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Diagnostic accuracy of different ultrasound signs for detecting adnexal torsion: systematic review and meta-analysis

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Contribution

What are the novel findings of this work?

Quality of studies assessing the role of different ultrasound signs for diagnosing adnexal torsion was moderate. There is significant heterogeneity among studies. Therefore, investigating this unique clinical issue using meta-analysis might lead to erroneous conclusions as to the diagnostic capabilities of sonographic signs in the diagnosis of adnexal torsion.

What are the clinical implications of this work?

This meta-analysis shows the current evidence about the role of ultrasound in diagnosing adnexal torsion. Most of the classical ultrasound signs are specific for diagnosing this entity. These findings support the use of ultrasound in this clinical setting

Abstract

Objective. To evaluate the diagnostic accuracy of different ultrasound signs for diagnosing adnexal torsion (AT), using surgery as the reference standard.

Methods. A search was performed in PubMed/MEDLINE, CINAHL, Scopus, Cochrane, ClinicalTrials.gov and Web of Science databases (January 1990 to November 2021) for studies evaluating the presence of ovarian edema, an adnexal mass, Doppler flow findings and the whirlpool sign as ultrasound signs (index tests) for detecting AT, using surgical findings as reference standard. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool was used to evaluate the quality of the studies. Pooled sensitivity, specificity, positive and negative likelihood ratios were calculated separately, and the post-test probability of AT following a positive or negative test also was determined.

Results. The search identified 1267 citations after excluding duplicates. Twenty studies were ultimately included in the qualitative and quantitative syntheses. Ten studies, comprising 983 patients, analyzed ovarian edema. Eleven studies, comprising 1295 patients, analyzed the presence of adnexal mass. Fifteen studies, comprising 2212 patients, analyzed the Doppler flow. Finally, seven studies, comprising 654 patients, analyzed whirlpool sign. Overall, quality was considered as moderate or good for most studies. However, there is a high risk of bias in Patient Selection and Index text (except for whirlpool sign) in a significant proportion of studies. Pooled sensitivity, specificity and positive and negative likelihood ratios of each ultrasound sign were 58%, 86%,4.0 and 0.49 for ovarian edema, 69%, 43%, 1.3 and 0.67 for adnexal mass, 65%, 92%, 8.0 and 0.38 for whirlpool sign, 53%, 95%, 11.0 and 0.49 for Doppler findings and 55%, 69%, 1.7 and 0.66 for pelvic fluid. Heterogeneity was high for all them.

Conclusion. Diagnostic accuracy of the presence of an adnexal mass or pelvic fluid as ultrasound signs for suspecting an adnexal torsion is moderate, while the presence of ovarian edema, whirlpool sign and decreased or absent Doppler flow show good specificity.

Introduction

Adnexal torsion is a relatively common problem in clinical practice accounting for about 3% of all gynecological emergencies (1). It consists of the abnormal rotation of the ovary and or fallopian tube on its supporting ligaments around the vascular axis. Four pathological patterns have been described: tubo-ovarian torsion, ovarian torsion, tubal torsion and mesentero-tubal torsion (2). It can occur **in** female patients of any age, being more frequent in the reproductive period and rare in postmenopausal women (3). The main concern of this entity is that adnexal torsion may lead to the loss of the adnexa, more specifically the ovary, which may pose relevant consequences to the woman.

The diagnosis of adnexal torsion is mostly based on clinical symptoms and it should be suspected in cases of acute unilateral lower abdominal pain associated with nausea and/or vomiting, together with several laboratory alterations, especially leukocytosis (1). However, these symptoms and signs were quite non-specific. The rotation of the adnexa on its pedicle implies a compromise in its blood supply that can be detected by Doppler ultrasound, analyzing the decrease or absence of blood flow, both arterial and venous (4). This situation causes a series of histological reactive changes in the ovary visible by ultrasound, such as enlarged ovaries, with hyperechogenic stroma and follicles arranged on the periphery, also known as ovarian edema (5). Adnexal torsion is more frequent in patients with ovarian cysts or masses, as well as in cases of ovarian hyperstimulation (3).

For all these reasons, ultrasound imaging plays a very important role in the correct diagnosis of adnexal torsion and it is considered as the imaging modality of choice in these patients (6). Many studies have been carried out to date to evaluate the diagnostic performance of this imaging test for this pathology. There are some meta-analyses reported analyzing the diagnostic performance of ultrasound in cases of adnexal torsion. However, except in the case of whirlpool sign (7), none of them performs an independent analysis for each of the classic ultrasound signs (8,9).

We aimed to perform a systematic review and meta-analysis about the diagnostic accuracy of several ultrasound signs for detecting adnexal torsion.

Material and Methods

1. *Protocol and registration*

This systematic review and meta-analysis was performed according to PRISMA statement (10) and according to SEDATE guidelines (11). All methods regarding inclusion/exclusion criteria, data extraction and quality assessment were defined a priori (Appendix S1). The methodology was registered in PROSPERO (registration number pending. Provisional ID 312976) before the study started. No amendments were made after registration. Institutional Review Board approval was waived because of study's nature and design.

2. *Data sources and search*

Three of the authors searched six electronic databases (PubMed/MEDLINE, CINHAL, Scopus, Cochrane, ClinitalTrials.gov and Web of Science) to identify potentially eligible studies published between January 1990 and November 2021. The search terms were as follows: "ultrasound", "adnexa", "ovary", "torsion" and "Doppler". Therefore, the following Boolean operators were used: ultrasound AND Doppler AND adnexa OR ovary AND torsion. Only articles published in English, Spanish and French were analyzed.

3. *Study selection*

Three authors screened the titles and abstracts of identified articles in order to exclude those that were irrelevant, such as duplicates, not strictly related to the topic of review, case reports, reviews, meta-analyses, and letters to the editor.

The full texts of relevant articles were then obtained and the reviewers applied independently the following inclusion criteria:

1. Prospective or retrospective cohort or case-control study with at least 20 women included (sample size was set arbitrarily)
2. Participants included girls, adolescents non-pregnant and pregnant women with clinical suspicion of adnexal torsion
3. The index test was ultrasound assessment performed either via transvaginal, abdominal or transrectal for detecting at least one of the following ultrasound signs related to adnexal torsion (12): ovarian edema (we considered "enlarged

ovary" as ovarian edema), adnexal mass (the presence of adnexal mass distinct of an enlarged ovary, such as a dermoid cyst, a simple cyst, a hemorrhagic cyst, etc…), whirlpool sign, ovarian flow Doppler assessment (ovarian color map –absent vs present- or pulsed Doppler assessment for either venous and arterial blood flow for detecting decreased or absent flow), intra-follicular fluid-debris level, follicular ring sign and fluid in the pelvis.

4. Surgery with or without pathological correlation was used as the reference standard
5. The reported data were sufficient to construct a 2 × 2 table of diagnostic performance as a minimum data requirement.

Studies that assessed isolated tubal torsion were not considered for this meta-analysis. Studies including fetal and/or neonates were also excluded.

The 'snowball strategy' was used to identify potentially relevant papers from the reference lists of those selected for full-text assessment. In cases of missing relevant data, we sought to contact the authors to request this information.

4. *Data collection process*

As stated above, seven ultrasound signs related to the presence of adnexal torsion were selected for this meta-analysis, namely: ovarian edema, follicular ring, intra-follicular fluid-debris level, presence of adnexal mass, ovarian Doppler flow findings, the whirlpool sign and the presence of pelvic free fluid.

The following data were extracted from each one of the studies included: first author's name, year of publication, study design (prospective or retrospective cohort or case-control study), population (girls, adolescents, premenopausal non-pregnant and pregnant women or postmenopausal women), recruitment period, sample size, index test (type of ultrasound route –transvaginal or transabdominal- , Doppler settings used, ultrasound sign evaluated), number and experience of examiners, blinding of examiners to clinical presentation or surgical outcome, surgical approach and total cases of torsion confirmed by surgical findings.

4. Qualitative synthesis.

Quality assessment was carried out using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool, adapted for use in this meta-analysis was used to assess the risk of bias in individual studies (13). The QUADAS-2 tool includes four domains: (1) patient selection; (2) index test; (3) reference standard; and (4) flow and timing. For each domain, the risk of bias and concerns regarding applicability were classified as high, low or unclear. The results of quality assessment were used for descriptive purposes to evaluate the overall quality of the included studies and to investigate potential sources of heterogeneity. Two authors assessed independently the methodological quality, using a standard form with quality assessment criteria.

Disagreements were solved by discussion moderated by a third author to reach a consensus. The authors determined the risk of selection bias based on the description of the inclusion and exclusion criteria of the studies. For the index text domain, we sought for the ultrasound sign definition used in the study that could be clear enough to be replicated in a different study. For evaluation of the reference-standard domain, the method that the study used to determine the presence of adnexal torsion was assessed. For evaluation of the flow-and-timing domain, the description of the time elapsed between the index-test assessment and the reference-standard result was evaluated.

5. Quantitative synthesis

Data about the diagnostic performance of all the ultrasound signs assessed in this meta-analysis were extracted or derived from the studies ultimately included. We considered the test result as positive when the sign assessed was visualized during the ultrasound examination. Consequently, we considered the test result as negative when the sign was not visualized or not specifically mentioned as visualized in the study under research. In this latter case, we assumed that the sign was searched for and it was not found. The reference standard was adnexal torsion found at surgery.

The primary outcome was pooled sensitivity, specificity and positive and negative likelihood ratios (LR+ and LR−) as well as the diagnostic odd ratio (DOR) of each ultrasound sign in the detection of adnexal torsion. True-positive, true-negative, false-positive and false-negative values were obtained from each study. Post-test probabilities were calculated and plotted on Fagan nomograms.

The presence of heterogeneity in sensitivity and specificity was assessed graphically, by plotting forest plots, as well as using Cochran's Q statistic and the I^2 index. Tests for heterogeneity examine the null hypothesis that all studies are evaluating the same effect; P < 0.1 indicates heterogeneity. According to Higgins et al. I^2 values of 25%, 50% and 75% are considered to indicate low, moderate and high heterogeneity, respectively (14). A summary receiver-operating-characteristics (sROC) curve was plotted to illustrate the relationship between sensitivity and false positive rate. In case where heterogeneity was observed, meta-regression was performed using as co-variables year of publication, sample size, adnexal torsion prevalence, study design and population studied.

Statistical analysis was performed using Meta-analytical Integration of Diagnostic Accuracy Studies (MIDAS) and METANDI commands in Stata version 12 for Windows (Stata Corp., College Station, TX, USA). P < 0.05 was considered as statistically significant.

Results

Search results

A flow-chart summarizing literature identification and selection of studies is shown in Figure 1. The electronic search identified 1949 citations (853 in *PubMed/MEDLINE, 16 in CINHAL, 796 in Scopus, 0 in Cochrane, 1 in ClinitalTrials.gov and 283 in Web of Science*). After removal of 682 duplicate records, 1267 citations remained. Of these, 1064 were excluded by title, while 100 additional papers were excluded after reading the abstract.

We examined the full text of the remaining 103 articles. Eighty-five studies were excluded because of several reasons: sample size ≤20 cases, same cohort of patients, case report or cases series, the index test was not ultrasound, the reference standard was not available or it was not surgical findings only, or there was insufficient data to construct a 2x2 table (for example, retrospective studies in which all cases included had adnexal torsion and therefore the false positive and true negative cases were zero by definition) (Appendix S2).

We observed that, from the seven ultrasound signs to be assessed; only one study assessed the intra-follicular fluid-debris level sign (15) and only three studies assessed the follicular ring sign (16-18). Therefore, we decided to exclude these signs from the meta-analysis because of the number of identified studies was insufficient to perform the quantitative synthesis.

Therefore, eighteen studies were ultimately included in the analysis (17-34). The studies included analyzed the accuracy of preoperative ultrasound presence or not of ovarian edema, adnexal mass, whirlpool sign ovarian Doppler flow and/or pelvic fluid in patients with clinical suspicion of adnexal torsion. Most studies assessed more than one ultrasound sign. The analysis was performed separately for each ultrasound sign. There was no need to contact the authors for any of the studies, as all relevant data to perform the meta-analysis were available.

Characteristics of included studies

The characteristics of the selected studies are shown in Table 1. The studies were published between 1998 and 2022 and reported on 2101 patients. Among these 2101 patients, 870 had adnexal torsion at surgery (by laparoscopic or laparotomy access).

The series was consecutive in all observational (no case-control) studies. Three of them were prospective in design (20,25,32), ten studies were observational retrospective cohort (18,19,22,23,27,28,29,30,31,34) and five were retrospective case-control studies (17,21,24,26,33), although only two out of these five studies actually matched by age (21,33) and three studies did not match cases with controls (17,24,26). Regarding the population studied, four studies analyzed only pediatric patients (17,26,28,31). Four studies included non-pregnant women and pregnant women (19,25,27,34), seven studies included only non-pregnant women (18,20,22,23,24,33,33) and three studies included a mix of any patient (pediatric, non-pregnant, pregnant and postmenopausal) (21,29,30). Two studies reported by the same group included a different set of patients, one study including primary cases of adnexal torsion (30) and other study including cases of recurrent adnexal torsion (29). The number of observers and whether they were blinded to reference standard is shown in Table 1.

The ultrasound examination was carried out transvaginal or transabdominal route in most studies, depending the population studies. In studies with mixed population, the percentage of patients explored by one or other of these routes was poorly or not specified at all in the vast majority of studies. One study did not describe the route used for ultrasound examination (27). The experience of examiners were reported in seven studies (17,18,24,27,30,31,33). In all studies ultrasound examinations were performed by expert examiners.The type of equipment used was reported in eight studies, all of them can be considered as high-brand for the time the study was performed (18,23-26,30,33,34).

Surgical findings have been taken as the reference standard. In most of the studies surgery was performed laparoscopically. The time between the establishment of the ultrasound suspicion and the surgical intervention was reported in ten studies, varying from thirty minutes to 60 hours.

Qualitative synthesis

The results of the evaluation of the risk of bias and concerns regarding applicability of the included studies, according to the QUADAS-2 tool, are summarized in Figure 2. Six studies were considered to have a high risk of patient selection bias because of the fact they were case-control studies (17,21,24,26,33) or had inadequate patient exclusion (20).

For the index test dominion, we analyzed the quality according to the ultrasound sign assessed. The definition of each ultrasound sign used by the authors in each study is shown in table 2. Regarding the ovarian edema sign, two studies were considered as high risk of bias because of ovarian edema was defined using only a quantitative criterion (21,26). In two studies no definition of ovarian edema was provided (23,28). Regarding the adnexal mass sign, six studies were considered as high risk of bias since just the presence of and "ovarian cyst or mass" without taking into consideration the size the mass and, therefore, potentially physiological ovarian follicles or corpora lutea cannot be ruled out (17,19,22,23,27,29). Regarding ovarian Doppler flow findings, five studies were considered as high risk of bias since the criterion reported was not clearly defined (for example, "decreased" or "pathological" or "abnormal" or "positive finding for torsion" are imprecise)(19,21,23,26,31). For studies assessing the whirlpool sign, all studies were considered as low risk of bias as all of them described correctly this sign. Regarding the presence of free fluid in pelvis, all seven studies were considered as high risk, since none of them provided an objective definition for this sign.

For the reference test, all studies were considered low risk of bias since all studies confirmed the presence or absence of adnexal torsion according to surgical findings.

Concerning the flow-and-timing domain, the time elapsed between the index test and the reference standard was reported in eight studies (18,19,22,25,28,32,33,34), seven of them were considered as low risk and one as high risk because of the median or mean time was more of 48 hours (19). The remaining studies were considered as unclear for risk bias, as they did not specify the time interval.

Regarding applicability, all studies were deemed to include patients that matched the review question. For the index-test domain, all studies were considered to have low concerns for applicability. Moreover, all studies presented low concerns regarding the reference-standard domain.

Quantitative synthesis

Table 3 summarizes quantitative synthesis for all five signs assessed.

1. Ovarian edema sign

Eight articles assessed ovarian edema as an ultrasound sign for adnexal torsion (18,21,23,26,27-30). All studies were retrospective, and two of them had a case-control design. The studies included for this analysis comprised 809 patients. The mean prevalence of adnexal torsion at surgery was 59% (range: 27% to 82%).

The pooled sensitivity, specificity, positive and negative likelihood ratios of ovarian edema in the detection of ovarian torsion were 58% (95% CI, 38-76%), 86% (95% CI, 61-96%), 4.0 (95% CI, 1.3-12.6), 0.49 (95% CI, 0.30-0.79). The diagnostic odds ratio was 8 (95% CI, 2-36). Heterogeneity was high for both sensitivity (Cochran´s Q=142.20, P=0.00; I^2=95.1%) and specificity (Cochran´s Q=73.87, P=0.00; I^2=90.5%) (Figure 3A). Based on meta-regression, prevalence could explain heterogeneity of specificity

The sROC curve is shown in Figure 4A. The area under the curve was 0.77 (95% CI, 0.66-0.85). The Fagan nomogram showed that a positive result on ultrasound regarding ovarian edema increased moderately the post-test probability of adnexal torsion, from 59% to 85%, while a negative test decreased the post-test probability only slightly, from 59% to 41%. No publication bias was observed (p= 0.52).

We attempted to perform a subgroup analysis according to the population assessed in the studies. However, this was not possible due to the small number of studies assessing a specific population. Two studies focused only on pediatric patients (26,28). Two studies focused only in non-pregnant pre- and/or postmenopausal women (18,23). One studiy mixed pregnant and non-pregnant women (27). In addition, three studies mixed pediatric patients, pregnant and non-pregnant premenopausal women and postmenopausal women (21,29,30).

2. Adnexal mass

Eight articles assessed the presence of an adnexal mass as an ultrasound sign associated to adnexal torsion (17,18,22,23,27-30). All studies were retrospective, and two of them had a case-control design. The studies included for this analysis comprised 1218 patients. The mean prevalence of adnexal torsion at surgery was 61% (range: 23% to 82%).

The pooled sensitivity, specificity, positive and negative likelihood ratios of adnexal mass in the detection of adnexal torsion were evaluated in all studies. The respective values were 69% (95% CI, 55-81%), 46% (95% CI, 22-61%), 1.3 (95% CI, 0.8-1.9), 0.67 (95% CI, 0.41-1.10). The diagnostic odds ratio was 2 (95% CI, 1-5). Heterogeneity was high for both sensitivity (Cochran´s Q=53.98, P=0.00; I^2=87.0%) and specificity (Cochran´s Q=247.72, P=0.00; I^2=97.2% (Figure 3B). Based on meta-regression, prevalence could explain heterogeneity of specificity.

The sROC curve is shown in Figure 4B. The area under the curve was 0.65 (95% CI, 0.52-0.75). The Fagan nomogram showed that a positive result on ultrasound regarding adnexal mass increased slightly the post-test probability of adnexal torsion, from 61% to 67%, despite a negative test decreased the post-test probability slightly, from 61% to 51%. No publication bias was observed (P=0.06).

We attempted to perform a subgroup analysis according to the population assessed in the studies. However, this was not possible due to the small number of studies assessing a specific population. Two studies focused only in pediatric patients (17,28). Three studies focused only in non-pregnant pre- and/or postmenopausal women (18,22,23). Two studies mixed pregnant and non-pregnant women (19,27). In addition, two studies mixed pediatric patients, pregnant and non-pregnant premenopausal women and postmenopausal women (29,30).

3. Whirlpool sign

Six articles assessed the whirlpool sign (18,24,25,29,30,34). The studies included for this analysis comprised 545 patients. The mean prevalence of adnexal torsion at surgery was 65% (range: 22% to 83%).

The pooled sensitivity, specificity, positive and negative likelihood ratios of whirlpool sing in the detection of adnexal torsion were evaluated in all studies. The respective values were 65% (95% CI, 18-94%), 92% (95% CI, 84-96%), 8.0 (95% CI, 4.2-15.4), 0.38 (95% CI, 0.1-1.44). The diagnostic odds ratio was 21 (95% CI, 4-119). Heterogeneity was high for both sensitivity (Cochran´s Q=216.19, P=0.00; I^2=97.2%) and specificity (Cochran´s Q=89.26, P=0.00; I^2=93.3%) (Figure 3C). Based on meta-regression, heterogeneity could not be explained by any of the variables analyzed.

The sROC curve is shown in Figure 4C. The area under the curve was 0.92 (95% CI, 0.81-0.97). The Fagan nomogram showed that a positive or negative result on ultrasound regarding whirlpool sign increased and decreased moderately the post-test probability of adnexal torsion, from 65% to 94%, and from 65% to 42% respectively. No publication bias was observed (p=0.20).

We attempted to perform a subgroup analysis according to the population assessed in the studies. However, this was not possible due to the small number of studies assessing a specific population. Two studies focused only in non-pregnant pre- and/or postmenopausal women (18,24). Two studies mixed pregnant and non-pregnant women (25,34). In addition, two studies mixed pediatric patients, pregnant and non-pregnant premenopausal women and postmenopausal women (29,30).

4. Ovarian Doppler flow

Fourteen articles assessed ovarian Doppler findings as an ultrasound sign for diagnosing adnexal torsion (17-23,26,27,29-33),. The studies included for this analysis comprised 1765 patients. The mean prevalence of adnexal torsion at surgery was 47% (range: 12% to 82%)

The pooled sensitivity, specificity, positive and negative likelihood ratios of ovarian Doppler flow were 53% (95% CI, 34-72%), 95% (95% CI, 86-98%), 11.0 (95% CI, 3.8-31.8), 0.49 (95% CI, 0.32-0.74). The diagnostic odds ratio was 22 (95% CI, 7-76). Heterogeneity was high for both sensitivity (Cochran´s Q=172.35, P=0.00; I^2=92.5%) and specificity (Cochran´s Q=199.31, P=0.00; I^2=93.5%). (Figure 3D). Based on meta-regression, prevalence could explain heterogeneity of Doppler specificity.

The sROC curve is shown in Figure 4D. The area under the curve was 0.86 (95% CI, 0.76-0.92). The Fagan nomogram showed that a positive result on ultrasound regarding Doppler flow increased significantly the post-test probability of adnexal torsion, from 47% to 91%, while a negative test decreased the post-test probability moderately, from 47% to 30%. Publication bias was observed (p=0.02).

We attempted to perform a subgroup analysis according to the population assessed in the studies. However, this was only possible for studies focusing only in non-pregnant pre- and/or postmenopausal women (18,20,22,23,32,33). In this population, diagnostic performance was similar to whole aggregate analysis, with pooled sensitivity, specificity, positive and negative likelihood ratios of ovarian Doppler flow were 51% (95% CI, 14-88%), 99% (95% CI, 89-100%), 35.6 (95% CI, 4.4-289.7), 0.49 (95% CI, 0.19-1.30). The diagnostic odds ratio was 72 (95% CI, 6-896). Heterogeneity was high for both sensitivity (Cochran´s Q=55.4, P=0.00; I^2=90.1%) and specificity (Cochran´s Q=52.7, P=0.00; I^2=90.5%).

5. Fluid in pelvis

Seven articles assessed the whirlpool sign (17,18,23,27-30). The studies included for this analysis comprised 981 patients. The mean prevalence of adnexal torsion at surgery was 59% (range: 23% to 82%).

The pooled sensitivity, specificity, positive and negative likelihood ratios of whirlpool sing in the detection of adnexal torsion were evaluated in all studies. The respective values were 55% (95% CI, 38-71%), 69% (95% CI, 54-80%), 1.7 (95% CI, 1.1-2.9), 0.66 (95% CI, 0.44-0.99). The diagnostic odds ratio was 3 (95% CI, 1-6). Heterogeneity was high for both sensitivity (Cochran´s Q=72.09, P=0.00; I^2=91.2%) and specificity (Cochran´s Q=129.02, P=0.00; I^2=95.3%) (Figure 3E). Based on meta-regression, heterogeneity could not be explained by any of the variables analyzed.

The sROC curve is shown in Figure 4E. The area under the curve was 0.67 (95% CI, 0.54-0.77). The Fagan nomogram showed that a positive or negative result on ultrasound regarding whirlpool sign increased and decreased moderately the post-test probability of adnexal torsion, from 59% to 72%, and from 59% to 49%, respectively. No publication bias was observed (p=0.14).

We attempted to perform a subgroup analysis according to the population assessed in the studies. However, this was not possible due to the small number of studies assessing a specific population. Two studies focused only in non-pregnant pre- and/or postmenopausal women (18,23). Two studies focused on pediatric population (17,28). One study mixed pregnant and non-pregnant women (27). In addition, two studies mixed pediatric patients, pregnant and non-pregnant premenopausal women and postmenopausal women (29,30).

Discussion

1. *Summary evidence*

According to our results ovarian edema, whirlpool sign and ovarian Doppler flow alterations are ultrasound signs with a high specificity but moderate sensitivity for the diagnosis of adnexal torsion. The presence or absence of an adnexal mass or pelvic fluid have poor diagnostic performance. On the other hand, objective diagnostic criteria for ovarian edema, adnexal mass, pelvic fluid and ovarian Doppler flow were not clearly stated in many studies.

2. *Interpretation of results*

An accurate diagnosis is essential for an optimal management of women with a clinical suspicion of adnexal torsion. A delayed or a false negative diagnosis might end in ovarian necrosis, while a false positive diagnosis may lead to unnecessary surgical intervention with potential complications (35).

We have observed that ovarian edema, whirlpool sign and ovarian Doppler findings show good specificity for diagnosing adnexal torsion. However, the sensitivity of these signs is rather moderate. Therefore, these signs should be assessed in every patient with a clinical suspicion of adnexal torsion. The presence of an adnexal mass and pelvic fluid may be a potential source of false positive cases and they should be interpreted taking into consideration other ultrasound signs. In fact, some studies have shown that combining more than one sign might improve the diagnostic performance (18,24).

The qualitative synthesis rises some concerns regarding the quality of the studies because of many studies included mixed population, did not provided clear definition of the index test and mixed data obtained by TAS and TVS.

3. *Strengths and limitations*

There are three meta-analyses about ultrasound diagnosis of adnexal torsion reported so far (7-9). However, we do consider that the main strength of this meta-analysis lies in the fact that this is the first meta-analysis that specifically performs a quantitative and qualitative synthesis about the diagnostic performance of several ultrasound signs separately.

Bronstein et al reported a meta-analysis assessing the role of B-mode ultrasound, Doppler ultrasound and CT scan for diagnosing adnexal torsion in pediatric population (7), including 18 studies using B-mode findings and 15 studies using Doppler. However, Bronstein et al did not perform a qualitative analysis of the studies and not all studies included used surgical findings as reference test. In fact, only three studies assessing B-mode findings and four studies assessing Doppler ultrasound findings would be used to estimate pooled specificity. Furthermore, for B-mode ultrasound, no specific ultrasound sign was evaluated.

Adu-Bredu et al reported a meta-analysis including eight studies assessing only the whirlpool sign (8). Albeit the authors stated that qualitative synthesis was performed, data from this analysis were not reported. Furthermore, in the quantitative synthesis the authors included six studies from which specificity could not be estimated because of all patients included had torsion or reference standard we not surgery.

Wattar et al reported on a meta-analysis assessing the diagnostic performance of ultrasound, CT scan and magnetic resonance imaging for diagnosing adnexal torsion (9), including 12 studies assessing ultrasound findings. In this meta-analysis reference standard in the studies included was not only surgical findings but also clinical follow-up. Including studies using clinical follow-up may pose a risk of bias because of spontaneous detorsion may occur and true cases could be considered as “true negative” cases. Additonally, no specific analysis of different ultrasound signs was done. Qualitative synthesis was only considered for case-control studies and the reported data did not differentiate among studies using ultrasound, CT scan or magnetic resonance imaging.

A common problem with studies assessing imaging in adnexal torsion is that not all suspicious cases undergo surgery, which can lead to ascertainment bias. This fact may affect mostly to the specificity of the test, which could be overestimated. However, all women in our meta-analysis underwent surgery; therefore, in our case this could be a strength.

The main limitations of this meta-analysis are the small number of studies and patients included. In addition, we could not assess diagnostic performance of the different ultrasound signs in different populations. We observed that there were few objective, quantifiable and reproducible criteria available to make the ultrasound diagnosis of adnexal torsion with high certainty. This is why we believe that it seems difficult to propose the development of a clinical guide for action in the face of this entity. From the methodological point of view, we did assume that a sign was negative in case the authors did not specifically mentioned as visualized. This assumption could be erroneous and potentially leading to underestimate sensitivity.

The results found regarding the diagnostic performance of these signs are rather disappointing. This could be explained by the significant heterogeneity found among the 20 studies ultimately selected. In fact, we could not assess whether factors such as quality of ultrasound machines used (there is a significant range of the year of publication of the studies assessed), experience of the examiner, route of the ultrasound exam (transvaginal versus transabdominal) and the population studied (girls, adolescents, non-pregnant premenopausal women, pregnant women and postmenopausal women. All of them, factors that clearly might affect the diagnostic performance of ultrasound in the diagnosis of adnexal torsion.

Certainly, many clinicians relay on ultrasound as imaging technique when evaluating women with suspected adnexal torsion. However, we found that sensitivity for all signs assessed in our meta-analysis is moderate at best. This fact means that false negative cases are frequent and this is quite relevant when we do consider the consequences of adnexal torsion (loss of the adnexa). We do believe that our findings should prompt the development of a sort of “scoring system” combining several clinical feature and ultrasound findings in an attempt to improve our diagnostic performance of this entity.

Interestingly, there are three meta-analyses reporting data about the diagnostic performance of other imaging techniques such as CT scan and MRI (7,9,36). Two meta-analyses reported overall diagnostic performance of these techniques but did not analyze specific signs (7,9), and one meta-analysis reported on the pooled proportion of different signs present in cases of adnexal torsion using CT scan, but did not assess the diagnostic performance of these signs. Therefore, we cannot compare our data with those reported in these meta-analyses.

4. *Conclusions*

The presence of ovarian edema, whirlpool sign and absent intraovarian blood flow as assessed by Doppler ultrasound are highly specific sonographic signs for diagnosing adnexal torsion. The presence or absence of an adnexal mass and pelvic fluid have a moderate diagnostic performance for detecting adnexal torsion. However, the quality of the evidence is limited. Future research is still needed to improve the diagnostic performance of ultrasound in diagnosing adnexal torsion

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Figures' legends

Figure 1. Flowchart summarizing selection of studies evaluating the diagnostic accuracy of different ultrasound signs to diagnose adnexal torsion.

Figure 2. Summary of quality assessment (risk of bias and concerns regarding applicability) for studies included in the meta-analysis, according to the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool

Figure 3A. Forest plots of sensitivity and specificity of ovarian edema in the detection of adnexal torsion.

Figure 3B. Forest plots of sensitivity and specificity of adnexal mass in the detection of adnexal torsion.

Figure 3C. Forest plots of sensitivity and specificity of whirlpool sign in the detection of adnexal torsion.

Figure 3D. Forest plots of sensitivity and specificity of intraovarian Doppler flow in the detection of adnexal torsion.

Figure 3E. Forest plots of sensitivity and specificity of pelvic fluid in the detection of adnexal torsion.

Figure 4A. Hierarchical summary receiver-operating-characteristics curve for ovarian edema in detecting adnexal torsion.

Figure 4B. Hierarchical summary receiver-operating-characteristics curve for adnexal mass in detecting adnexal torsion.

Figure 4C. Hierarchical summary receiver-operating-characteristics curve for whirlpool sign in detecting adnexal torsion.

Figure 4D. Hierarchical summary receiver-operating-characteristics curve for intraovarian Doppler flow in detecting adnexal torsion.

Figure 4E. Hierarchical summary receiver-operating-characteristics curve for pelvic fluid in detecting adnexal torsion.

Appendix S1 Protocol template

Appendix S2 Papers excluded after reading full text

Table 1. Characteristics of the studies included in the present meta-analysis

Author	Year	Study period	Study design	Patients (N)	Population	N of AT	N of examiners	Examiner Blinded	Time from US to surgery	Index test	US route	Reference test
Lee	1998	NA	Prospective	47	Pregnant and non-pregnant premenopausal women and postmenopausal women	32	NA	Yes	< 48 hours	Whirlpool sign	TAS/TVS	Surgical findings
Ben-Ami	2002	NA	Prospective	65	non-pregnant premenopausal women	15	NA	Yes	NA	Doppler flow	TVS	Surgical findings
Linam	2007	1998-2005	Case-control	74	Girls and adolescents	46	NA	NA	NA	Ovarian edema, Doppler flow	TAS	Surgical findings
Valsky	2010	2006-2009	Retrospective	80	Pregnant and non-pregnant premenopausal women	18	NA	Yes	< 24 hours	Whirlpool sign	TAS/TVS	Surgical findings
Bar-On	2010	2006-2008	Retrospective	77	Pregnant and non-pregnant	36	NA	NA	< 60 hours	Doppler flow	TVS	Surgical findings

					premenopausal women							
Mashiach	2011	2002-2008	Retrospective	63	Pregnant and non-pregnant premenopausal women	47	Five	NA	NA	Ovarian edema, adnexal mass and Doppler flow	NA	Surgical findings
Naiditch	2013	2007-2011	Retrospective	113	Girls and adolescents	14	Twelve	NA	< 12 hours	Doppler flow	TAS	Surgical findings
Rostamzadeh	2014	2011-2012	Prospective	323	Non-pregnant premenopausal women	43	One	Yes	<6 hours	Doppler flow	TAS	Surgical findings
Swenson	2014	2005-2010	Case-control	40	Non-pregnant premenopausal women and postmenopausal women	15	Two	Yes	<48 hours	Doppler flow	TVS	Surgical findings
Melcer	2018	2009-2016	Retrospective	87	Girls and adolescents	53	NA	NA	< 16 hours	Ovarian edema and Adnexal mass	TAS	Surgical findings

Gu	2018	2012-2017	Case-control	54	Non-pregnant premenopausal women	28	Two	Yes	NA	Whirlpool sign	TAS/TVS	Surgical findings
Budhram	2019	2000-2014	Case-control	184	Girls, adolescents, pregnant and non-pregnant premenopausal women and postmenopausal women	92	NA	No	NA	Ovarian edema and Doppler flow	TAS/TVS	Surgical findings
Ghulmiyyah	2019	2009-2015	Retrospective	37	Non-pregnant premenopausal women	10	One	Yes	NA	Ovarian edema, adnexal mass and Doppler flow	TAS/TVS	Surgical findings
Otjen	2020	2004-2015	Case-control	430	Girls and adolescents	99	Twelve	No	NA	Adnexal mass and Doppler flow	TAS	Surgical findings
Yatsenko	2021	NA	Retrospective	129	Non-pregnant premenopausal women	106	One	Yes	<24 hours	Ovarian edema, adnexal mass,	TAS/TVS	Surgical findings

										whirlpool sign and Doppler flow		
Carugno	2021	2014-2018	Retrospective	63	Non-pregnant premenopausal women and postmenopausal women	47	NA	No	Median 10-16 hours	Adnexal mass and Doppler flow	TAS/TVS	Surgical findings
Meyer	2021	2011-2020	Retrospective	115	Girls, adolescents, pregnant and non-pregnant premenopausal women and postmenopausal women	86	NA	NA	NA	Ovarian edema, Adnexal mass, whirlpool sign and Doppler flow	TAS/TVS	Surgical findings
Meyer	2022	2011-2020	Retrospective	120	Girls, adolescents, pregnant and non-pregnant premenopausal women and postmenopausal women	83	NA	Yes	NA	Ovarian edema, Adnexal mass, whirlpool sign and Doppler flow	TAS/TVS	Surgical findings

AT: Adnexal torsion. US: ultrasound. N: number. NA: not available. TAS: transabdominal sonography. TVS: transvaginal sonography

Table 2. Definitions of different ultrasound signs in the studies included in the present meta-analysis

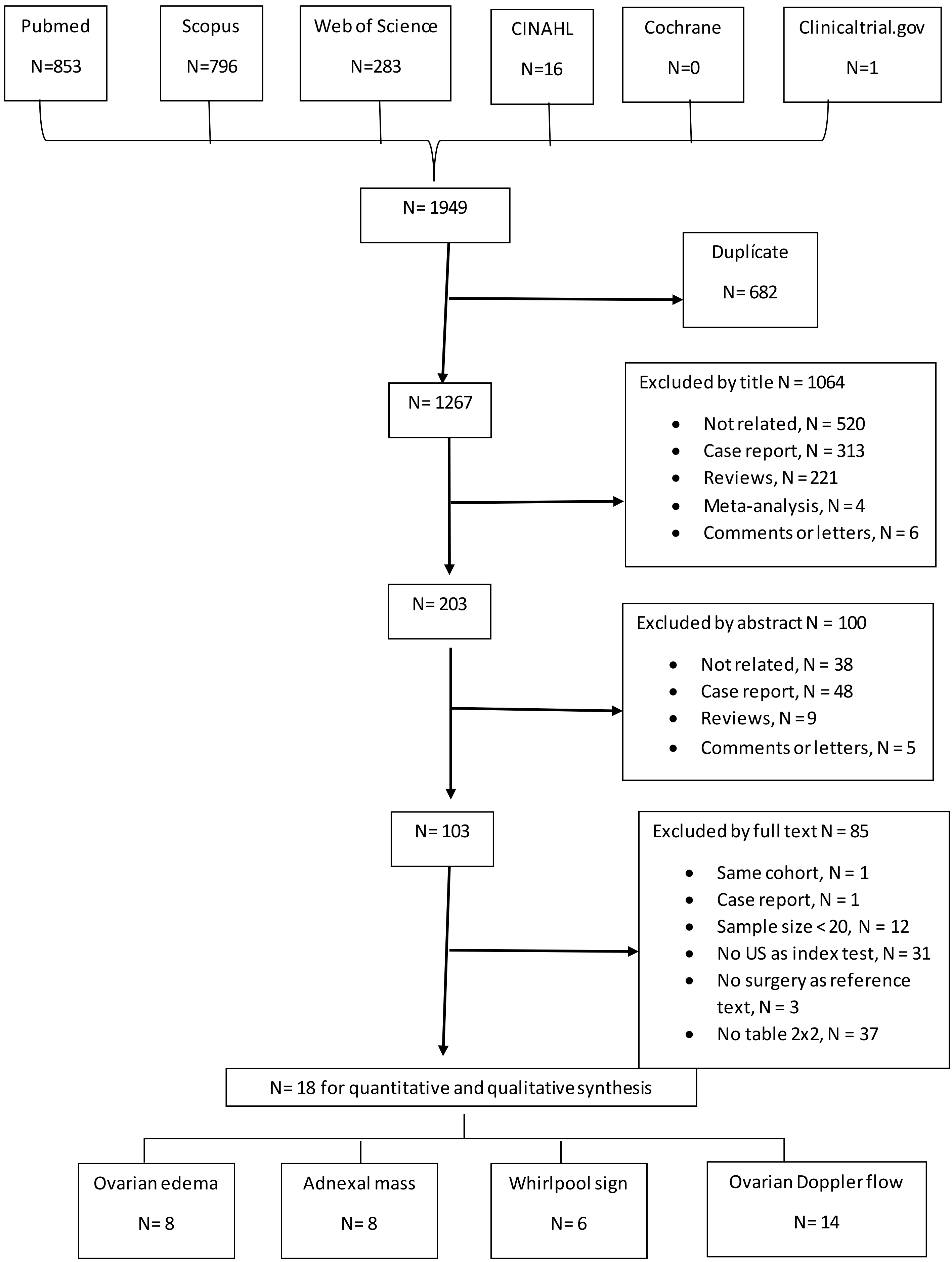
Author	Year	Ovarian edema	Adnexal mass	Ovarian Doppler flow	Whirlpool sign	Pelvic fluid
Lee	1998				Twisted vascular pedicle	
Ben-Ami	2002			Absent venous and/or arterial flow		
Linam	2007	Adnexal volume > 20mL		Decreased or absent venous flow		
Bar-On	2010		Ovarian cyst or mass	“pathological” or absent flow		
Valsky	2010				Twisted vascular pedicle	
Maschiach	2011	Hypoechoic or heterogeneous stroma with small peripheral follicles	Ovarian cyst or mass	Absent venous and/or arterial flow		Not defined objectively
Naiditch	2013			“positive” or “negative”		
Rostamzadeh	2014			Absent venous and/or arterial flow		
Swenson	2014			Absent venous and/or arterial flow		
Melcer	2018	Not defined	Ovarian cyst or mass describing features			Not defined objectively

Gu	2018				Twisted vascular pedicle	
Ghulmiyyah	2019	Not defined	Ovarian cyst or mass	“Abnormal” flow		Not defined objectively
Budhram	2019	Ovarian maximum diameter of 3 or 5 cm		“Abnormal” flow		
Otjen	2020		Ovarian cyst or mass	Absent flow		Not defined objectively
Yatsenko	2021	Hypoechoic or heterogeneous stroma with small peripheral follicles	Ovarian cyst or mass > 3 cm	Absent venous and/or arterial flow	Twisted vascular pedicle	Not defined objectively
Meyer	2021	Hyperechoic or heterogeneous stroma with small peripheral follicles	Adnexal cyst	Absent flow	Twisted vascular pedicle	Not defined objectively
Carugno	2021		Ovarian cyst or mass	Absent flow		
Meyer	2022	Hypoechoic or heterogeneous stroma with small peripheral follicles	Ovarian cyst > 3 cm	Absent flow	Twisted vascular pedicle	Not defined objectively

Table 3. Summary of quantitative synthesis

Ultrasound sign	SENSITIVITY (95%CI)	SPECIFICITY (95%CI)	AUC (95%CI)	DOR
Edema	57% (41%-72%)	88% (69%-96%)	0.77 (0.67-0.85)	10
Adnexal mass	72% (61%-81%)	39% (20%-61%)	0.64 (0.53-0.74)	2
Doppler flow	55% (34%-72%)	94% (84%-95%)	0.85 (0.74-0.91)	20
Whirpool sign	65% (18%-94%)	92% (84%-96%)	0.92 (0.81-0.97)	21
Pelvic fluid	55% (38%-71%)	69% (54%-80%)	0.67 (0.54-0.77)	3

ACU: Area under the curve. DOR: Diagnostic odd ratio



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No table 2x2, N = 37
N= 18 for quantitative and qualitative synthesis
Ovarian edema N= 8
Adnexal mass N= 8
Whirlpool sign N= 6
Ovarian Doppler flow N= 14

Study	RISK OF BIAS								APPLICABILITY CONCERNS						
	PATIENT SELECTION	INDEX TEST OVARIAN EDEMA	INDEX TEST ADNEXAL MASS	INDEX TEST WHIRLPOOL SIGN	INDEX TEST OVARIAN DOPPLER FLOW	INDEX TEXT PELVIC FLUID	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST OVARIAN EDEMA	INDEX TEST ADNEXAL MASS	INDEX TEST WHIRLPOOL SIGN	INDEX TEST DOPPLER	INDEX TEST PELVIC FLUID	REFERENCE STANDARD
Lee, 1998	☺			☺			☺	☺	☺			☺			☺
Ben-ami, 2002	☹				☺		☺	?	☺				☺		☺
Linam, 2007	☹	☹			☹		☺	?	☺	☺			☺		☺
Bar-On, 2010	☺		☹		☹		☺	☹	☺		☺		☺		☺
Valsky, 2010	☺			☺			☺	☺	☺			☺			☺
Mashiach, 2011	☺	☺	☹		☺	☹	☺	?	☺	☺	☺		☺	☺	☺
Naiditch, 2013	☺				☹		☺	☺	☺				☺		☺
Rostamzadeh, 2014	☺				☺		☺	☺	☺				☺		☺
Swenson, 2014	☹				☺		☺	☺	☺				☺		☺
Gu, 2018	☹			☺			☺	?	☺			☺			☺
Melcer, 2018	☺	?	☺			☹	☺	☺	☺	☺	☺			☺	☺
Budhram, 2019	☹	☹			☹		☺	?	☺	☺			☺		☺
Ghulmiyyah, 2019	☺	?	☹		☹	☹	☺	?	☺	☺	☺		☺	☺	☺
Otjen, 2020	☹		☹		☺	☹	☺	?	☺		☺		☺	☺	☺
Meyer, 2021	☺	☺	☹	☺	☺	☹	☺	?	☺	☺	☺	☺	☺	☺	☺
Carugno, 2021	☺		☹		☺		☺	☺	☺		☺		☺		☺
Yatsenko, 2021	☺	☺	☺	☺	☺	☹	☺	☺	☺	☺	☺	☺	☺		☺
Meyer, 2022	☺	☺	☺	☺	☺	☹	☺	?	☺	☺	☺	☺	☺	☺	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

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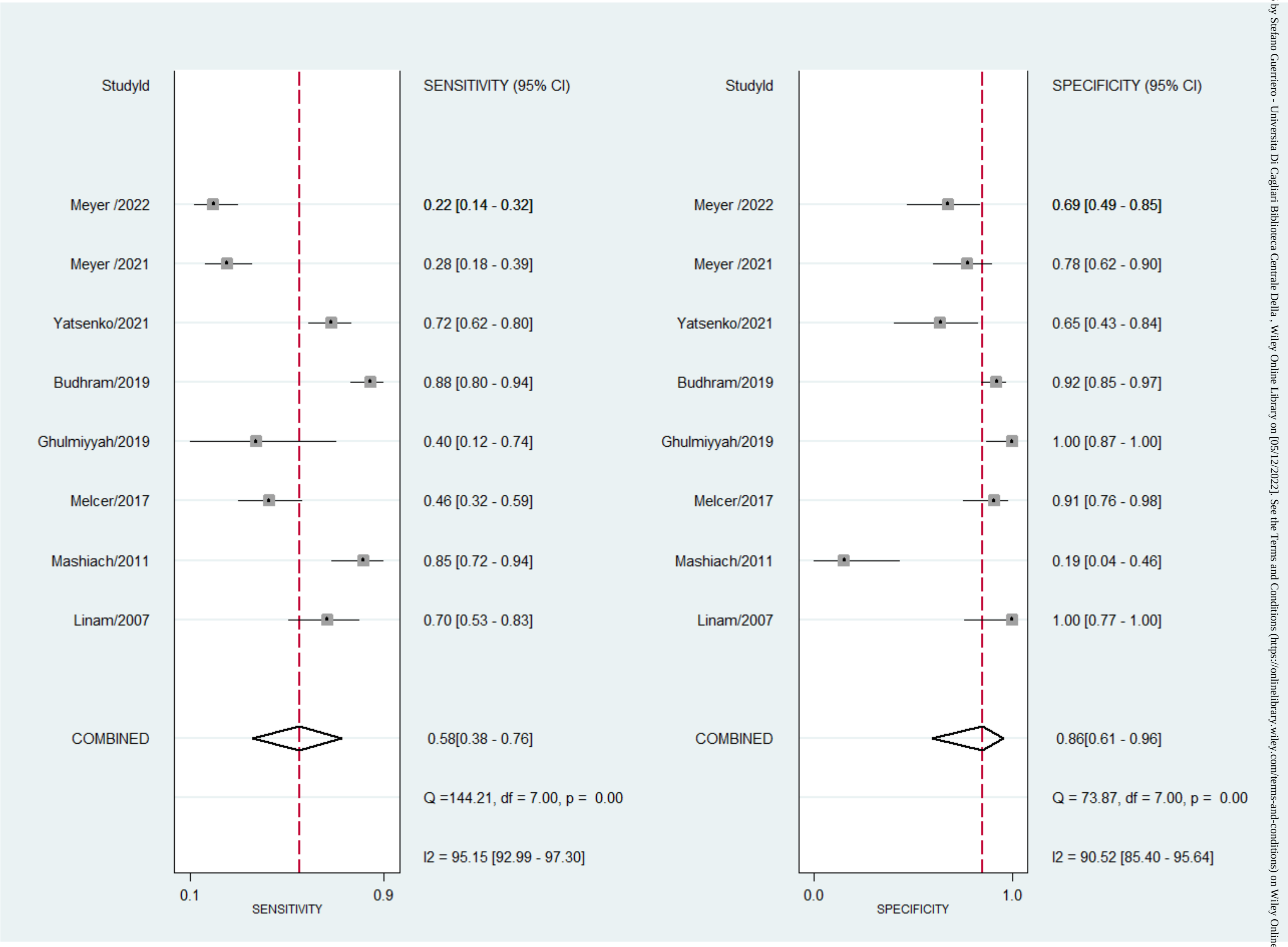

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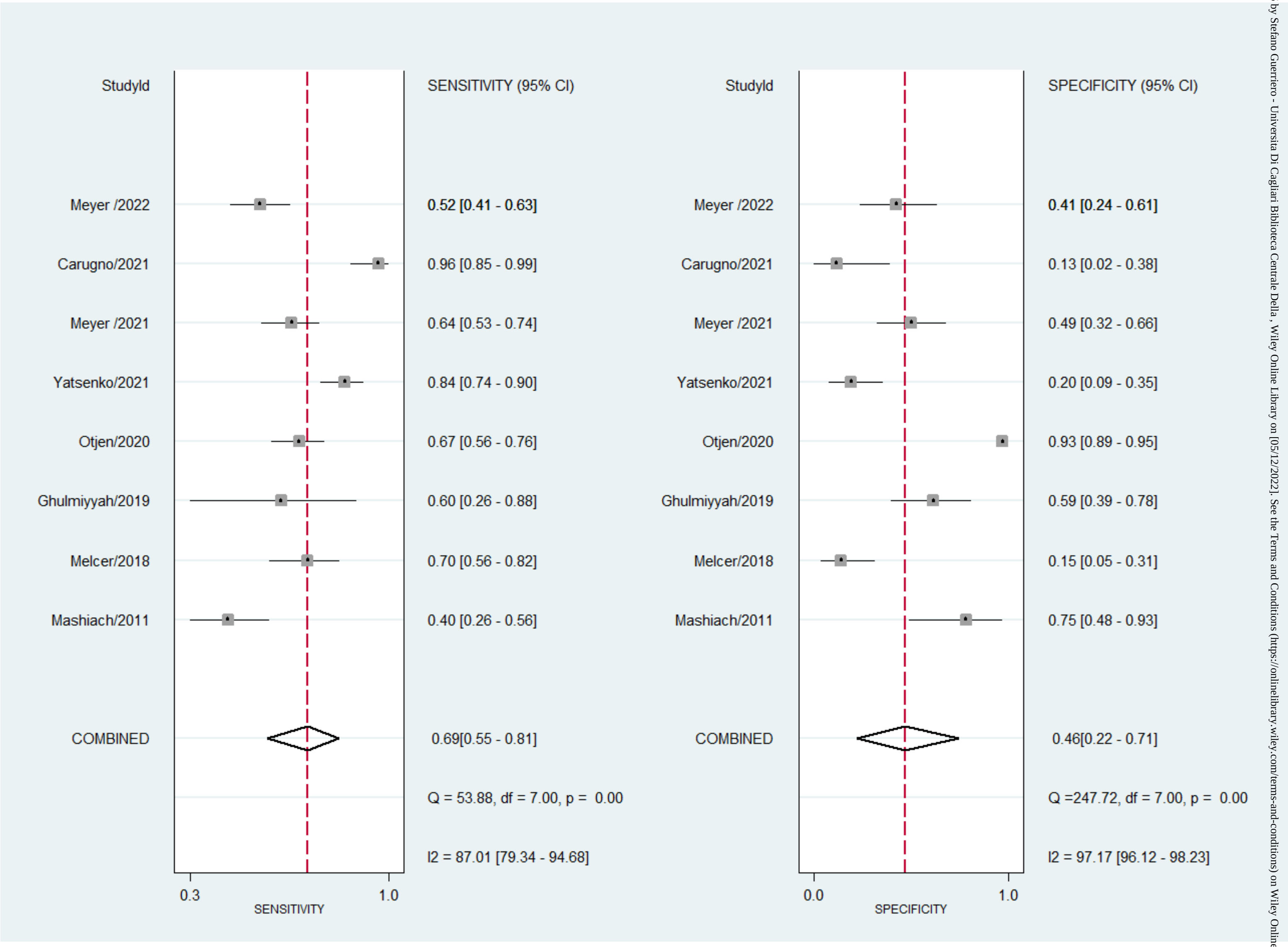

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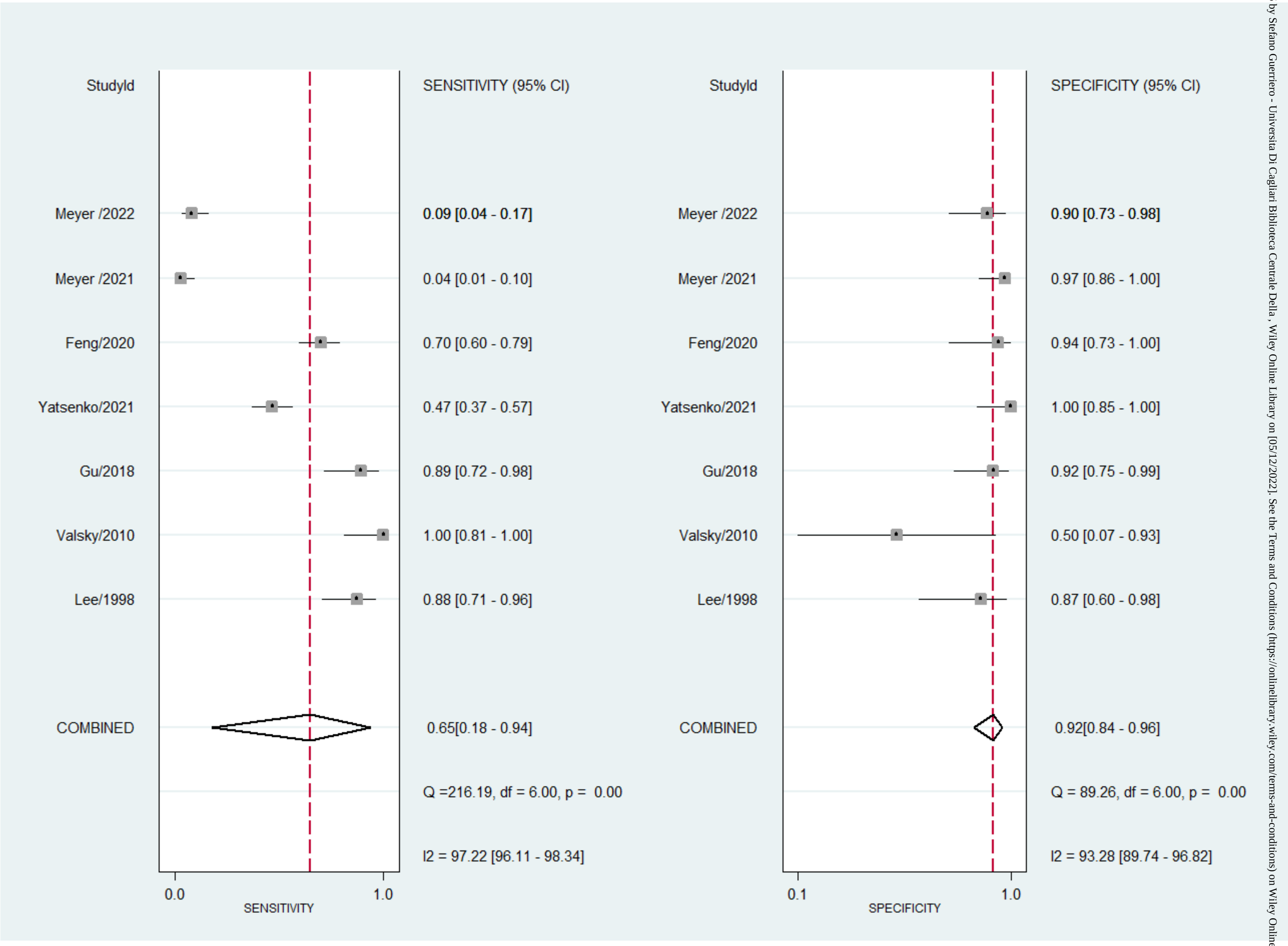

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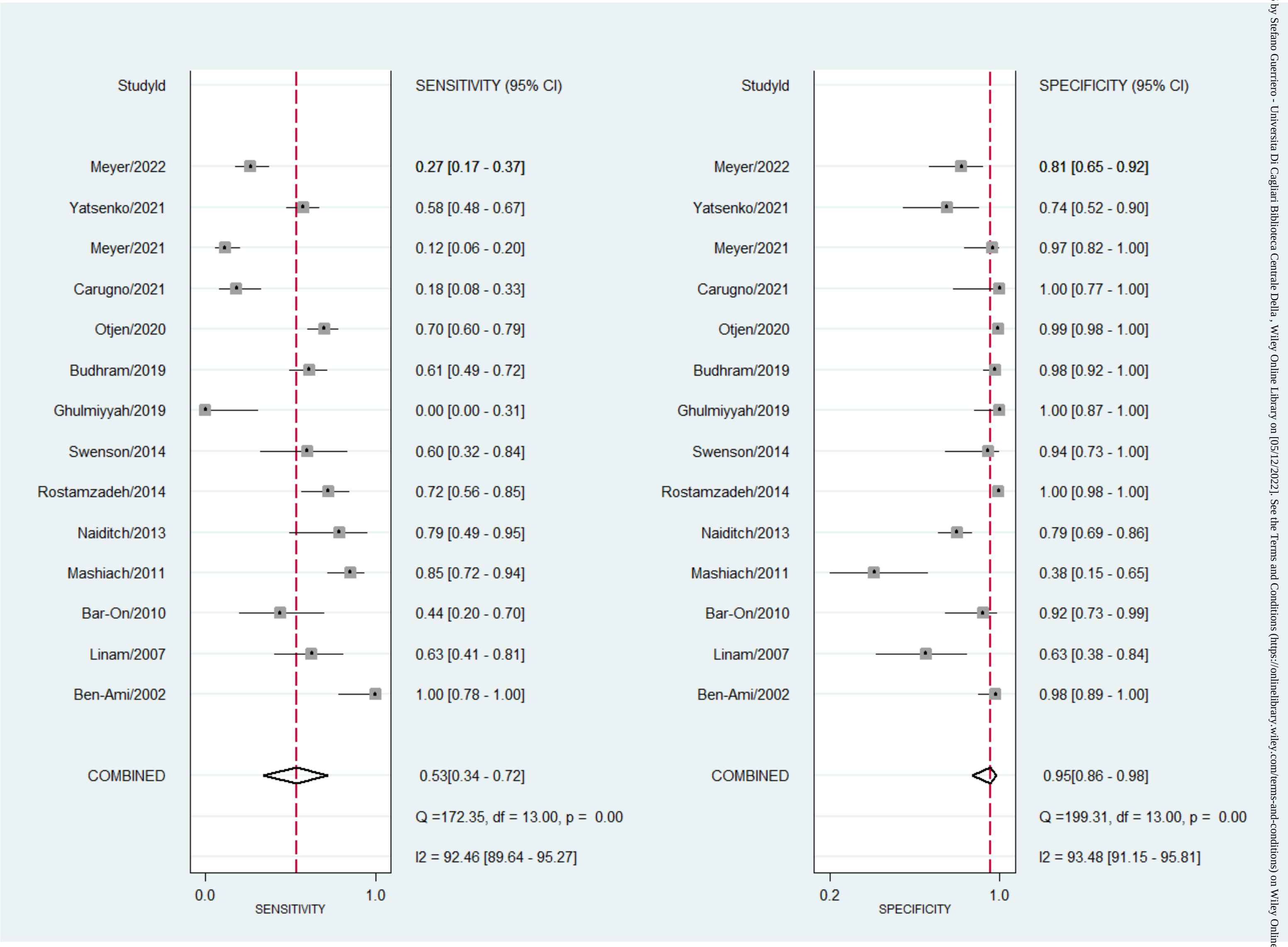

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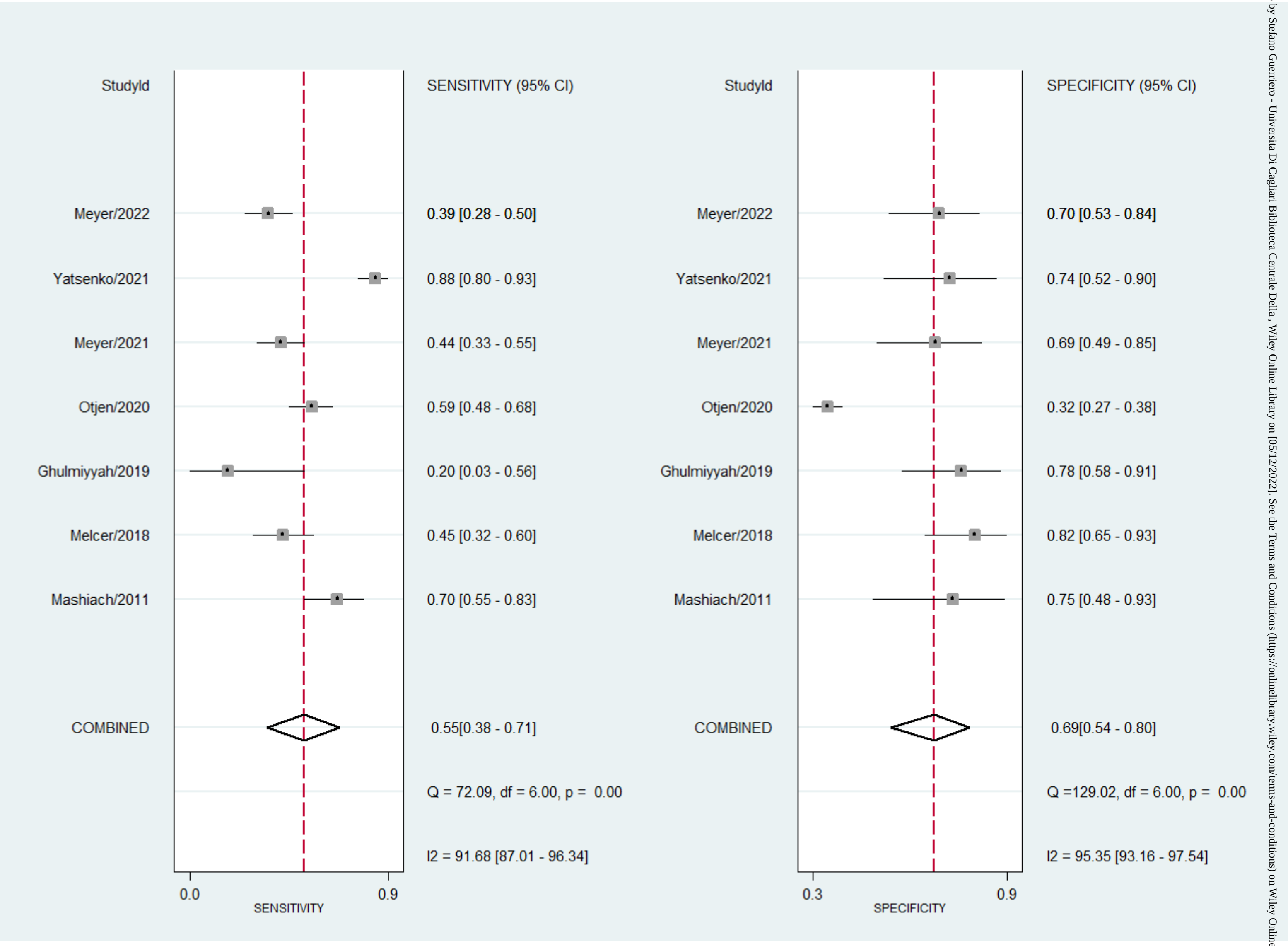

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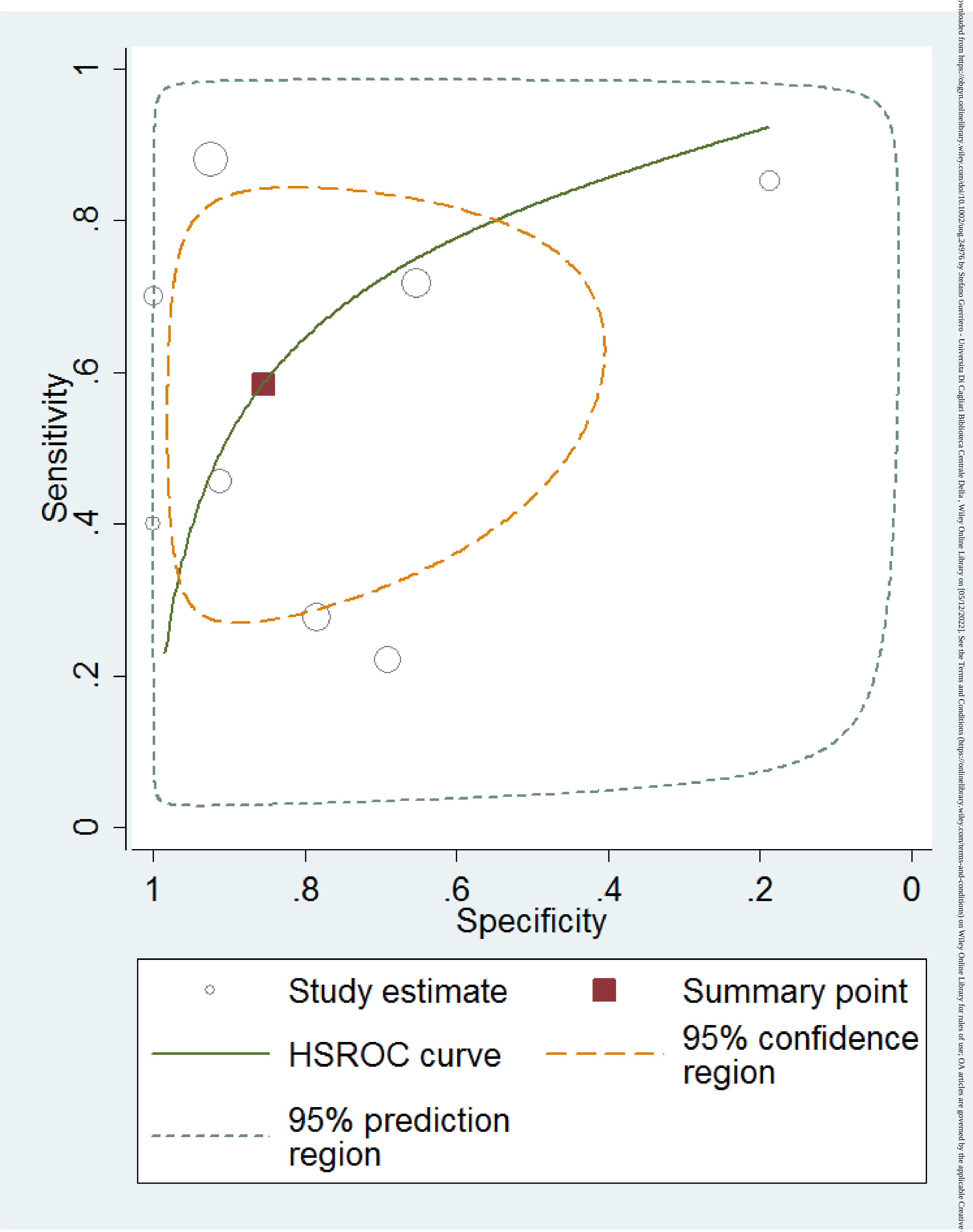

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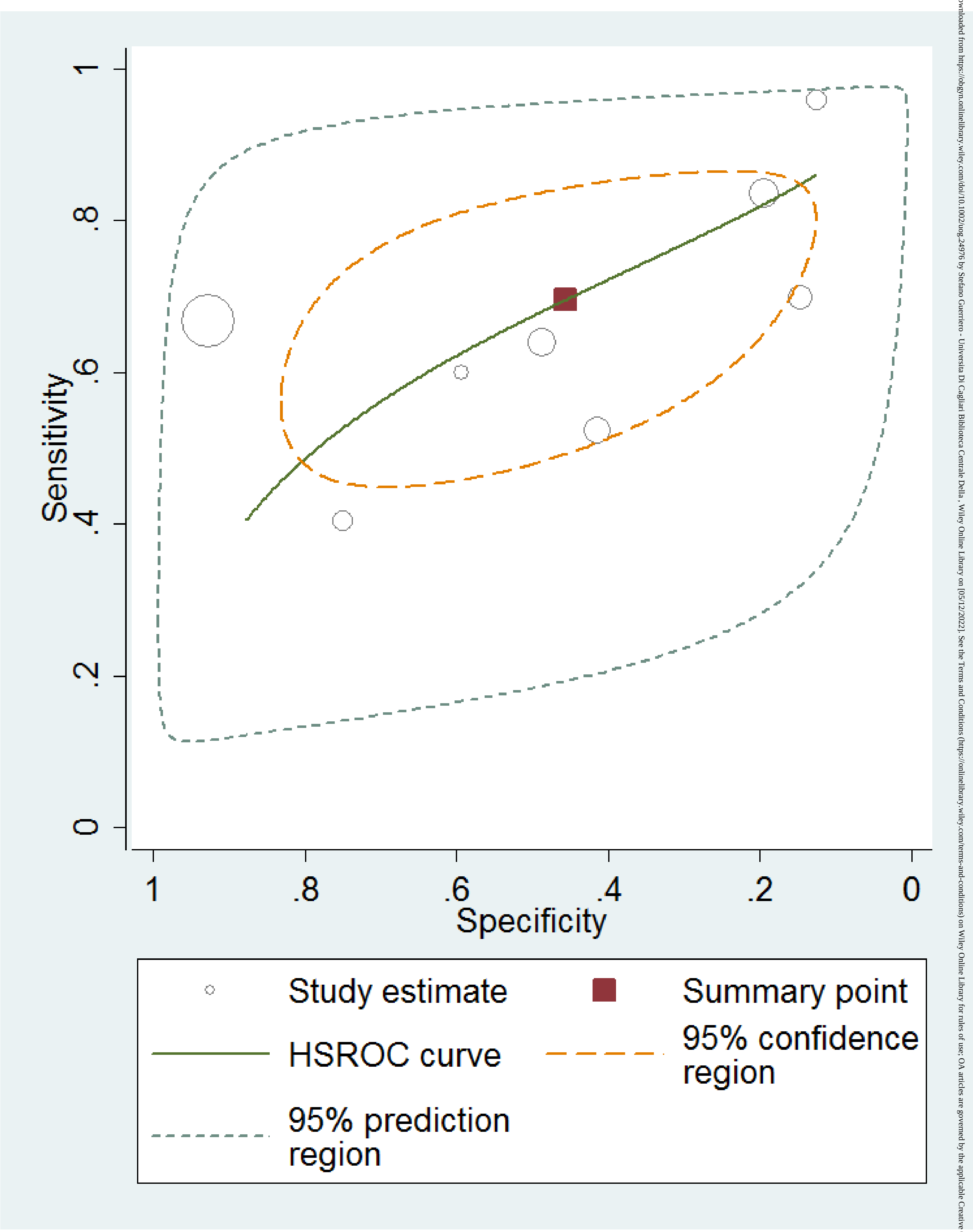

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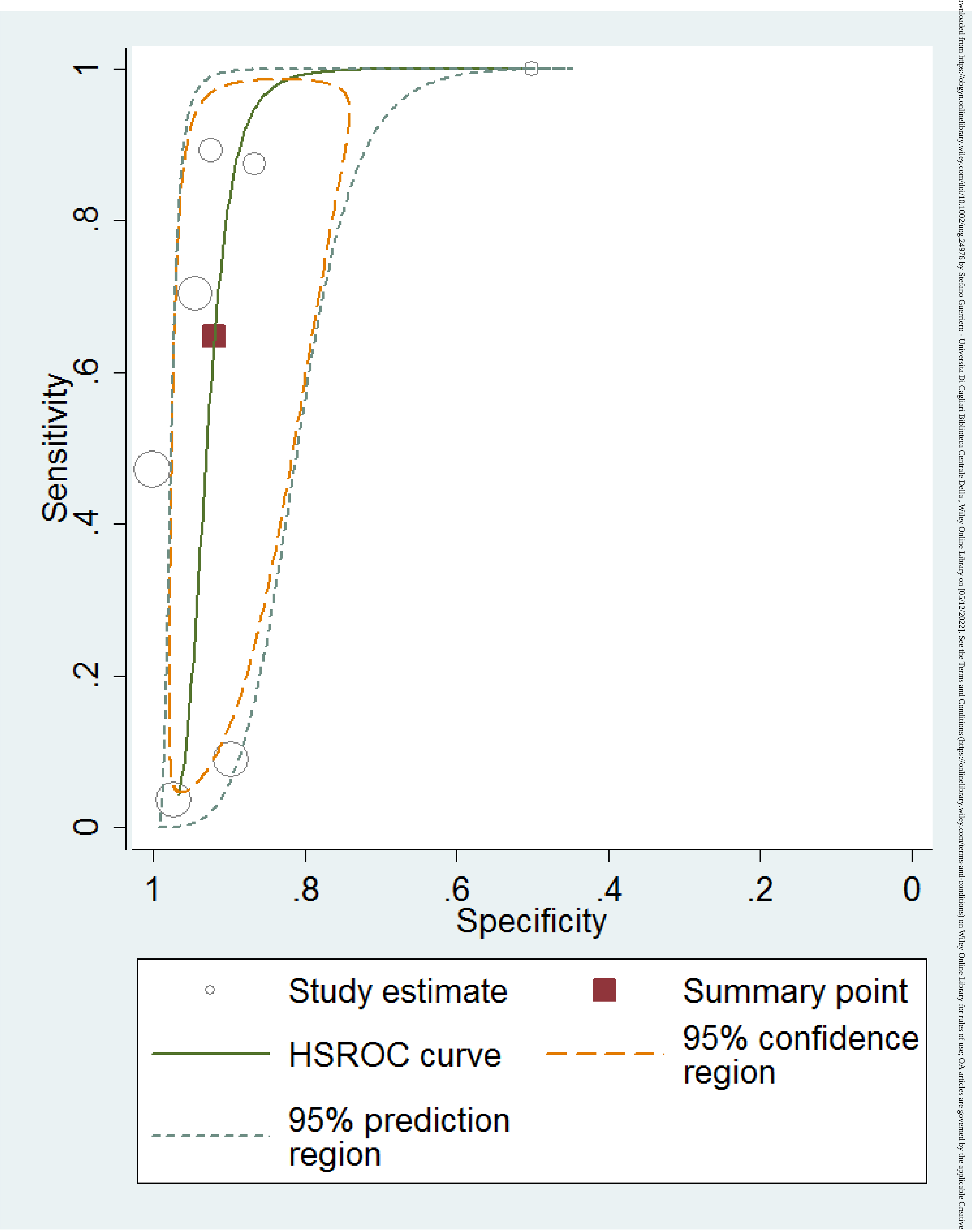

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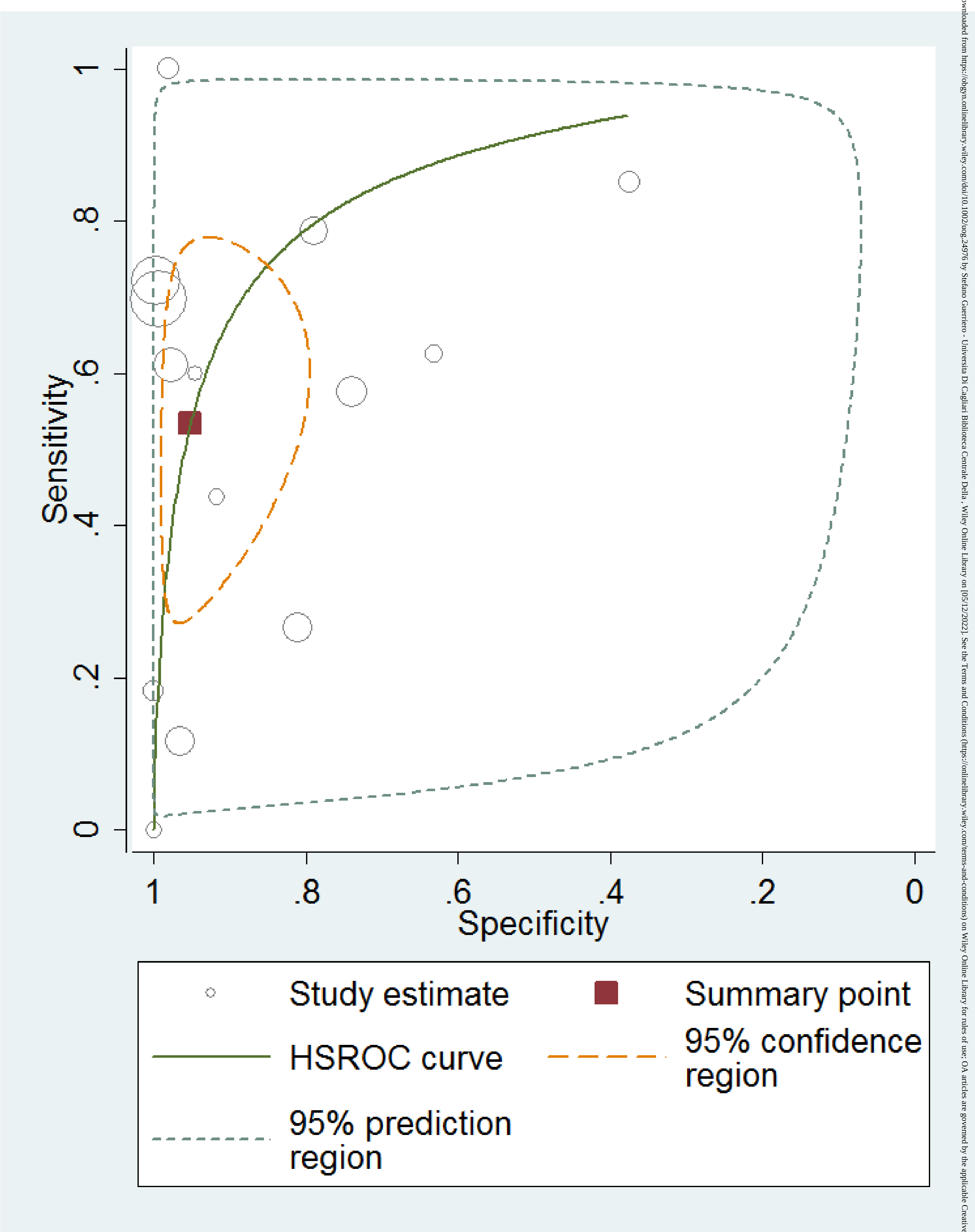

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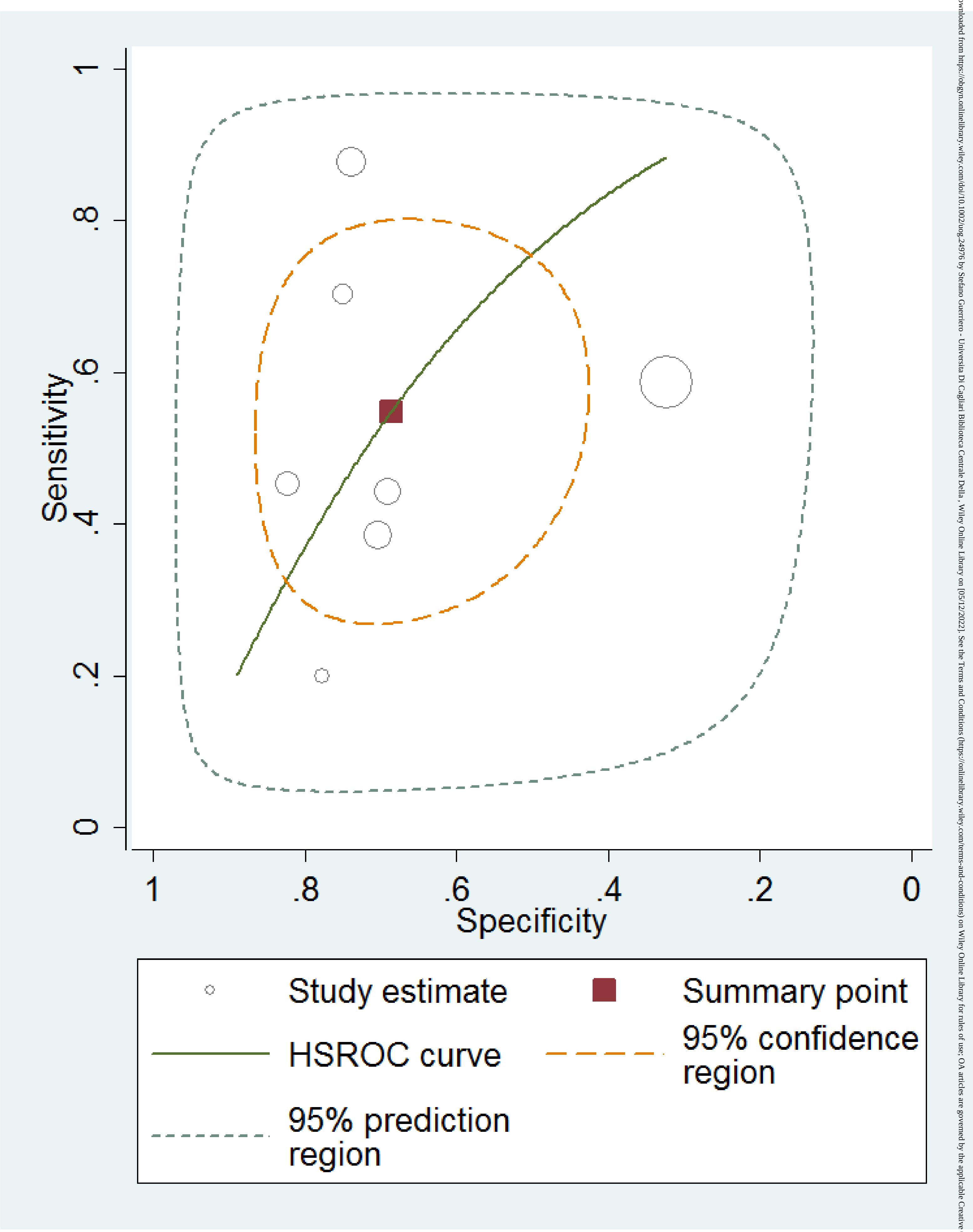

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