Allergic rhinitis diagnosis: skin-prick test versus laboratory diagnostic methods

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Aim
To verify the specificity, sensitivity, and accuracy of the skin-prick tests (SPTs) in allergic rhinitis (AR) compared with blood tests and nasal smears.
Study design
It is a cohort, prospective, nonrandomized study.
Patients and methods
A total of 180 patients were enrolled. Group A included 135 patients having AR symptoms for more than 1 year. Group B included 45 patients without AR symptoms candidate for septoplasty surgery who served as controls. All patients were subjected to detailed history, scoring for AR, endoscopic examination, complete blood count, nasal smear eosinophilia, and SPT.
Results
SPT was positive in 94.1% (*n*=127) of allergic patients and 20% (*n*=9) of the controls at least for one allergen. Most of cases were allergic to mixed pollens (66.7%), cotton dust (41.5%), and housefly particles and house dust mite (28.9% equally). The absolute eosinophil count was positive in 70.4% of allergic patients (*n*=95) and 33.3% of the control (*n*=15). Nasal smear eosinophilia was positive in 82.9% (*n*=112) of allergic patients and 20% (*n*=9) of the controls. SPT possesses high sensitivity and specificity that reached 94.1 and 80%, respectively, and 90.6% accuracy. However, absolute eosinophil count showed the lowest results, where sensitivity and specificity reached 70.4 and 66.7%, respectively, and 69.4% accuracy.
Conclusion
SPT is accurate for diagnosing AR and possesses high sensitivity and specificity; however, adding a nasal swap test will raise the sensitivity, specificity, and accuracy of diagnosis.

Keywords:
absolute eosinophilic count, allergic rhinitis, nasal smear eosinophilia, skin-prick test

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Introduction

Allergic rhinitis (AR) is a global health problem and one of the most common disorder seen by otolaryngologists, the prevalence rate of AR had been reported as 10–30% of adults and up to 40% of children [1]. AR is an immunoglobulin E (IgE)-mediated disease, which is predominantly caused by environmental allergen exposure in a genetically predisposed individual. Common allergens implicated in AR are mainly proteins and glycoproteins found in airborne particles. Important allergens causing intermittent or persistent symptoms may be airborne dust mite, cockroach residues, animal dander, and grass pollens [2].

AR is characterized by the presence of nasal obstruction, congestion, rhinorrhea with or without facial pain, and reduction or loss of smell [3,4]. These symptoms are reversible either spontaneously or with treatment. AR is diagnosed by the clinical examination of patients and their response to medical treatment [5]. Proof of sensitization to an allergen includes coupling of skin or blood testing and patient's exposure history [6].

Skin-prick testing (SPT) is advised as a diagnostic tool for AR as it is less invasive and easy to administer [7]. When SPT result is negative, AR as an IgE-mediated disease is largely excluded. Moreover, the results of SPT are important, especially if avoidance measures or immunotherapy are to be considered. There is a lack of international consensus regarding the accuracy of skin testing in the diagnosis of allergies [8,9], including AR [10,11]. The disagreement in the precision of SPT in the diagnosis of AR among studies can be clarified by

the inconsistency of standardization in the composition of allergens, the device used in the test, the differences in the characteristics of tested population, or the design of the study [12].

When SPT is not available, or the patient is receiving antihistamines, other tests should be considered including: complete blood picture to detect absolute eosinophil count (AEC), total and allergen-specific IgE concentrations in the blood, and nasal smears for cytology, which may show high concentrations of eosinophils [13]. SPT has the following advantages when compared with an in-vitro measurement of specific IgE antibodies: it can be interpreted within 15–20 min versus in-vitro test results (days or weeks); it can also be used to test less common allergens that lack specific IgE antibody measurements, such as fresh fruits and vegetables, and certain medications; the test gives a visual indication of the sensitivity which can be used to affect the patient's behavior [14]; it is less expensive; and it is a more specific screening method for detecting the presence of IgE antibodies in patients who had appropriate exposure history [15].

The commercially available respiratory allergens have few systemic adverse effects; however, a physician or other health care professional and emergency equipment should be immediately available when such tests are performed, and in patients with a history of severe systemic allergic reactions to food or drugs, an intravenous line for immediate circulatory access can be recommended. Patients, especially those taking a beta blocker, or less often, angiotensin converting enzyme-inhibitor, may be at a higher risk because of less response to epinephrine that might be needed to treat a systemic allergic reaction [16].

Relative contraindications for SPT include pregnancy [17], a peak flow of less than 70% in patients with asthma, patients with dermographism and severe eczema, or patients who are taking medications such as antihistamines or antidepressants or calcineurin inhibitors, which can interfere with the proper interpretation of the test results [18].

The current study is implemented with the aim to verify the specificity, sensitivity, and accuracy of SPT compared with inexpensive laboratory tests and nasal smears in the diagnosis of AR.

Patients and methods

The current study is a cohort, prospective, nonrandomized study. Data were collected from patients attending otorhinolaryngology outpatient clinic of Fayoum University Hospital, during the period from September 2016 to September 2018. This study was approved by local ethical committee. Written consents were provided by all the patients.

Patients are scored according to the quantitative scoring for allergic rhinitis (SFAR) [19]. Patients with SFAR score of more than or equal to 7 are considered to have AR, whereas patients with SFAR score of less than 7 are considered to have no AR.

Patients were divided into two groups: group A included 135 patients presented with AR symptoms for more than 1 year and had SFAR score of more than or equal to 7; they served as AR patients. Group B included 45 patients candidate for septoplasty surgery without evidence of previous history of AR with SFAR score of less than 7; they served as control patients. Both groups did have similar criteria regarding no medical treatment either oral, topical corticosteroids, or oral antihistamines at least 4 weeks before the first visit. Patients with severe dermatographism, patients on beta-blockers, uncooperative patients, those unable to stop antihistamines, pregnant patients, patients with severe asthma, patients with drug-induced rhinitis, or those with cardiac disease, with contraindication to the use of epinephrine, were excluded from the present study. All patients were subjected to detailed history, endoscopic examination, complete blood count (CBC), nasal smear eosinophilia (NSE), and SPT.

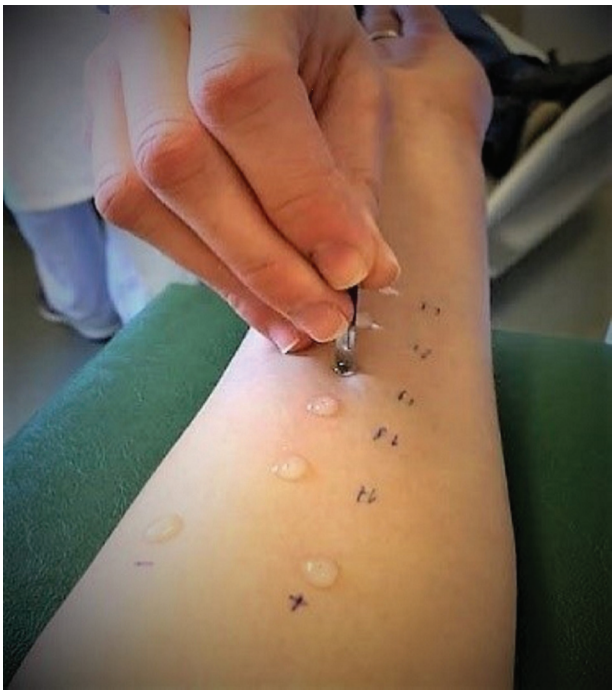
Skin-prick test

SPT was done by introducing specific allergens like house dust, house dust mite, cotton dust, mixed pollens, mixed molds, housefly particles, and grass pollens into the volar part of the forearm of patient's skin. The test solutions were allergen extracts (in 50% glycerine), one negative control (nonextract containing diluent with 50% glycerine), and one positive control (histamine base 6 mg/ml) purchased from Greer Laboratories Inc. (Lenoir, North Carolina, USA).

The process of skin inoculation with allergens was done using a single-head metal lancet (ALK-Abello Inc., Horshlom, Denmark) (Fig. 1).

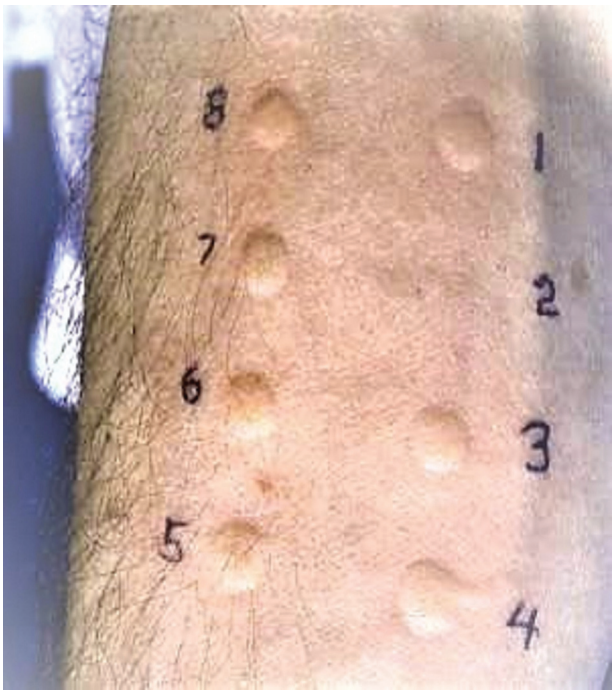
Positive and negative controls were measured first. The (positive) histamine control was used to make sure that the test materials are applied correctly and to exclude negative SPT results owing to medications taken by the test participant. The negative control excludes the presence of dermographism, which, when present, makes the tests difficult to interpret. The largest

Figure 1



The process of skin inoculation with different allergens using a single-head metal lancet (ALK-Abello Inc.).

Figure 2



The result of SP after 15 min.

diameter of the wheal of each particular test is measured. A positive result being a wheal of more than or equal to 3 mm. Then the wheal is outlined with a pen blotted onto a cellophane tape and transcribed onto paper and stored electronically, as recommended by the American Academy of Allergy, Asthma and Immunology, and the American College of Allergy, Asthma, and Immunology [7] (Fig. 2 and Table 1).

CBC was performed to detect AEC, which refers to the number of circulating eosinophils in the peripheral blood in cells per cubic millimeter (cells/mm^3). The cutoff value used in this study was positive if AEC was more than or equal to 440 cells/mm^3 [20].

Nasal smear was taken by swab sticks from medial surface of middle part of inferior turbinate. The slide was fixed in 95% ethyl alcohol, and then stained with hematoxylin and eosin stain. Finally, the slide was subjected to NSE count study. The cutoff value used in this study was positive if more than or equal to 10 eosinophil cells were detected by high power field (E ≥10/HPF) [21].

The collected data were organized, tabulated, and statistically analyzed using SPSS software statistical computer package, version 18 (SPSS Inc., Chicago, Illinois, USA). Qualitative data were presented as number and percentages. Sensitivity, specificity, and total accuracy measures of different tests in differentiating patients of AR from normal were presented as %, with 95% confidence interval, and calculated using OpenEpi (Open Source Epidemiologic Statistics for Public Health, Developed by the open Epi project, Atlanta, Georgia) version 3.01.

Table 1 Self-completed questionnaire for the scoring for allergic rhinitis [19]

Items	Score (points)	Total score
Nasal symptoms (blocked nose, runny nose, and sneezing) in past year	1 for each symptom	3
	1 for perennial	4
	1 for pollen season	5
Nasal symptoms plus itchy-watery eyes	2	7
Triggers		
Pollens, house dust mites, and dust	1	
Epithelia (cat and dog)	1	9
Previous allergic status	2	11
Previous positive allergic tests	2	13
Previous medical diagnosis of allergy	1	14
Familial history of allergy	2	16

Results

This study was carried out on 180 patients, who were divided into two groups. Group A included 135

patients having AR and group B included 45 cases who served as the control. The first group (group A) had 92 males and 43 females, with an average age of 25.2 years, whereas the control group (group B) had 34 males and 11 females, with an average age of 25.4 years (Table 2).

Overall, 60% of patients with AR (n=81) had severe allergic symptoms that affected their daily life whereas only 5.9% of patients (n=8) had mild symptoms. None of the control group had any allergic symptoms.

Regarding the SPT, 94.1% of allergic patients (n=127) showed positivity at least for one allergen, whereas 5.9% of them (n=8) showed no reaction to any allergen but had positive eosinophil nasal smears. On the contrary, 20% of the control group (n=9) showed skin reaction to at least one allergen, with maximum of three allergens (Table 3).

Most of cases were allergic to mixed pollens (66.7%), cotton dust (41.5%), and housefly particles and house dust mite equally (28.9%). In many patients there was reaction to multiple allergens. Most of the control group participants were allergic to mixed pollen also (6.75%) and grass and house dust mite equally at 4.4% (Fig. 3).

The AEC in the allergic patients was positive (>440 cell/mm^3) in 70.4% of them (n=95), whereas it was negative (<440 cell/mm^3) in 29.6% (n=40). In the control group, only 33.3% of patients (n=15) were positive (Table 4).

Regarding the NSE count, in the AR group, 82.9% of patients (n=112) had positive nasal smear results (<10 eosinophils/HPF), whereas 17.1% of patients (n=23) had negative results (>10 eosinophils/HPF). In the control group, 20% of patients (n=9) were positive (Table 5).

Table 2 The demographic data

	Group A	Group B
No	135	45
M	92	34
F	43	11
Average age	25.2	25.4

Table 3 A comparison between skin-prick test among allergic rhinitis and control groups

SPT	Group A (cases) [*n* (%)]	Group B (control) [*n* (%)]
Positive	127 (94.1)	9 (20)
Negative	8 (5.9)	36 (80)
Total	135 (100)	45 (100)

SPT, skin-prick test.

The sensitivity, specificity, and accuracy among the three types of tests are summarized in Table 6. SPT possess the highest result, as sensitivity and specificity reached 94.1 and 80%, respectively, and 90.6% accuracy. On the contrary, AEC showed the lowest results, where sensitivity and specificity reached 70.4 and 66.7%, respectively, and 69.4% accuracy (Fig. 4).

Discussion

AR can be defined clinically as an inflammatory condition of the nose characterized by nasal obstruction, sneezing, itching, or rhinorrhoea [13]. A recent large-scale, cross-sectional study in six western European countries found that the overall prevalence of AR was 23%. The study also showed that the condition is often undiagnosed, as 45% of patients with investigator-confirmed AR had not previously received a diagnosis from their physicians [22].

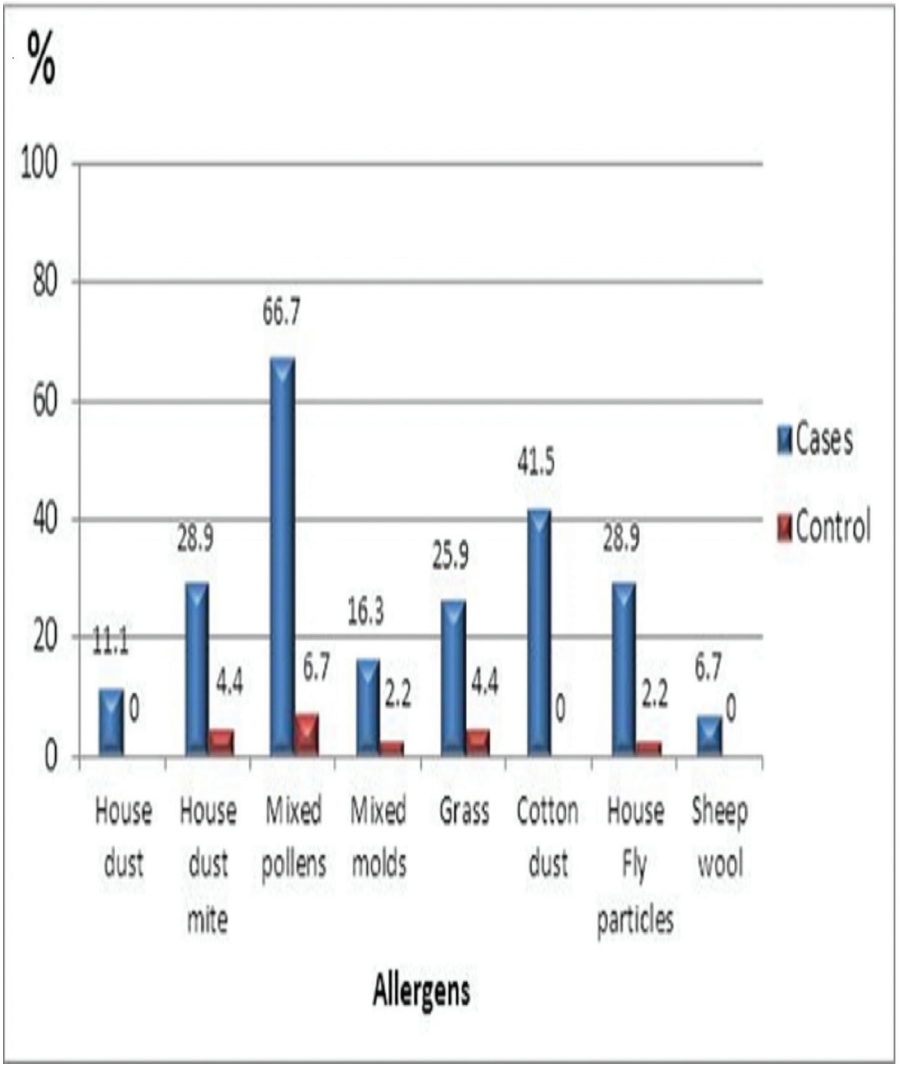
Since the first publication about SPT by Ebruster [23], who extensively researched this diagnostic test, it has been used as a primary diagnostic tool to detect type I hypersensitivity reactions. Although the principle of SPT still largely resembles the original methods described, a wide array of interpretations and modifications has led to diminished comparability when SPT results are reported [24].

Adopting the Global Allergy and Asthma European Network (GA (2) LEN) protocol, Heinzerling *et al.* [14] found SPT is highly specific and sensitive, reaching 70–95% and 80–97%, respectively, to diagnose inhalant allergies. The positive predictive value to diagnose AR based only on the clinical history is 77% for persistent allergy and 82–85% for intermittent seasonal allergy, this increases to 97–99% if SPT is utilized [25].

It was reported in a meta-analysis done by Nevis *et al.* [26] to verify the sensitivity and specificity of SPT in the diagnosis of AR that there is a lack of consensus regarding the performance of SPT, and the combined estimates of the sensitivity and specificity for SPT in various studies were 88.4 and 77.1%, respectively.

When we compare the results reached in the present study with the aforementioned meta-analysis, it showed great concordance, as in the current study, SPT is reasonably accurate reaching 90.6% in identifying patients with suspected symptoms of AR. It carries sensitivity and specificity of 94.1 and 80%,

Figure 3



Results of the SPT among AR cases and controls for different allergens (%). AR, allergic rhinitis; SPT, skin-prick test.

Table 4 A comparison between absolute eosinophil count results among allergic rhinitis and control groups

	Group A [*n* (%)]	Group B [*n* (%)]
>440 cell/mm^3	95 (70.4)	15 (33.3)
<440 cell/mm^3	40 (29.6)	30 (66.7)
Total	135 (100)	45 (100)

Table 5 Comparison of percentage of eosinophils in nasal smears among allergic rhinitis and control groups

	Group A [*n* (%)]	Group B [*n* (%)]
E≤10/HPF	112 (82.9)	9 (20)
E< 10/HPF	23 (17.1)	36 (80)
Total	135 (100)	45 (100)

respectively. On the contrary, nasal smears had sensitivity and specificity of 82.9 and 80%, respectively, whereas AEC had sensitivity and specificity of 70.4 and 66.7%, respectively, which are lower than SPT.

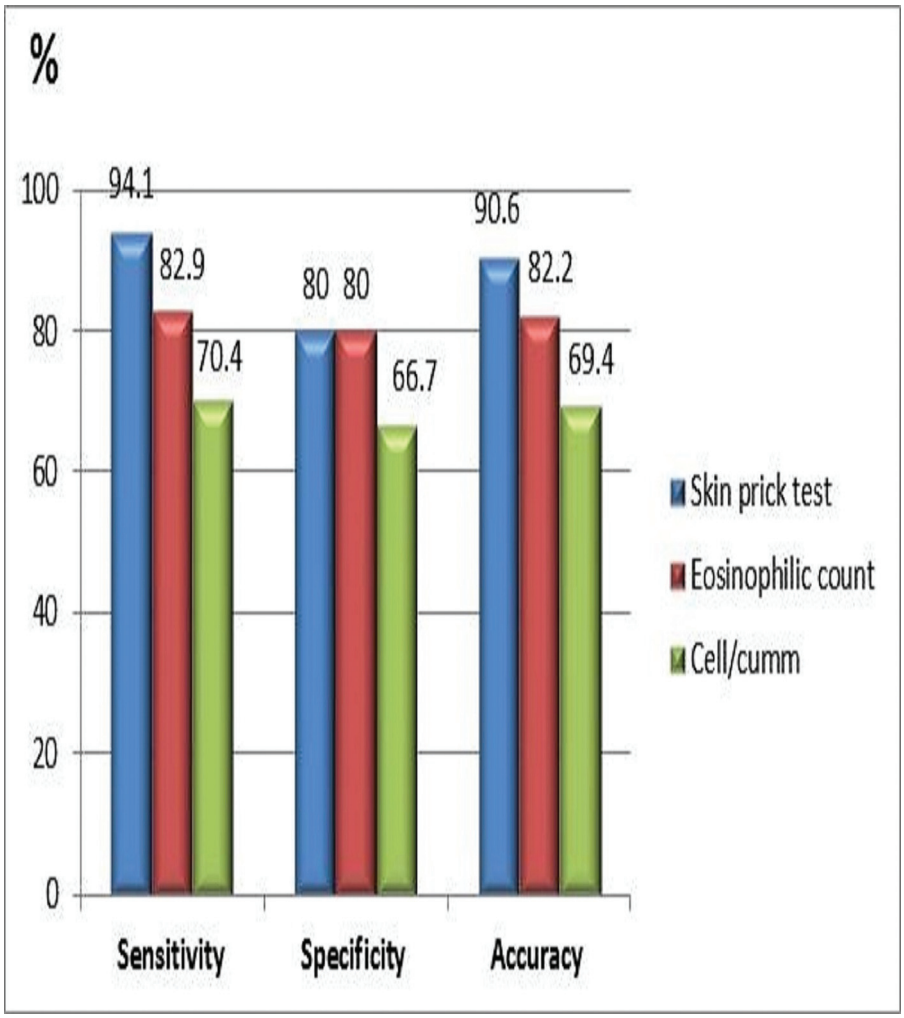
Table 6 Results of sensitivity, specificity, and accuracy among the three types of tests

	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)
SPT	94.1 (88.7–96.9)	80.0 (66.2–89.1)	90.6 (85.4–94.2)
NSE	82.9 (75.7–88.4)	80.0 (66.2–89.1)	82.2 (75.9–87.1)
AEC	70.4 (62.2–77.4)	66.7 (52.1–78.6)	69.4 (62.4–75.7)

AEC, absolute eosinophil count; CI, confidence interval; NSE, nasal smear eosinophilia; SPT, skin-prick test.

It is well known that the proper diagnosis of allergen in patients with AR will facilitate the decision of further management of patients in the form of immunotherapy, allergen avoidance, or pharmacotherapy. Consequently, financial burden can be alleviated and the patients' quality of life can be improved. This raises the importance of SPT compared with serum eosinophilia and nasal swab, as the SPT can diagnose the AR in addition to suspected allergen. On the contrary, CBC (AEC)

Figure 4



Sensitivity, specificity, and accuracy of SPT, AEC, and NSE. AEC, absolute eosinophil count; NSE, nasal smear eosinophilia; SPT, skin-prick test.

and nasal smear (NSE) only detect AR without detection of allergen, but adding CBC (AEC) and nasal smear (NSE) to SPT will increase the accuracy, sensitivity, and specificity of diagnosis in AR.

The current study can add to the results of several studies that support the role of SPT as an accurate test in the diagnosis of AR. The present study was done on a small number of patients, and further studies are needed on large numbers of patients to evaluate the role of SPT, CBC (AEC), and nasal smear (NSE) in the diagnosis of AR.

Conclusion

The specificity, sensitivity, and accuracy of the SPT in the diagnosis of AR are higher than blood tests and nasal smear. Adding the blood test (AEC) and nasal smear (NSE) to SPT will increase the specificity, sensitivity, and accuracy of diagnosis in AR. SPT should be further standardized to include standardized procedures and allergen panels that cover suspected allergens in different geographic areas.

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Conflicts of interest
There are no conflicts of interest.

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