

Positive allergen reaction in allergic and nonallergic rhinitis: a systematic review

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Background: The diagnosis of allergic rhinitis (AR) is based on cutaneous and serological assessment to determine immunoglobulin E (IgE)-mediated disease. However, discrepancies between these tests and nasal provocation exist. Patients diagnosed as non-allergic rhinitis (NAR) but with positive nasal allergen provocation test (NAPT) may represent a local allergic condition or entopy, still suitable to allergy interventions. The objective of this study was to determine the frequency of nasal reactivity toward allergens among AR and NAR patients, and to describe the diagnostic characteristics of NAPT methodologies.

Methods: EMBASE (1947–) and Medline (1946–) were searched until December 8, 2015. A search strategy was used to identify studies on AR or NAR patients subjected to diagnostic local nasal provocation. All studies providing original NAPT data among the AR or NAR population were included. Meta-analysis of proportion data was presented as a weighted probability % (95% confidence interval [CI]).

Results: The search yielded 4504 studies and 46 were included. The probability of nasal allergen reactivity for the AR population was 86.3% (95% CI, 84.4 to 88.1) and in NAR was 24.7% (95% CI, 22.3 to 27.2). Reactivity was high with

pollen for both AR 97.1% (95% CI, 94.2 to 99.2) and NAR 47.5% (95% CI, 34.8 to 60.4), and lowest with dust for both AR 79.1% (95% CI, 76.4 to 81.6) and NAR 12.2% (95% CI, 9.9 to 14.7). NAPT yielded high positivity when defined by subjective end-points: AR 91.0% (95% CI, 86.6 to 94.8) and NAR 30.2% (95% CI, 22.9 to 37.9); and lower with objective end-points: AR 80.8% (95% CI, 76.8 to 84.5) and NAR 14.1% (95% CI, 11.2 to 17.2).

Conclusion: Local allergen reactivity is demonstrated in 26.5% of patients previously considered non-allergic. Similarly, AR, when defined by skin-prick test (SPT) or serum specific IgE (sIgE), may lead to 13.7% of patients with inaccurate allergen sensitization or non-allergic etiologies.
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Key Words: allergen inhalation challenge; aeroallergens; rhinitis; allergic rhinitis; local allergic rhinitis; entopy

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Antigen skin-prick testing (SPT) and serological identification of specific immunoglobulin E (sIgE) are assessments routinely used for diagnosis of allergic rhinitis (AR). Non-allergic rhinitis (NAR) is often defined in

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patients with symptoms of rhinitis with negative SPT and/or serum sIgE. However, systemic tests do not necessarily reflect nasal pathophysiology. There is extensive evidence that allergen-specific IgE responses develop in the nasal mucosa, giving rise to local production of sIgE. In nasal mucosa explants from AR patients, sIgE was synthesized, *ex vivo*, and were similar to the patient's known allergen sensitization.¹ A B-cell enzyme essential for class switch recombination and somatic hypermutation, AID, has been demonstrated in the nasal mucosa of rhinitis patients, enabling a sufficient self-production of local sIgE.¹ Therefore, these sIgE may not be detected in blood nor by SPTs. Thus, local assessments of the nose are important to determine the etiology of rhinitis.

A nasal allergen provocation test (NAPT) is a local assessment where the suspected allergen is administered directly onto the nasal mucosa and the subsequent nasal reactivity is measured. It is used to determine the causative allergen in AR especially when there are multiple sensitizations detected by systemic tests or false-negative skin and serum results are present.² In these cases, NAPT is used to diagnose local allergic rhinitis (LAR). LAR is a phenotype of rhinitis where patients have negative SPT or the absence of serum sIgE but are proven to have a local allergen-specific-induced response in the nose.³ This has also been termed "entopy".³ LAR is thought to occur due to local production of sIgE via the mechanisms discussed above.¹ The frequency of LAR using NAPT as a diagnostic tool varies between studies.

We sought to systematically review the literature for evidence of local nasal allergen reactivity, defined by a positive NAPT, in relation to systemic evaluation of allergy among patients with rhinitis. The main objective of this study was to describe the characteristics of NAPT outcomes in patients diagnosed with AR or NAR by SPT or serum sIgE. The secondary objective of this study was to determine if positive NAPT was influenced by definitions of rhinitis, type of administered allergen, and the tools utilized to measure a positive response.

Materials and methods

A systematic review was performed to identify studies on patients with AR or NAR with reported outcomes on NAPT. This review was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).⁴ The methodology from Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy⁵ was followed where possible.

Eligibility criteria

Studies on patients diagnosed with rhinitis who were subjected to NAPT were included. Only studies with frequency data were selected. Participants were rhinitis patients of any age with a history of physician-diagnosed rhinitis or chronic symptoms of rhinitis. These patients must have been further

identified as having either AR or NAR based on systemic evaluation for allergy (either SPT or serum sIgE). Chronic rhinosinusitis, asthma without rhinitis, and infectious rhinitis were excluded from this review. Diagnostic studies of either case series, case-control, or cross-sectional design were included. Only manuscripts published in English were included; case reports, reviews, guidelines, letters, and editorials with no original data were excluded as well as animal studies.

Information sources

A systematic electronic search was performed on both the EMBASE (1947–) and Medline (1946–) databases until December 8, 2015. A search strategy was designed for each database (Supporting Appendix 1) to identify all studies on a rhinitis population with nasal assessment for allergy.

Missing studies were searched manually from the bibliography of included studies.

Study selection

The search results were reviewed by 2 authors (A.W.H. and R.J.H.), and selected according to the eligibility criteria. Titles were screened for relevant articles followed by abstract review. Uncertain abstracts were then discussed between the reviewers. Full texts of the selected abstracts were then analyzed and excluded if they did not fulfill the selection criteria. Three main types of nasal intervention tests were used in the studies: NAPT, tests for nasal sIgE, and nasal cytology. Studies that utilized NAPT were then selected.

Data collection

An Excel datasheet (Microsoft Corp., Redmond, WA) was used to extract relevant data from the selected studies in a standardized data-sheet. Variables recorded were: study type, number of subjects per population group, disease-state definition, type of provocation intervention (allergen type, dose), response measure (tools of measure and criteria to determine positive response), and the outcome.

Rhinitis populations were determined to be either AR or NAR based on the presence of symptoms and systemic allergy evaluation or when it was predefined by the study authors. For the analysis, patients with rhinitis were grouped as AR when the systemic evaluation (serum sIgE and/or skin test) was positive and NAR if these tests were negative. When studies had both seasonal and perennial AR patients in the population, they were analyzed collectively as AR. Patients who were sensitized to aeroallergen without rhinitis symptoms were excluded.

For definitions of a positive NAPT, the committee of Spanish Society of Allergy and Clinical Immunology was used as a guide. Their recommendation stated 'the Symptom score should be combined with objective measure but can be considered positive when positivity criteria of objective measures are satisfied.'⁶ The cutoff point for the different measures of assessment were as follows:

1. Symptom: score increase ≥ 5 ;
2. Acoustic rhinometry: minimal cross-sectional area (MCA) 2 to 6 cm decrease $\geq 25\%$;
3. Active anterior rhinomanometry (AAR): NAR/airflow increase $\geq 100\%$;
4. Peak nasal inspiratory flow (PNIF): decrease flow $\geq 40\%$.

The European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA²LEN)⁷ guideline on positivity criteria for nasal challenge with aspirin was also used. This guideline required both symptoms and objective measure criteria to be fulfilled. Symptoms are considered positive when there is appearance of nasal symptoms after nasal provocation.

Objective measurements are considered positive if they fulfill the below criteria:

1. Acoustic rhinometry: decrease 25% total nasal volume at 12 cm; OR
2. AAR: decrease 40% bilateral reduction nasal inspiratory flow; OR
3. PNIF: flow decrease 40%.

As no included studies used total nasal volume at 12 cm, we adapted the criteria for acoustic rhinometry using the volume at 2 to 6 cm.

Quality assessment

The quality of the included studies were assessed using the 11 items from the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist⁸ as recommended by the Cochrane handbook.⁹ Quality assessment items were scored as either “yes,” “no,” or “unclear.” Three additional quality assessments were added for this review. Added items were the following:

- Item 12. Was a pre-challenge with control solution performed prior to allergen challenge?
- Item 13. Was the population defined based on Allergic Rhinitis and its Impact on Asthma Guidelines (ARIA)¹⁰ recommendations?
- Item 14. Were the cutoffs for positivity criteria predefined?
- Item 12 was added as it is important to perform a nasal challenge with control solution prior to allergen administration to rule out nonspecific nasal reactivity. This must be clearly stated in the study. Item 13 was added to assess if the study population had the accepted characteristics of AR or NAR. We summarized the ARIA definition¹⁰ of AR as a symptomatic disorder of the nose after an allergen exposure by an IgE-mediated inflammation. This is demonstrated by allergen sIgE in skin or blood. Studies that did not elaborate on the patient selection or merely mention known diagnosis of the disease received a score of “unclear.” Item 14 assessed for bias in interpreting outcome of nasal reactivity. Authors must have clearly stated that the same methods and positivity criteria was applied to all patients who underwent NAPT in their study.

Risk of bias

Heterogeneity was assessed graphically using forest plots (seen as scattered distribution without overlap of confidence interval) and tested using the I^2 . The heterogeneity was then explored by performing subgroup analysis. This analysis was done to identify discrepancies that resulted from different population definitions, adult or children population, allergen types, and methods to determine a positive test result.

Statistical analysis

The data was analyzed with Excel 2016 with a statistical add-on application package MIX2.0 (Bax L: MIX 2.0–Professional software for meta-analysis in Excel. Version 2.015. BiostatXL, 2016, Mountain View, CA; <https://www.meta-analysis-made-easy.com>). The studies that involved patients diagnosed as AR or NAR were pooled as 2 separate populations. The frequency of positive nasal allergen reactive (n/N) in these studies were converted into Freeman Tukey double arc sines. To allow data transformation, a value of 0.1 was used to replace 0 for studies that reported no positive NAPT result in their population. Data output was generated as a weighted probability both within individual studies and as overall cumulative tests among AR and NAR population. The data was presented as a percentage with the 95% confidence interval (CI). The methodological quality assessment data was analyzed using IBM SPSS Statistics for Windows, version 24.0. (IBM Corp., Armonk, NY) and summarized as a methodological quality assessment graph.

Results

Study selection

The search strategy yielded a total of 4504 studies. Studies were reduced to 3607 after 904 duplicates were removed. These titles were then screened, which left 282 abstracts for assessment. There were 218 full-text studies that were assessed for eligibility; 39 studies from the original search were included for analysis. Additionally, 7 studies that met the eligibility criteria were selected from the bibliographic review. A total of 46 studies were included (Fig. 1). These studies involved 3230 participants, of which 1685 were patients with AR, 1380 NAR, and 165 healthy controls.

Characteristics of included studies

The included studies consisted of case-controls (n = 33) or case series (n = 13). Case-control studies compared either AR vs NAR populations (n = 21),^{11–31} AR vs healthy controls (n = 10),^{32–41} or NAR vs healthy control (n = 2).^{42,43} The case series assessed either AR-only (n = 12)^{44–55} or NAR-only (n = 1)⁵⁶ populations. There were 43 studies that involved patients with AR^{11–41,44–55} and 24 studies that involved patients with NAR.^{11–31,42,43,56} There were 6 studies^{14,18–20,34,50} that involved exclusively children under 16 years of age. All of the studies were original articles

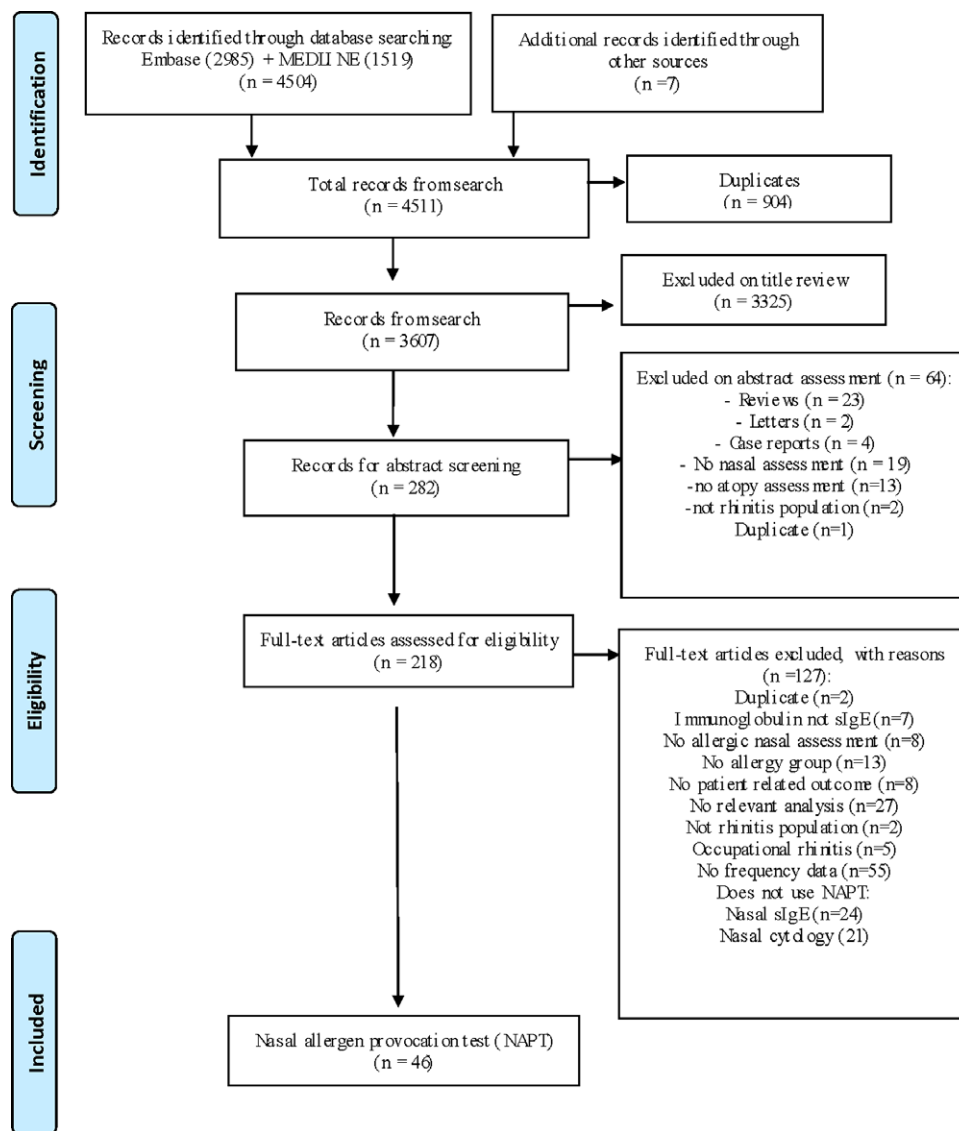


FIGURE 1. PRISMA flowchart depicting study selection process. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses.

except for 6 that were conference abstracts.^{11,12,14,36,38,56} The characteristics of included studies are presented in Supporting Appendix 2.

Intervention

NAPT was performed with either dust (n = 22),^{12,16,17,19–23,25–28,34,36–38,42,45,49,50,56} grass/tree pollens (n = 13),^{29,31,33,35,39–41,44,46,48,53–55} or *Alternaria* mold (n = 2).^{18,24} Three studies used allergens dependent on the patient's most likely sensitization.^{32,47,52} Single-allergen challenges were performed except for 6 studies where multiple allergens were administered 1 week apart (n = 5),^{11,13,15,30,51} or consecutively 15 minutes apart.⁴³ All studies performed a control nasal challenge with the respective diluent to rule out nonspecific nasal hyper-reactivity except for 9 studies where it was not clearly stated.^{11,12,14,19,36,38,40,51,56}

Outcome measures and positivity criteria

The measurement tools used to determine nasal reactivity were either subjective (n = 12),^{11,17–19,31,33,35,39,40,44,46,48} objective (n = 9),^{15,16,22,24,34,41,47,50,56} or a combination of both (n = 21).^{13,20,21,23,26–30,32,36,37,42,43,45,49,51–55} The outcome measures were unclear for 4 studies.^{12,14,25,38} For the studies with subjective endpoints, nasal symptoms were used (sneezing, itching, blockage, runny nose, and ocular symptoms). The symptoms measure either simple dichotomous outcome (present or absent symptoms),^{40,48} visual analogue scale (VAS),¹⁷ or ordinal categories. For VAS, a change of 3 or more from baseline was considered positive. For ordinal categories,^{31,33,35,44} a change varied between 2.5 to 5 from a normalized total of 10 categories, was used to define a positive nasal response. Another subjective assessment used was the number of sneezes induced (positive if >5 sneezes).¹⁹

The majority of studies used a combination of symptom assessment and/or objective assessments. Objective assessments utilized either acoustic rhinometry,^{13,16,22,24,28,29,42,43,47,56} rhinomanometry,^{15,20,26,27,30,32,34,36,37,41,47,49–52} or PNIF.^{14,17,21,49} A combined scoring system of both induced symptoms and severity of increased nasal airway resistance from rhinomanometry was also used.^{45,53–55} Among these, only 16 studies fulfilled the Spanish recommendation for positivity criteria on NAPT^{13,16,22,23,28–30,33,34,36,42–44,47,50,56} and 6 studies fulfilled the EAACI/GA²LEN 2007 recommendation for positivity criteria.^{13,28–30,42,43}

Quality assessment of included studies

The included studies were of good quality to assess the results of NAPT among patients diagnosed to have AR and NAR (Fig. 2). In general, studies used the same reference test to diagnose allergy (SPT and/or serum sIgE). The study population was in concordance with the ARIA definition and their allergy status was verified by either a skin or serological test for sIgE. Most studies also performed a control nasal challenge and explained any intermediate results.

However, the spectrum of disease was variable. There were studies that restricted their population to extreme spectrum of disease (eg, high cutoff values to determine positive SPT or serum IgE results, severe symptoms only) or those with a healthy control population that does not represent patients in clinical practice. The duration between index (NAPT) and reference test (SPT/serum sIgE) were also unclear in most studies. Studies done also conducted the index test without blinding, but this was to be expected as NAPT is an additional test to confirm nasal allergy.

Positive nasal allergen reaction among patients with AR and NAR

The weighted probability of positive nasal allergen reaction among studies was summarized in forest plots representing the AR (Fig. 3) and NAR population (Fig. 4). Positive nasal allergen reaction for all studies on AR was 86.3% (95% CI, 84.4 to 88.1) and for NAR it was 24.7% (95% CI, 22.3 to 27.2) (Supporting Tables 1 and 2). All healthy controls had negative NAPT. There were 2 studies that reported 0 positive NAPTs among their NAR population.^{14,20}

Study bias

Among studies on the AR population, the positive nasal allergen reactivity for case-control (AR vs NAR) studies was 81.3% (95% CI, 78.8 to 83.8), for case-control (AR vs normal control) studies was 93.7% (95% CI, 89.6 to 97.1), and for case series was 94.3% (95% CI, 91.2 to 96.8). Among studies on the NAR population, the positive nasal allergen reactivity for case-control (AR vs NAR) studies was 23.2% (95% CI, 20.4 to 26.1), case-control (NAR vs normal control) studies 36.8% (95% CI, 31.5 to 42.3), and for case series was 10.91% (95% CI, 5.7 to 17.5).

Population bias

The nasal allergen reaction was subanalyzed by refined definitions of AR and NAR. Studies were screened for a more stringent criterion to define AR^{15,20,28,46,48} and NAR^{13,15,28,29,43} patients. Stringent criteria for AR population was defined as symptoms of rhinitis with strong positive results on SPT (wheal diameter of more than 5 mm) or high level of serum sIgE (more than class 3). Stringent criteria for NAR population was defined as presence of symptoms with both negative SPT and serology toward a panel of aeroallergens. Studies with these definitions had high positive nasal allergen reactivity in both AR 100.0% (95% CI, 98.0 to 100) and NAR 56.7% (95% CI, 51.7 to 61.6) population.

Positive nasal allergen reaction among children

Nasal allergen reactivity among studies on children under 16 years old with AR was 93.0% (95% CI, 81.9 to 86.0), while in the NAR population it was 16.1% (95% CI, 9.5 to 24.0). Studies on the adult-only group with AR returned a probability of 84.0% (95% CI, 81.9 to 86.0), and for NAR it was 25.0% (95% CI, 22.5 to 27.6).

Positive nasal allergen reaction between types of allergen

Nasal allergen reactions were highest when multiple allergen challenges were administered for both AR 100% (95% CI, 98.1 to 100.0) and NAR 52.5% (95% CI, 47.1 to 57.9) population. When pollen allergens were used, the positive nasal responses were comparatively high for both AR 97.1% (95% CI, 94.2 to 99.2) and NAR 47.5% (95% CI, 34.8 to 60.4) population. Nasal allergen challenges with dust showed the least reactivity for both AR 79.1% (95% CI, 76.4 to 81.6) and NAR 12.2% (95% CI, 9.9 to 14.7) population.

Positive nasal allergen reaction based on tools to measure nasal reactivity

The different tools used to measure positive nasal allergen reactions were explored. Subjective tools of measure returned the highest nasal allergen reactivity for both AR 91.0% (95% CI, 86.6 to 94.8) and NAR 30.2% (95% CI, 22.9 to 37.9) populations. The nasal reactivity using objective tools for the AR was 80.8% (95% CI, 76.8 to 84.5) and in NAR was 14.1% (95% CI, 11.1 to 17.2). When a combination of both methods was used the nasal allergen reactivity for AR was 85.0% (95% CI, 82.3 to 87.5) and in NAR was 35.1% (95% CI, 31.3 to 39.1).

Positive nasal allergen reaction based on established guideline for positivity criteria

When only studies that fulfilled the Spanish society recommendation for positivity criteria were combined, the prevalence returned for AR was 89.3% (95% CI, 86.8 to 91.6) and in NAR was 24.5% (95% CI, 21.9 to 27.2). However,

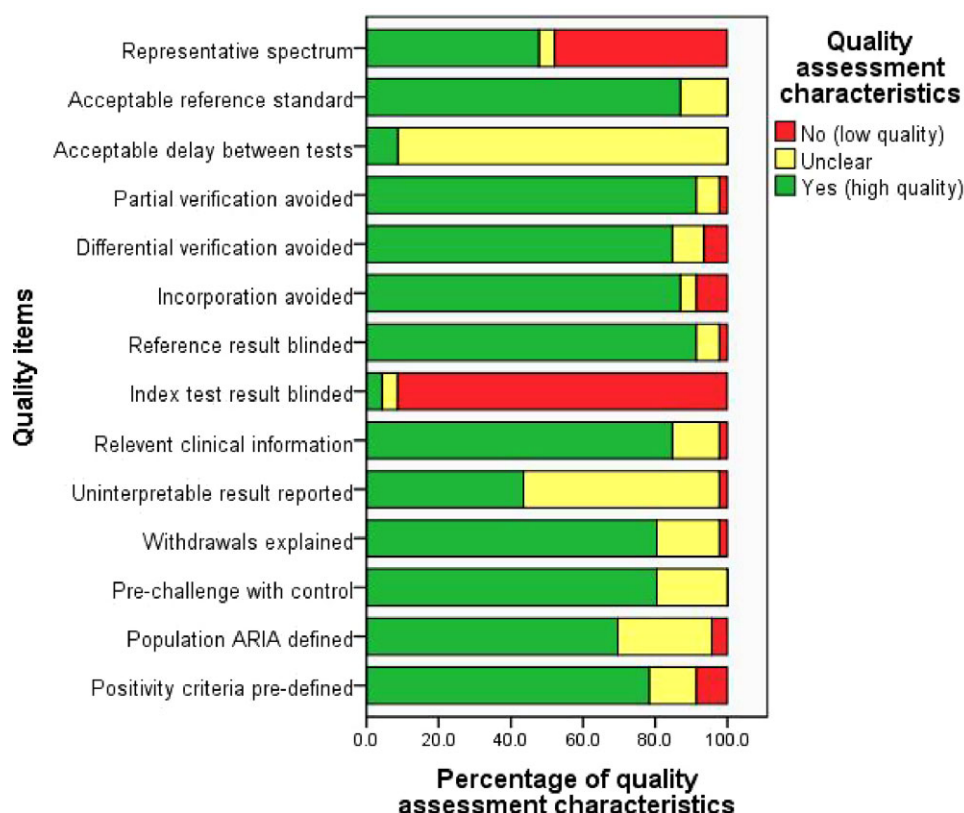


FIGURE 2. Methodological quality assessment of included studies using 11 items from the QUADAS checklist⁸ and 3 added quality assessment items relevant to this review. Assessments are categorized as either “yes”, “no,” or “unclear” based on QUADAS recommendations. QUADAS = Quality Assessment of Diagnostic Accuracy Studies.

it was higher when EAACI/GA²LEN 2007⁷ positivity criteria was applied (99.9%; 95% CI, 98.1 to 100.0) and 40.3% (95% CI, 36.0 to 44.6) for AR and NAR, respectively.

Heterogeneity of studies

The forest plots (Figs. 2 and 3) indicated heterogeneity for both populations with greater disparity among the NAR population. The I^2 values for studies on the AR and NAR populations were 92.3% (95% CI, 90.5 to 93.7) and 94.7% (95% CI, 93.2 to 95.9), respectively, which showed extreme heterogeneity among both study populations.

Discussion

Discrepancies exist between nasal reactivity toward inhaled allergens and systemic sensitization among patients with airway reactivity. Patients diagnosed with NAR may exhibit positive nasal reaction toward an allergen, which could be due to local allergic rhinitis (LAR).¹⁶ NAPT as a test to diagnose patients with local nasal allergy need to be further standardized. As presented in this review, NAPT results could vary depending on patient selection, age group, allergen type, tools to measure nasal response, and importantly the cutoff to determine a positive result. There was

also greater disparity in nasal allergen reactivity among the NAR population. Key findings of this study are that using allergen sensitization (SPT, serum sIgE) alone can result in a misdiagnosis occurring in 13.7% of AR patients and 24.7% of NAR.

Among patients with AR, false-negative NAPT may be due to inadequate allergen dose, concomitant use of medications, varying definitions of positivity criteria, or nonrelevant sensitizations in the skin or serum. Applying a cutoff wheal diameter of 5 mm or more was reported to correlate more accurately with positive NAPT with high positive predictive value.²³ Chusakul et al.¹⁷ increased the frequency of positive nasal reactivity toward allergens from 68.8% to 90% among AR patients in his study when a cutoff wheal diameter of 7 mm was applied. Similarly, we found increased nasal reactivity which reached 100.0% (95% CI, 98.0 to 100) when only studies that used strong test magnitude from SPT or serum sIgE to define the AR population were used.

Positive NAPT among NAR patients could be due to either a false-negative systemic test, or local nasal allergy. A false-positive NAPT, due to nonspecific reactivity, is unlikely because 80.4% of included studies used a control delivery to exclude nonspecific nasal reactivity. A more stringent definition that ruled out inhaled allergen sensitization by both SPT and serology to define NAR population

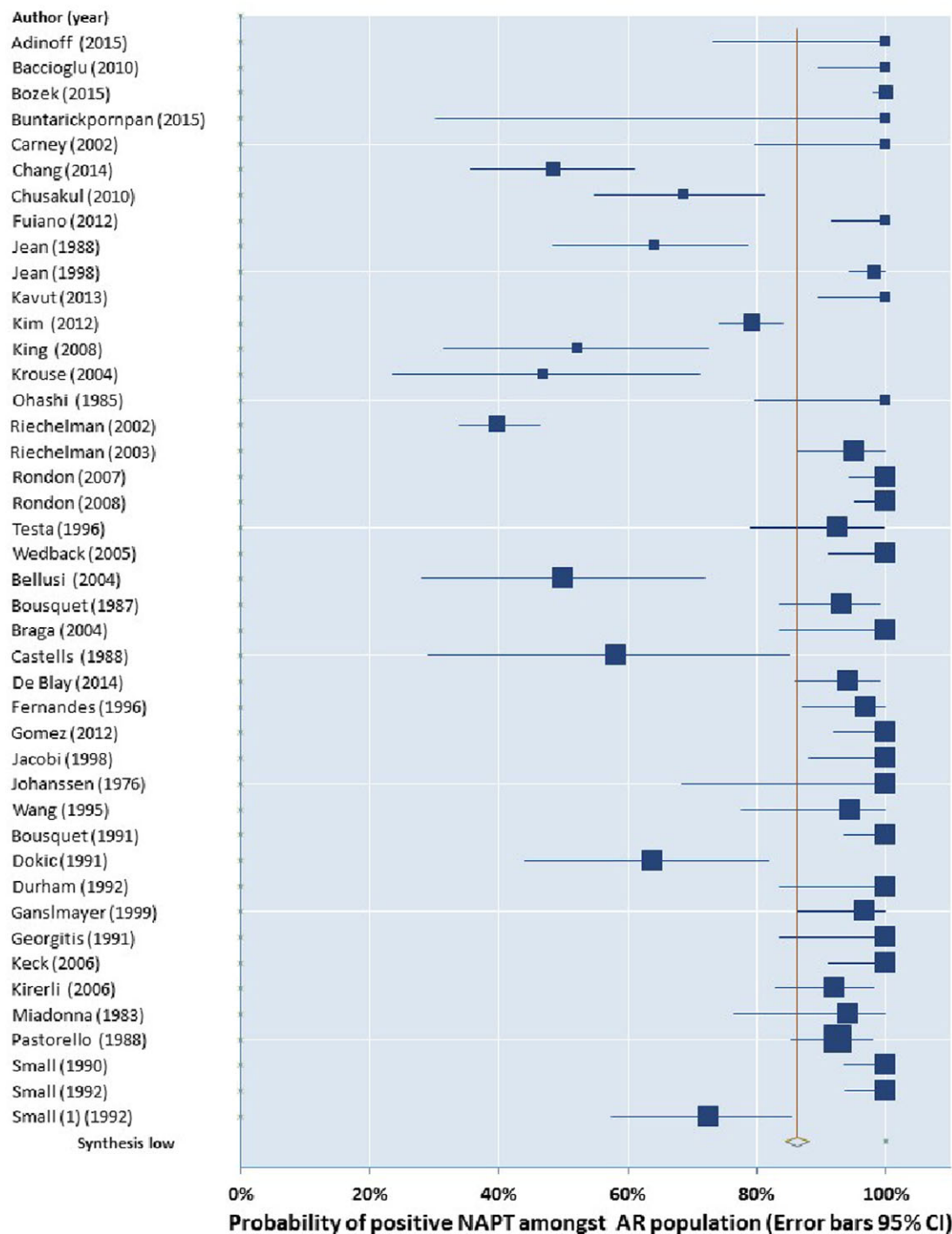


FIGURE 3. Forest plot representation of positive nasal allergen reactivity among patients diagnosed as having AR. Studies are primarily ordered by study type (from top: case control [AR vs NAR], case control [AR vs healthy control], followed by case series [AR only]), in alphabetical order. The diamond represents a pooled summary estimate of the probability of positive nasal allergen provocation test among the AR population. Heterogeneity was present between studies (I^2 92.26%; 95% CI, 90.45 to 93.73). AR = allergic rhinitis; CI = confidence interval; NAR = nonallergic rhinitis.

only increased the positive NAPT results. This high positive NAPT was more evident for pollens (97.1% and 47.5% for AR and NAR, respectively). Therefore a high suspicion for LAR is needed among patients with seasonal rhinitis symptoms but negative systemic tests.

The tools to measure positive nasal responses differed between studies. To address the variability among NAPT methodologies, guidelines have been made available for test harmonization. The Spanish Society guidelines⁶ and GA²LEN guideline have provided recommendation on

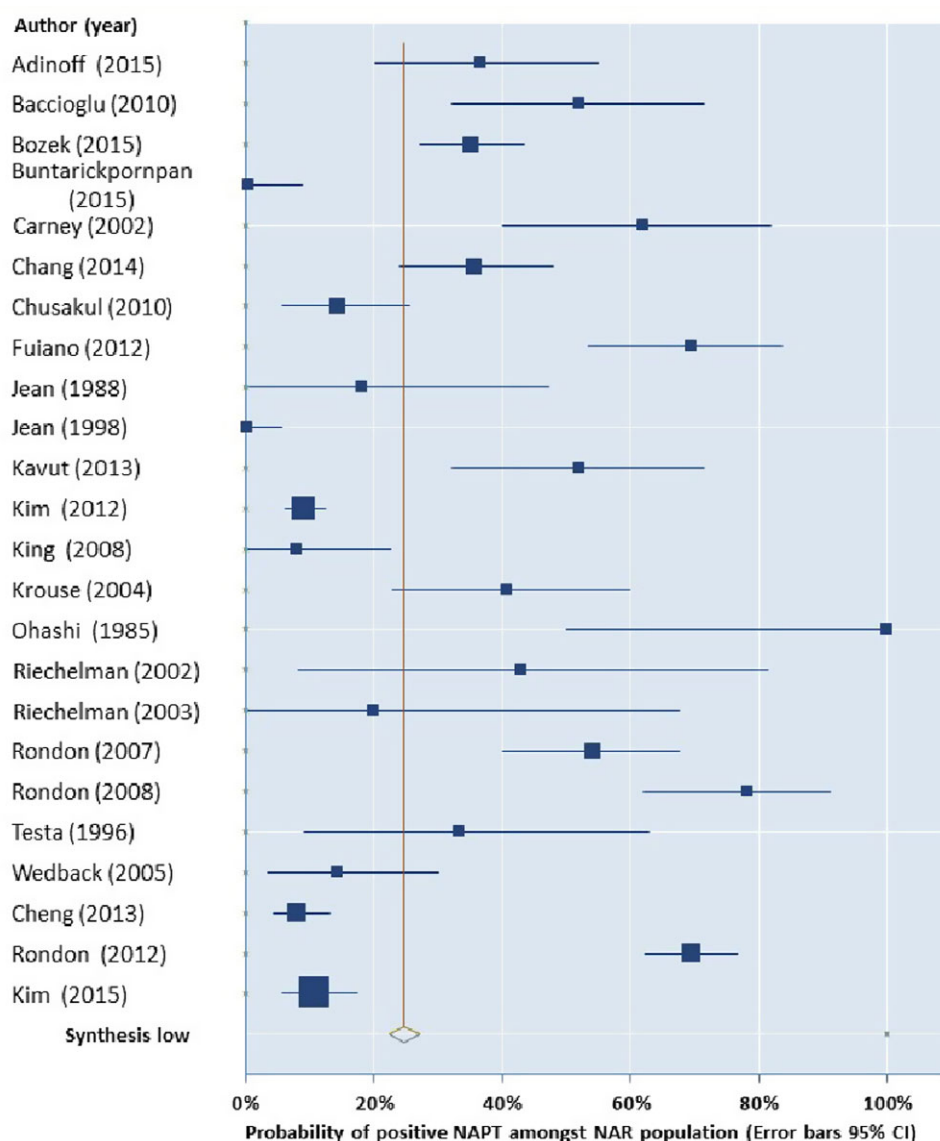


FIGURE 4. Forest plot representation of positive nasal allergen reactivity among patients diagnosed as having NAR. Studies are primarily ordered by study type (from top: case control [AR vs NAR], case control [AR vs healthy control], followed by case series [AR only]), in alphabetical order. All were case-control studies except the final study (Kim and Jang⁵⁶). The diamond represents a pooled summary estimate of the probability of positive nasal allergen provocation test among the NAR population. Heterogeneity was high among the NAR population (I^2 94.7%; 95% CI, 93.2 to 95.9). AR = allergic rhinitis; CI = confidence interval; NAR = nonallergic rhinitis.

cutoff to determine a positive response (positivity criteria). The Spanish guidelines place more emphasis on objective measures to determine a positive nasal reaction. The probability of positive NAPT among the AR and NAR population across studies that met the Spanish guidelines were more consistent with the overall pooled summary estimate.

Heterogeneity was greater in the NAR population. This was explained by 3 main factors, which were the following: differing criteria to define NAR; how the allergens were selected; and the methods used to determine a positive NAPT. Definitions for NAR were variable between studies. Although studies used either SPT or serum sIgE to

exclude allergy toward the allergen of interest, some studies used other methods to define their NAR population. Some studies were more stringent in ruling out allergen sensitization by employing both serology for sIgE and SPT for a panel of aeroallergens.^{13,15,28,29,43} There were also studies that used intradermal test^{21,24,35,43} or nasal smear for eosinophils²¹ to exclude allergy. Allergen selection was variable, in that studies either picked an allergen based on symptom or used a whole panel of common aeroallergens. The differing methods and positivity criteria also played a role and impacted the outcome of NAPT. These were tested using the subgroup analyses, which found that these variations influenced the probability of positive NAPT.

Demographic factors may also influence the probability of a positive NAPT. Studies that involved children under 16 years old with AR were found to have a higher nasal reactivity toward allergens compared to adults (93.0% vs 84.0%). This was the reverse for children with NAR (16.1% vs 25.0%). However, further age or gender stratification was not done due to unavailable data. These data were reported as summarized data for both the AR and NAR population in the case-control studies and could not be differentiated between the positive or negative NAPT results group.

Regardless of the methods for NAPT, there remains a third (26.5%) of the NAR population who reacted to allergens applied to the nasal mucosa. These patients could

represent a subtype of rhinitis termed as LAR. On the flip side, patients incorrectly identified as AR may lead to ineffective management and wasted resources. Therefore, a more accurate patient selection to define airway allergy is warranted to optimize therapy.

Conclusion

Systemic allergic test results do not necessarily reflect the true etiology of rhinitis. Local allergen reactivity is demonstrated 24.7% of patients previously considered nonallergic. Similarly, AR, when defined by SPT or serum sIgE, may lead to 13.7% of patients with inaccurate allergen sensitization or nonallergic etiologies. 

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