptive) in 19% and item 21 (generalizability) in 30% of all included studies (table 1).

We included the following features in univariate analysis based on their reasonably possible impact on the reporting quality of the poorly reported items: Society journal, Journal reporting recommendation, population of the study, IF, research question, and continent of the study. We collected information regarding the affiliation with a scientific/medical society and the reporting recommendations from the journals' webpages.

## RESULTS

Of the 265 manuscripts identified through PubMed searching, 101 full text manuscripts were finally included in our review. Out of the 164 articles excluded, 16 had no observational design, 21 were not discussing celiac disease, 3 were not written in English and 4 were not found in full text. 144 were systematic reviews and meta-analyses and we had to go through their references and extract 24 observational studies published in 2018- 2022 (figure 1).

Most studies were located in Europe (64%) and much fewer came from Asia (15%) and North America 12%. The median (106-947) sample size was 237. The main research question in the included studies was "extraintestinal manifestations of celiac disease and associated diseases" (44%) followed by "etiology" (18%) and "follow up" (16%). The population of the studies was evenly distributed, 41% of the studies had adult participants and 47% included only pediatric population. Most of thestudies (52%) were cohort ones (including birth cohort studies) and the rest of the studies were mainly distributed equally between case control and cross-sectional studies (figure 2).

Sample size of the study population did not vary much by research question. Irrespective of the research question, included studies were based mainly on a sample ranging between 100 and 999 participants, while studies with the research question of "gluten free diet" and "follow up" had comparatively a higher proportion of samples < 100 participants (figure 3).



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Thirty two per cent (n=32) of included studies were published in journals with an IF ≥ 6 and 68% (n=69) in lower ranked journals .

The reporting quality of the manuscripts was variable and in general inadequate. Only 2 % of the 101 papers used the STROBE statement as guidance. However none of them mentioned having used any other reporting statement. Only one paper (1%) of the included ones went through all the 22 items of the STROBE checklist.

Table 1 shows and compares the proportion of reporting of all sub-items of the STROBE list among the IF categories of journals. In particular, a statistically significant difference was found in the quality of reporting with regards to the following fields: study's design reporting in the title or abstract, methods of assessment and their comparability, study size, addressing potential bias and missing data, presentation of flow diagram, summarizing follow up time and translating estimates of relative risk into absolute risk. Moreover other analyses done were reported more commonly in high ranked journals.

However the proportions of reporting even in the journals with higher IF were quite low for some of the above items. They amounted to 47% for efforts to address bias, 21% for absolute risk estimation, 44% for study size determination and 31% for the item of analyzing missing data. Only 25% and 22% of the studies in high ranked journals indicated the number of participants with missing data and discussed the potential of generalizability, as shown in table 2.

Table 2 shows the association between the journal and manuscript characteristics (research question, continent of study, IF, society journal, the population under study and journal reporting recommendation) and the reporting of six specific items (the ones that had the lower reporting rate in the articles). As illustrated, the IF is the common denominator of the quality of reporting of these specific items. Nevertheless most of the journal and manuscript characteristics were not associated with the reporting of any of the above six items.

In particular, regarding the item of statistics, manuscripts published in journals with higher IF were more likely to report statistics in detail. Interestingly attaching the strobe list *vs* giving no special recommendation had a lower odds of reporting this item. Manuscripts published in journals with a higher IF were more likely to report addressing potential sources of bias than manuscripts published in lower ranked journals. Reporting of



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descriptive statistics was positively associated with the journal's high IF, however following any recommendations *vs* no recommendations, as indicated in the journal's author instructions, showed smaller odds for the above reporting. The reporting of the calculation of the study size, was more commonly discussed in studies with adult population, however it appeared less in journals affiliated with a medical society. The reporting of details regarding participants was positively and statistically significantly associated only with the journal's high IF.

## DISCUSSION

This is to our knowledge the first study that attempts to explore the quality of reporting of observational studies focused on celiac disease over the last 5 years. The STROBE guidance and its elaboration have been published more than a decade ago, a time frame which should reasonably allow for its generalized implementation.

The reporting quality of the studies included was insufficient in certain items and sub-items of the STROBE checklist. Although the median STROBE score was 17 ( 15-18), only 1% of the examined papers included all items and 72-85 % of the papers did not address items, such as statistical methods, management of study size and bias, descriptive data (missing data and follow up time), data regarding participants and generalizability.

Most of the studies (44%) focused on the extraintestinal manifestations of celiac disease and diseases that accompany this heterogeneous clinical entity. Clinical research has been increasingly exploring the wide spectrum of celiac disease, as its classical type tends to comprise the minority of the possible manifestations of this disorder [14]. Since the treatment is quite straightforward, that is the avoidance of gluten in diet, the majority of the remaining studies addressed the question of etiopathogenesis (18% of studies ), including the immunophenotypes linked to the appearance of celiac disease, and the follow up (16% of studies) that should probably be prioritized given the lifelong nature and management of the disease.

Most of the studies were based in Europe (64%), though the incidence of celiac disease does not seem to differ much in other continents e.g. Africa



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[15], a finding that could be attributed to the availability of funding for research in Europe. The increasing diagnosis of celiac disease in the adult population seems to have steered research towards the adult population, as shown by the increased proportion of included studies concerning this age group.

Most of the included studies (52%) were cohort studies, though many authors, even in high ranked journal, did not clearly state the study design, especially when it involved diverse features e.g. cohort or case control studies with cross sectional analysis. In particular only 67% of the authors included the study design in the title or abstract, they preferablymentioned it in the "introduction" or "methods" section.

Although the STROBE statement was supposed to improve the quality of study reporting, many studies in accordance to our study have demonstrated that the adherence to the STROBE criteria of reporting has been suboptimal in certain items [8-10,16-21]. Whether the STROBE statement and its elaboration and explanation [22] have improved, the reporting quality after its publication in 2007 remains equivocal [10, 23].

In our review most of the items of the STROBE list were inadequately reported in the included manuscripts. However some of them, for instance the reporting of the study design in the section of title or abstract, do not actually influence the validity or methodological quality of the study and relate only to the transparency of data. The methodological quality can be evaluated with other assessment tools such as ROBINS-I, GRACE and MORE [24].

It is important that bias, as a systemic error that can lead to an incorrect interpretation, be considered during the design and conduct of study. The fact that it cannot be corrected afterwards renders nearly necessary the proactive addressing of potential sources of bias early in its design. We have observed that in the majority of the studies the authors did not address specific to the study design types of bias, a consideration that could ideally improve the validity of the studies. 29% of studies in our review have missed to address bias in accordance with other previous studies [8-10,17-20].

Regarding the sample size authors must "indicate the considerations that determined the study size or formal sample size calculations if they were done" [22]. When sample size calculation is not mentioned, reviewers may well assume that it was not addressed properly. While a small sample



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lessens the external validity and clinical value of the study, a very large sample size may be considered ethically inappropriate.

Although missing data and loss to follow up are common inherent weaknesses in cohort studies, not much seems to have been done in the direction of addressing this issue. In our review the corresponding items were insufficiently reported, in particular only reported in 17% (20% for the number of participants with missing data) and 42% of manuscripts accordingly. The statistical methods used to attenuate the above issues, such as multiple imputation or augmented inverse probability weighting [25] seem to be implemented quite rarely in the observational studies, as ascertained in our review. The lack of long term follow up and consequently of long term population outcomes owing to the great difficulties in adherence to the gluten free diet remains one of the special features of celiac disease that should be addressed in the future.

"The limitations of the study" and "the generalizability of the study results" were reported in 78% and 30% of studies accordingly. Adequate reporting of these items is considered a prerequisite for the study's internal and external validity. Interestingly the item of generalizability was less adequately reported in high ranked journals compared to the lower ranked ones. Though observational studies, unlike randomized controlled trials, are typically supposed to offer valid data for extrapolation to other populations, few studies in our review have commented on the generalizability of their findings.

Another observation that is worth consideration is that, although some authors attached the STROBE checklist completed on submission of their manuscript, they actually did not include accurately all the items. This probably implies that attachement of the STROBE list does not always guarantee quality in reporting. In our study even in journals that required the attachement of the completed STROBE list, the median score of completed items was 17 (15-21). Similarly Swords et al. showed that the endorsement of STROBE guidelines was useful but not sufficient to guarantee a high quality of reporting [10]. Probably a stricter verification of adherence to the STROBE guidance, implemented carefully by the journal editors is required in this direction.

The quality of reporting of many items of the STROBE checklist in the included studies seems to be associated with the journal's impact factor as confirmed in both statistical analyses. This has been shown to a variable



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extent in other studies specifically as for the reporting of the estimates and their precision [16] and the reporting of statistical methods [9].

The limitations of our study should be clearly mentioned. First we limited our search to PubMed database and studies published in English increasing the possibility of publication bias. Other databases like Embase could have provided more studies probably with different features and results. However PubMed database is thought to contain quite representative research papers. Our feeling is that the number of studies included is adequate for safe assumptions.

Second we have not been strict in our appraisal of the adherence to some of the STROBE checklist's items and sub-items. For instance we have not taken into account the report of the confidence intervals in terms of precision or the rationale for the selection of certain confounding factors in each study when evaluating the quality of reporting of the corresponding item. Even before the STROBE guidance publication Pocock et al. had already commented that the selection of and adjustment for potential confounders needs greater clarity, consistency, and explanation in observational studies [6].

Third the writers were not blinded to the name of the journal which might have affected their judgement regarding the appraisal of adherence to the STROBE checklist.

Notwithstanding the clear statement of the purpose of STROBE guidance, it has been used inappropriately as a tool for the assessment of methodological quality or as a guide to plan biomedical research [26]. Nevertheless the STROBE checklist should remain a formal reporting guideline of observational research and not degenerate into a typical process.



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## CONCLUSION

The findings of this study could provide both authors and writers with important information on which aspects of reporting they should focus in order to increase the reporting quality of observational studies in celiac disease. Appropriate and detailed implementation of the STROBE checklist from the journals' side and increased awareness of inadequately reported items by the authors can optimize the quality of observational research.

It is widely accepted that a well-designed observational study canoutweigh a poorly designed randomized study design on a equivalent research objective [27]. This renders imperative the prioritization of the implementation of high methodological and reporting quality standards in observational research.



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Figure 1. Flow diagram of included and excluded studies

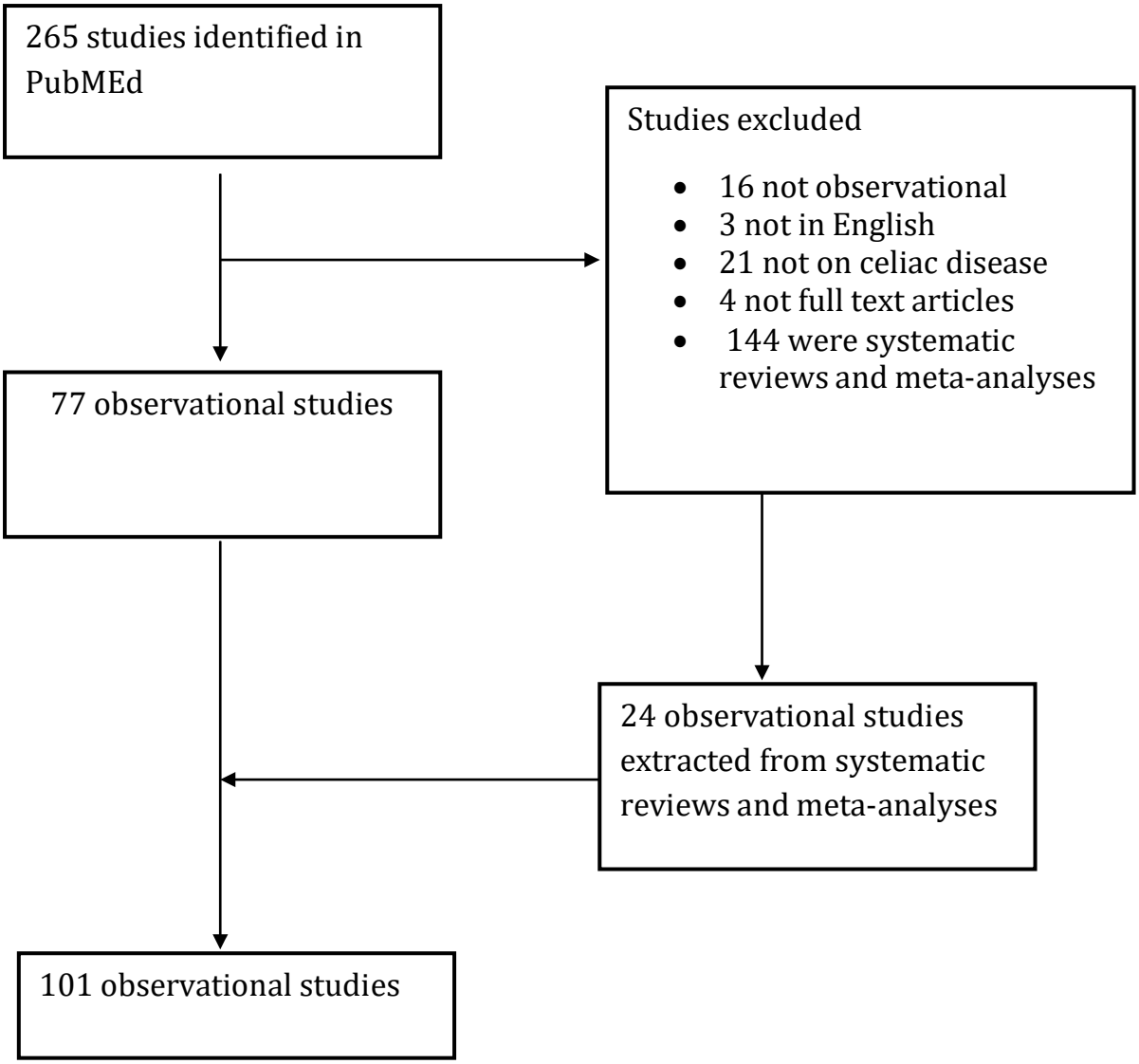




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Figure 2. Characteristics of observational studies on celiac disease in 2018-2022

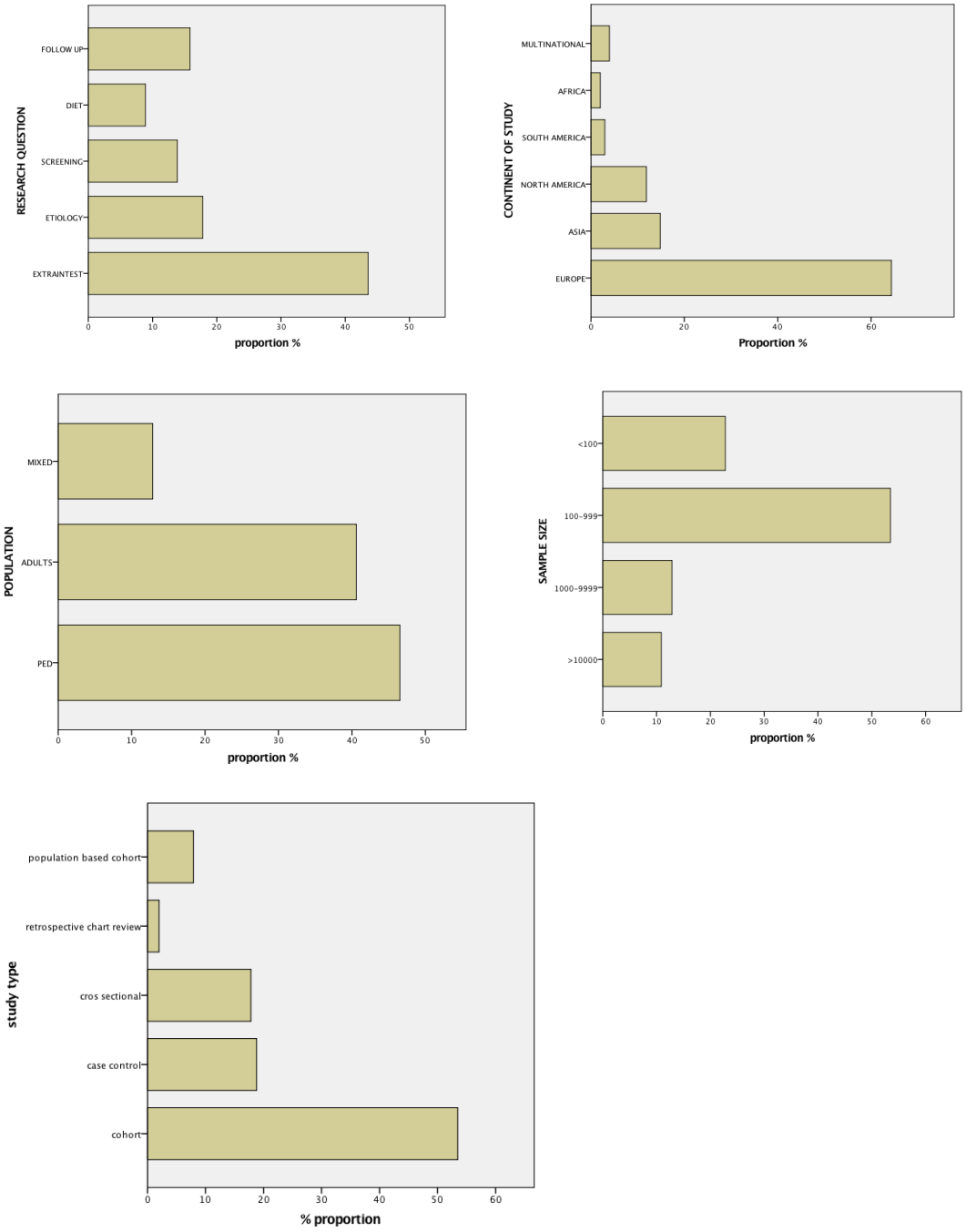




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Figure 3. Sample size by type of research question of observational studies on celiac disease in 2018-2022

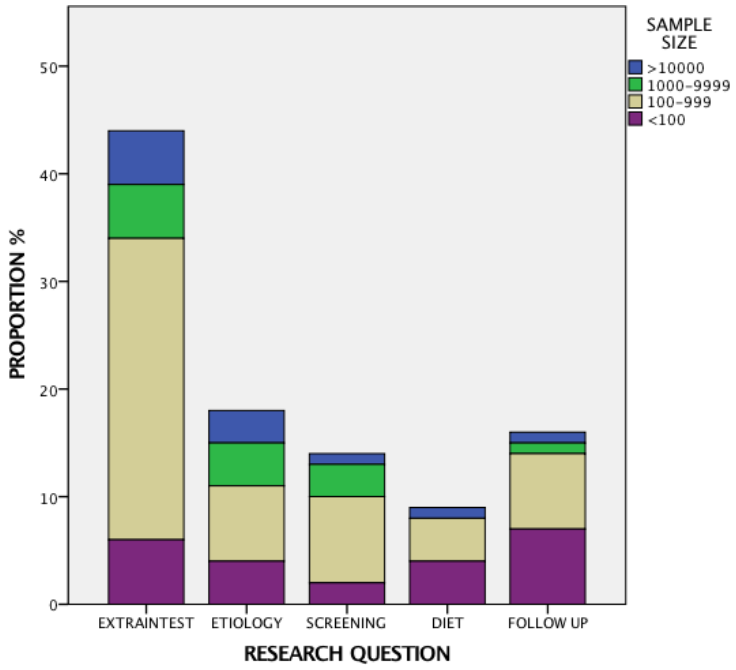




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**Table 1.** % Proportion of papers that addressed adequately each of the STROBE checklist items and sub-items from the whole sample of included studies (n =101)

| | Item No | Recommendation | Studies % |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 66% |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 96% |
| | | | 66% in total |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 97% |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 97% |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 95% |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 97% |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br><br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br><br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants | 94% |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br><br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case | 100% |
| | | | 94% in total |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 96% |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 90% |
| Bias | 9 | Describe any efforts to address potential sources of bias | 29% |
| Study size | 10 | Explain how the study size was arrived at | 29% |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 98% |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 99% |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 99% |
| | | (*c*) Explain how missing data were addressed | 17% |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br><br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br><br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy | 42% |
| | | (*e*) Describe any sensitivity analyses | 66% |
| | | | 14% in total |



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| **Results** | | | **Studies** |
|---|---|---|---|
| | | | **%** |
| Participants | 13 | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 68% |
| | | (b) Give reasons for non-participation at each stage | 62% |
| | | (c) Consider use of a flow diagram | |
| | | | 58% in total |
| Descriptive data | 14 | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 85% |
| | | (b) Indicate number of participants with missing data for each variable of interest | 20% |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) | 71% |
| | | | 19% in total |
| Outcome data | 15 | *Cohort study*—Report numbers of outcome events or summary measures over time | 97% |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure | |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures | |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 97% |
| | | (*b*) Report category boundaries when continuous variables were categorized | 97% |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 8% |
| | | | 96% in total |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 74% |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 98% |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 78% |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 87% |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 30% |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 79% |



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**Table 2.** Proportion of reporting of the sub-items in the STROBEstatement in a total of 101 observational studies involving celiac diseaseby impact factor group

| | % Reporting sub-item | | |
|---|---|---|---|
| **STROBE items** | **Lower IF PAPERS (IF<6)(n=69)** | **Higher IF papers (IF>6)(n=32)** | **P Value** |
| 1. a. Study's design | 59% | 81% | 0,03 |
| b. Summary | 98% | 99% | 0,95 |
| 2. Scientific background | 97% | 97% | 0,95 |
| 3. Objectives | 97% | 97% | 0,95 |
| 4. Key elements of study design | 94% | 97% | 0,56 |
| 5. Setting of the study | 95% | 100% | 0,23 |
| 6. Participants | | | |
| a. selection | 91% | 100% | 0,08 |
| b. matching criteria | 100% | 100% | 1 |
| 7. Definition of all variables | 94% | 100% | 0,16 |
| 8. Data sources/measurements | 86% | 100% | 0,02 |
| 9. Efforts to address bias | 22% | 47% | 0,01 |
| 10. Study size | 23% | 44% | 0,03 |
| 11. Quantitative variables | 97% | 100% | 0,32 |
| 12. Statistical methods | | | |
| a. Details of all statistical methods used | 99% | 100% | 0,5 |
| b. Subgroups and interactions | 99% | 97% | 0,6 |
| c. Missing data | 12% | 31% | 0,02 |
| d. loss to follow-up/matching/sampling strategy | 36% | 52% | 0,21 |
| e. Sensitivity analyses | 59% | 79% | 0,22 |
| RESULTS | | | |
| 13. Participants | | | |
| a. Reporting of their numbers at each stage of the study | 84% | 97% | 0,06 |
| b. Reasons for non-participation at each stage | 61% | 63% | 0,81 |
| c. Flow diagram | 31% | 55% | 0,02 |
| 14. Descriptive data | | | |
| a. Characteristics of study participants | 84% | 88% | 0,65 |
| b. Number of participants with missing data | 17% | 25% | 0,37 |
| c. Follow-up time | 62% | 85% | 0,045 |
| 15. Outcome data | 97% | 97% | 0,95 |
| 16. Main results | | | |
| a. Estimates and their precision | 96% | 100% | 0,23 |
| b. Category boundaries | 95% | 100% | 0,21 |
| c. Absolute risk estimation | 3% | 21% | 0,0049 |
| 17. Other analysis done | 65% | 94% | 0,002 |
| 18. Summary of results | 97% | 100% | 0,3 |
| 19. Limitations of study | 78% | 78% | 1 |
| 20. Overall interpretation | 91% | 78% | 0,065 |
| 21. Generalizability | 33% | 22% | 0,24 |
| 22. Funding | 78% | 81% | 0,73 |

IF=Impact Factor



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Chi-square test p – values were used to express the association between proportions for reporting an item among the two categories of papers

**Table 3.** Logistic regression analysis on the association between study and journal characteristics and the reporting of the six most inadequately reported items in the included studies (n=101)

| | OR (95% Cl) for reporting items | | | | | |
|---|---|---|---|---|---|---|
| | Item 9 (bias) | Item 10 (size) | Item12 (statistics) | Item 13 (participants) | Item 14 (descriptive) | Item 21 (generalizability) |
| **Society journal** | 0,4(0,2-1,0) | **0,3(0,1-0,8)** | 1,4 (0,4-4,4) | 0,5(0,2-1,3) | 1,0(0,3-3,0) | 0,7(0,3-1,7) |
| **Journal reporting recommendation** | | | | | | |
| None | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) |
| Follow any guideline | 0,9(0,2-3,5) | 1,7(0,5-5,9) | 0,2(0,03-1,1) | 1,7(0,5-5,6) | **0,1(0,01-0,8)** | 0,8(0,2-2,5) |
| Follow STROBE | 0,6(0,2-2,0) | 1,5(0,4-5,5) | 0,4(0,1-1,5) | 0,9(0,2-3,5) | 0,3(0,08-1,3) | 0,4(0,1-1,5) |
| Attach STROBE checklist | 0,9(0,2-3,2) | 0,9(0,2-4,3) | **0,1(0,02-0,9)** | 1,0(0,2-4,1) | 0,3(0,08-1,5) | 0,8(0,2-3,2) |
| **Impact Factor** | **1,2(1,07-1,4)** | 1,06(0,9-1,2) | **1,1(1,03-1,3)** | **1,1(1,01-1,2)** | **1,1(1,07-1,2)** | 1,0(0,9-1,1) |
| **Research question** | | | | | | |
| Extraintestinal/correlations | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) |
| Etiology | 1,4(0,3-6,0) | 0,9(0,3-3,1) | 0,2(0,04-1,1) | 3(0,9-9,4) | 0,4(0,08-2,2) | 1.026 (0,3-3,5) |
| Screening | 3,4(0,7-16,5) | 1,0(0,3-3,7) | 1,5(0,3-6,7) | 0,8(0,2-3,4) | 0,8(0,1-5,0) | 1,48 (0,4- 5,3) |
| Gluten free diet | 3,2(0,6-16,7) | 0,0 | 0,5(0,07-3,2) | 1,5(0,3-7,0) | 1,2(0,2-7,0) | 2,1 (0,5-9,3) |
| Follow up | 0,5(0,05-6,1) | 0,4(0,1-1,8) | 0,3(0,03-3,9) | 1,8(0,5-6,1) | 2,1(0,3-14,0) | 0,9 (0,2-3,3) |
| **Population of the study** | | | | | | |
| Pediatric | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) |
| Adults | 1,6(0,6-4,2) | **3,0(1,1-8,2)** | 0,7(0,2-2,3) | 1,2(0,5-2,9) | 1,4(0,5-4,5) | 1,8(0,4-2,6) |
| Mixed | 1,3(0,3-5,0) | 3,6(0,9-13,4) | 0,3(0,03-2,8) | 0,5(0,1-2,4) | 0,4(0,05-3,9) | 1,4(0,4-5,1) |
| **Continent on study** | | | | | | |
| Europe | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) | (ref.) |
| Asia | 0,5(0,1-3,8) | 0,6(0,1-2,5) | 0,2(0,03-1,9) | 0,4(0,1-1,7) | 0,6(0,06-7,1) | 0,3(0,06-1,4) |
| North America | 0,2(0,01-1,8) | 1,3(0,3-4,8) | 0,0 | 0,9(0,2-3,3) | 0,4(0,03-6,9) | 0,9(0,3-3,6) |
| South America | 0,3(0,03-3,5) | 0,0 | 0,09(0,005-1,5) | 0,0 | 0,2(0,01-5,7) | 0,9(0,08-11,3) |
| Africa | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 | 0,0 |
| Multinational | 0,0 | 0,0 | 0,0 | 1,8(0,2-13,8) | 0,0 | 0,6(0,06-6,6) |

Bold type represents OR estimations whose 95% confidence interval did not include 1

OR values close to zero were attributed to the small number of multinational studies and studies located in Africa, South America and were not included in the results of the statistical analysis



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