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Histologic Uncertainty to Surgical Clarity: Institutional Insights Into Malignancy Risk in Papillary Breast Lesions

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Abstract

Background

Papillary lesions of the breast pose a diagnostic and management challenge. Although these lesions have been discussed in the international literature, local data remain limited. This study provides targeted insights to support informed surgical decision-making and improve patient outcomes.

Methods

A retrospective review of a prospectively maintained pathology database was conducted from January 2023 to December 2025, and cases of papillary breast lesions diagnosed on core needle biopsy were extracted. Papillary cancers and incidental papillary lesions identified in surgical specimens were excluded. Patients who underwent subsequent diagnostic surgical excision were included in the final database, and their medical notes, radiology reports, and histology reports were reviewed. The rate of upgrade to DCIS or invasive cancer was recorded, and clinical or radiological predictors of upgrade were explored.

Results

A total of 132 patients were identified with isolated papillary breast lesions. Five patients underwent surveillance and were excluded from the analysis. The final cohort comprised 127 patients who underwent diagnostic surgical excision. The mean age was 52 ± 12.8 years. Overall, malignant upgrade was identified in 14/127 lesions (11.0%). Papillomas with atypia (B3b) demonstrated a significantly higher upgrade rate than papillomas without atypia (B3a) (20.5% vs 6.8%, p = 0.032). On multivariable analysis, the presence of atypia remained an independent predictor of malignant upgrade (adjusted OR 3.99, 95% CI 1.22-13.00, p = 0.022), while increasing age was significantly associated with upgrade.

Conclusion

Papillary lesions with atypia on core biopsy have significant potential to harbour malignant disease, supporting further diagnostic excision, particularly in patients aged over 50 years. The low upgrade rates observed in younger patients without atypia, warrant future studies evaluating the safety of surveillance in a similar large cohort.

Categories: General Surgery
Keywords: atypia, breast cancer, core biopsy, excisional biopsy, papillary lesions

Introduction

Papillary lesions of the breast represent a heterogeneous group of intraductal proliferations ranging from benign intraductal papillomas (IDPs) to atypical papillomas and papillary carcinomas. Their clinical significance lies in the variable but non-negligible risk of malignant upgrade when lesions diagnosed on core needle biopsy undergo surgical excision. This uncertainty continues to challenge breast surgeons, radiologists, and pathologists in determining which patients require excision and which may be safely observed.

International literature over the past decade demonstrates wide variation in upgrade rates, reflecting differences in biopsy technique, radiological-pathological concordance, and histological classification. A large meta-analysis of 7,371 biopsy-diagnosed benign IDPs reported an overall upgrade rate of 6.94% to high-risk lesions or carcinoma, and identified key predictive factors including age, lesion size ⩾10 mm, palpable mass, calcifications, and personal or family history of breast cancer [1]. These findings reinforce the need for individualised risk stratification rather than a uniform management strategy.

More contemporary data continue to refine this risk profile. A 2026 real-world analysis evaluating predictors of upgrade in IDPs highlights the ongoing effort to develop more accurate models for clinical decision-making, underscoring persistent uncertainty in managing these lesions [2]. Similarly, a recent European cohort study examining pure IDPs confirmed that even papillomas without atypia are clinically significant, given their persistent albeit low risk of upstaging, thereby justifying continued vigilance in management decisions [3].

Despite these international insights, local institutional data remain limited, particularly within Irish breast units. Given the variability in population demographics, imaging pathways, and biopsy practices, local upgrade rates may differ from those reported internationally [4]. Understanding these patterns is essential to developing evidence-based, context-specific recommendations that optimise oncologic safety while minimising unnecessary surgical intervention [5].

Our study addresses this gap by evaluating papillary breast lesions diagnosed over a three-year period in a busy tertiary-care breast unit. By examining upgrade rates, radiological and clinical predictors, and the influence of atypia and age, this work provides critical institutional evidence to guide MDT decision-making and refine management pathways for papillary breast lesions.

Materials And Methods

This study is a retrospective, cross-sectional review of a prospectively maintained database conducted at University Hospital Limerick (UHL), Ireland. The study sample comprised patients diagnosed with papillary breast lesions on core biopsy within the breast unit at UHL from January 2023 to December 2025. Formal approval was obtained from the Research Ethics Committee, UL Hospitals Group, Mid-West Region (Ref: 0394).

Inclusion criteria were based on the diagnosis of a papillary lesion on core biopsy and subsequent diagnostic excision. Patients who underwent surveillance or had incidental findings of a papillary lesion in other surgical specimens were excluded from the study. The primary outcome was the proportion of cases upgraded to ductal carcinoma in situ (DCIS) or invasive carcinoma upon surgical excision. Secondary analyses explored potential clinical and radiological predictors of malignant upgrade.

The variables recorded included patient age, presenting symptoms and clinical findings, incidental versus symptomatic detection, radiological characteristics, core needle biopsy findings, and final histopathological diagnosis following surgical excision. These data were extracted to characterise the study cohort and to evaluate potential clinical, radiological, and pathological predictors of malignant upgrade. Final excision histology was used as the reference standard for determining upgrade to DCIS or invasive carcinoma.

All patients underwent standard triple assessment, consisting of clinical examination, breast imaging, and tissue diagnosis. Clinical assessment was performed in consultant-led breast clinics. Radiological evaluation included bilateral mammography and targeted breast ultrasonography of the affected breast followed by a core needle biopsy. All cases were reviewed at the weekly multidisciplinary team (MDT) meeting comprising breast surgeons, radiologists, pathologists, medical oncologists, radiation oncologists, and breast care nurses.

The sample size was determined by the number of eligible cases identified within the predefined study period rather than by an a priori power calculation. This reflects the retrospective design and primary objective of estimating institutional malignant upgrade rates in papillary breast lesions diagnosed on core needle biopsy. Although the final cohort was sufficient for descriptive analysis and comparison of upgrade rates between B3a and B3b lesions, the limited number of malignant upgrade events reduced statistical power for subgroup analyses and necessitated a restricted multivariable model.

Statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY). Continuous variables were summarised as mean ± standard deviation when approximately normally distributed, and as median with interquartile range or range when non-normally distributed. Categorical variables were presented as frequencies and percentages. Group comparisons were performed using Fisher's exact test for categorical variables, given the small number of malignant upgrade events. Age was assessed as both a continuous and clinically stratified variable, using Welch's t-test or the Mann-Whitney U test as appropriate according to distributional assumptions. Univariable logistic regression was used to estimate odds ratios and 95% confidence intervals for potential predictors of malignant upgrade. Multivariable logistic regression was restricted to a limited number of clinically relevant variables to reduce the risk of overfitting in the context of low event numbers. A two-sided p-value <0.05 was considered statistically significant.

Results

The results are presented in accordance with the study objectives, commencing with cohort identification and baseline clinicopathological characteristics, followed by an assessment of malignant upgrade in relation to histological subtype, age, clinical presentation, and radiological features. The derivation of the final

excision cohort is described first to provide context for the subsequent analyses.

During the study period, 132 patients with isolated papillary breast lesions diagnosed on core needle biopsy were identified. Five patients were managed with radiological surveillance alone and were excluded from the upgrade analysis, resulting in a final excision cohort of 127 patients. Figure *1* illustrates this case-selection pathway and demonstrates that the analysed population represents patients in whom tissue confirmation was obtained through diagnostic surgical excision. Table *1* further characterises this cohort and shows that most lesions were classified as B3a papillomas without atypia, while approximately one-third were B3b papillomas with atypia. The overall age distribution was similar between the B3a and B3b groups, suggesting that differences in upgrade risk were not explained by major baseline age imbalance between histological categories.

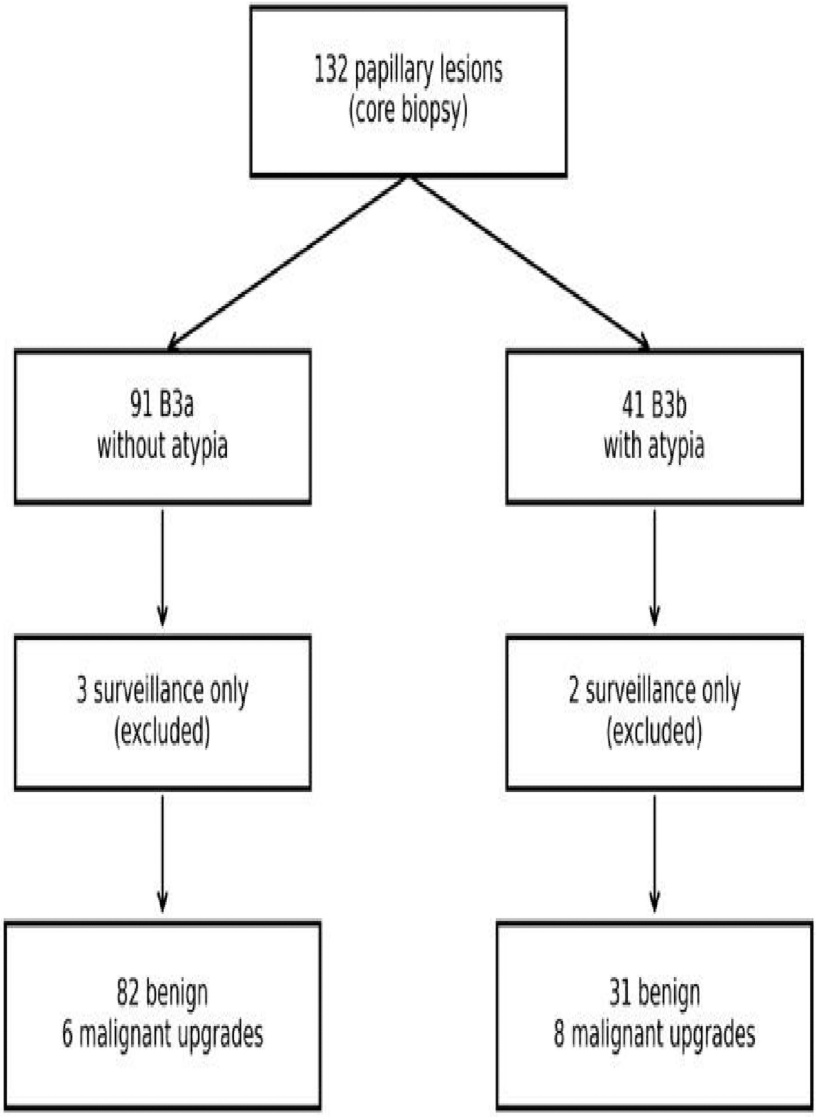


FIGURE 1: Flow diagram showing study cohort and final outcomes.

Cohort	n	Age mean +/- SD	Age median (IQR)	Incidental	Symptomatic	Malignant upgrade
All lesions	127	52.0 +/- 12.8	49.0 (44.0-57.0)	46 (36.2%)	81 (63.8%)	14 (11.0%)
B3a without atypia	88	52.2 +/- 13.0	49.0 (44.0-56.0)	28 (31.8%)	60 (68.2%)	6 (6.8%)
B3b with atypia	39	51.4 +/- 12.5	49.0 (43.5-59.5)	18 (46.2%)	21 (53.8%)	8 (20.5%)

TABLE 1: Baseline characteristics of the excised cohort stratified by atypia status.

Figure 2 summarises the final malignant histology among upgraded cases and shows that upgrades included both DCIS and invasive carcinoma. DCIS was the predominant pathology with eight cases, followed by three cases of invasive ductal carcinoma (IDC), two cases of papillary carcinoma, and one case of invasive lobular cancer. This distinction is clinically important because it confirms that papillary lesions diagnosed on core biopsy may harbour a spectrum of malignant pathology at excision. The presence of invasive disease among upgraded cases further supports continued caution in selected higher-risk patients, particularly where atypia, older age, or imaging concern is present.

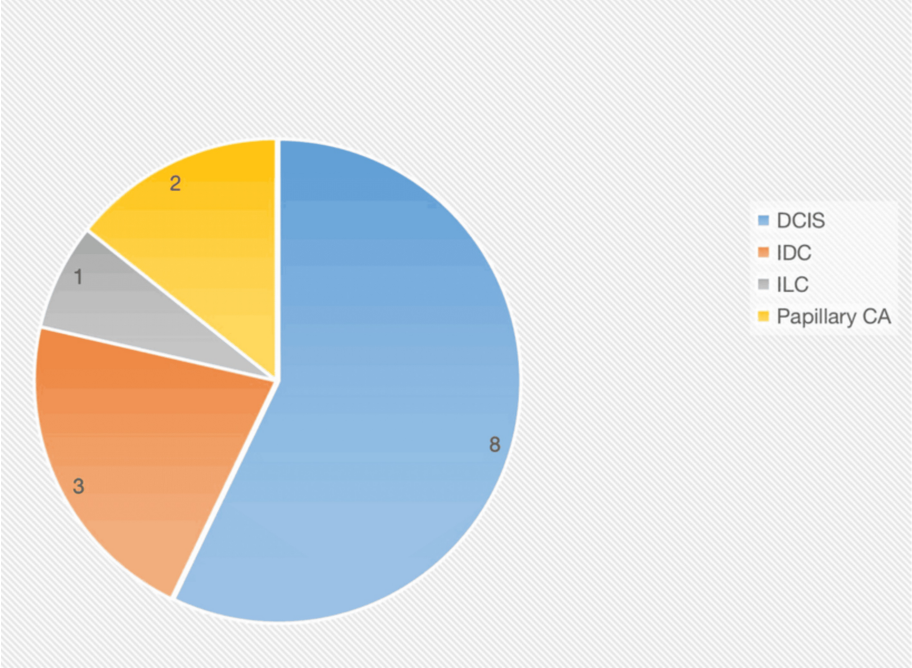


FIGURE 2: Pie-chart of various malignant histological findings upon excision

The univariable analysis presented in Table 2 reinforces this pattern. Among the evaluated clinical, pathological, and radiological parameters, the presence of atypia showed the clearest association with malignant upgrade. Incidental presentation demonstrated a higher observed upgrade proportion than symptomatic presentation, but this difference did not reach statistical significance, suggesting that mode of detection alone should not be used as an isolated determinant of management. Radiological findings, including calcifications, solid nodules, intraductal abnormalities, cystic lesions, and architectural distortion, showed variable upgrade proportions but no statistically significant independent association in this dataset. These findings suggest that imaging appearances should be interpreted in conjunction with histology and radiological-pathological concordance rather than as stand-alone predictors.

Variable	Exposed upgrade, n/N (%)	OR (95% CI)	p-value
B3b: papilloma with atypia	8/39 (20.5)	3.53 (1.13-10.99)	0.032
Incidental presentation	8/46 (17.4)	2.63 (0.85-8.13)	0.138
Calcifications present	2/23 (8.7)	0.73 (0.15-3.51)	1.000
Solid nodule	0/20 (0.0)	0.00 (0.01-2.91)†	0.124
Intraductal abnormality	2/22 (9.1)	0.78 (0.16-3.74)	1.000
Cystic lesion	1/7 (14.3)	1.37 (0.15-12.30)	0.568
Architectural distortion	0/5 (0.0)	0.00 (0.04-14.89)†	1.000

TABLE 2: Univariable predictors of malignant upgrade.

OR, odds ratio; CI, confidence interval; Fisher's exact test; p < 0.05 significant. † Zero-event OR estimates should be interpreted with caution.

Age-stratified predicted risk estimates are summarised in Table 3. Across all age bands, predicted upgrade risk was consistently higher for B3b than B3a lesions, and the difference between these groups widened with increasing age. The predicted risk rose gradually after 50 years and was highest in patients older than 70 years, particularly when atypia was present. This pattern supports the interpretation that age modifies the clinical relevance of atypia, with older patients with B3b lesions representing the subgroup most likely to benefit from diagnostic excision.

Age band	B3a predicted risk	B3b predicted risk
≤40	2.60%	9.80%
41–50	4.30%	15.30%
51–60	6.70%	22.60%
61–70	10.50%	32.10%
>70	15.60%	42.80%

TABLE 3: Predicted malignant upgrade risk by age band and atypia status

Overall, the results demonstrate that malignant upgrade occurred in approximately one in nine excised papillary lesions, with risk concentrated among lesions showing atypia on core biopsy and increasing with age. In contrast, papillomas without atypia, particularly in younger patients and in the absence of concerning radiological features, showed a lower upgrade profile. These findings provide institutional evidence to support risk-adapted MDT decision-making rather than a uniform management pathway for all papillary breast lesions.

A restricted multivariable logistic regression analysis was performed to assess the association of histological atypia and patient age with malignant upgrade (Table 4). Given the limited number of malignant upgrade events (n=14), the model was restricted to two clinically relevant predictors to limit overfitting. After adjustment for age, the presence of atypia (B3b) was associated with increased odds of malignant upgrade (adjusted OR 3.99, 95% CI 1.22-13.00; p=0.022). Increasing age was also associated with malignant upgrade (adjusted OR 1.049 per year, 95% CI 1.005-1.094; p=0.027). Although both associations reached conventional statistical significance, the limited event count and relatively wide confidence intervals warrant cautious interpretation. These findings should be regarded as exploratory and require validation in larger cohorts.

Predictor	Adjusted OR	95% CI	p-value
Atypia (B3b versus B3a)	3.99	1.22-13.00	0.022
Age (per year)	1.049	1.005-1.094	0.027

TABLE 4: Multivariable predictors of malignant upgrade

Discussion

The present study provides contemporary institutional data on the malignant upgrade risk of papillary breast lesions diagnosed on core needle biopsy, demonstrating an overall upgrade rate of 11%, comprising 6.3% DCIS and 4.7% invasive carcinoma. This rate falls towards the lower end of the wide range reported in international literature, suggesting that, within a structured breast unit pathway, many papillary lesions may be managed safely using careful risk stratification rather than a uniform approach to excision. Importantly, our findings reinforce that upgrade risk is not evenly distributed across all papillary lesions, but is influenced by histological subtype, radiological features, and patient age. These factors should therefore be considered together during MDT discussion to identify patients who are most likely to benefit from diagnostic surgical excision while avoiding overtreatment in appropriately selected low-risk cases.

Our findings confirm that atypia is the dominant predictor of malignant upgrade, with B3b lesions showing a significantly higher upgrade rate than B3a lesions (20.5% vs 6.8%, OR 3.53, p = 0.032). Detailed univariate analysis of different variables is shown in Table *2*. This finding is consistent with multiple large studies over the past decade. A 2024 meta-analysis of 7,016 intraductal papillomas reported pooled upgrade rates of 5.0% for benign intraductal papillomas and up to 36% for atypical intraductal papillomas, identifying atypia as the strongest histological driver of malignancy risk [4]. Lin et al. similarly demonstrated a substantially higher upgrade risk among papillomas with atypia diagnosed on core needle biopsy, reinforcing the need for definitive histological assessment in this subgroup [6]. Corbin et al. also reported higher upgrade rates in atypical papillomas and identified clinicopathological features that may help refine risk stratification after core biopsy [7]. Together, these studies support routine diagnostic excision for atypical papillary lesions and strengthen the external validity of our institutional findings.

Age was also an important clinical factor in our cohort. Although upgrade risk began to increase after age 50, the rise was most pronounced beyond age 70, particularly among patients with B3b histology (Table *3*). This pattern is consistent with Lee et al., who reported that older age was associated with malignant upgrade among benign papillomas diagnosed on core biopsy, supporting selective surgical excision in higher-risk patients [8]. Similarly, Chen et al. found that age and histological atypia were relevant considerations in determining management and outcome for papillary breast lesions [9]. Taken together, these findings suggest that age should be considered alongside atypia, imaging features, and radiological-pathological concordance when assessing upgrade risk. In practical terms, our data support a lower threshold for diagnostic excision in older patients, especially when atypia is present.

Radiological features also contributed to risk stratification. Hypoechoic nodules, representing the most common imaging finding in our cohort, were benign in more than three-quarters of cases, consistent with imaging-pathology concordance studies showing that well-circumscribed hypoechoic nodules without atypia carry a low upgrade risk [10]. In contrast, suspicious or discordant imaging appearances should prompt greater caution, particularly when accompanied by atypia or older patient age. These observations highlight the importance of integrating radiological assessment with histology and clinical context during MDT decision-making. Although limited by sample size, these findings are consistent with the broader literature.

The overall upgrade rate of 11% observed in our institution is lower than many historical series reporting rates of 15-30% but remains comparable to more recent high-quality cohorts in which improved imaging resolution, vacuum-assisted biopsy techniques, and more refined histopathological criteria have reduced diagnostic uncertainty [11]. This trend reflects the evolving diagnostic landscape and underscores the importance of local audit, as institutional upgrade rates are shaped by biopsy technique, radiological expertise, specimen adequacy, and pathology reporting thresholds. Institution-specific data can therefore guide risk-adapted MDT management by aligning excision decisions with contemporary local outcomes and patient-specific risk factors.

Recent European guidelines on the diagnosis, treatment, and follow-up of breast lesions of uncertain malignant potential (B3 lesions) recommend vacuum-assisted biopsy (VAB) as a less invasive diagnostic and therapeutic option for papillary lesions without atypia, provided there is radiological-pathological concordance and adequate sampling. In contrast, surgical excision remains the preferred approach for atypical papillary lesions, given their consistently higher risk of malignant upgrade [12]. These

recommendations support a risk-adapted strategy that avoids unnecessary surgery in carefully selected low-risk patients while maintaining oncological safety in higher-risk groups. As VAB is not currently available at our institution, surgical excision remains the recommended management approach for all papillary lesions within our local pathway.

The main strengths of this study include the use of a prospectively maintained pathology database, which improves case ascertainment and reduces the risk of incomplete data capture. All patients were managed within a consistent institutional imaging and MDT pathway, allowing radiologic, pathologic, and surgical decision-making to be interpreted within a standardised clinical framework. The inclusion of near-complete follow-up and final surgical histology provides reliable confirmation of malignant upgrade status. In addition, the study reflects real-world practice in a tertiary breast unit and provides relevant local data on papillary breast lesions, an area where Irish institutional evidence remains limited. The findings are clinically meaningful because they align with contemporary international evidence while also supporting context-specific MDT decision-making, particularly in relation to atypia and increasing age as markers of higher upgrade risk.

Limitations

Limitations of this study include its retrospective and single-centre design, which may limit generalisability to other breast units with different imaging protocols, biopsy techniques, pathology thresholds, and access to vacuum-assisted biopsy. The modest sample size, and particularly the small number of malignant upgrade events, limited the statistical power for subgroup comparisons and restricted the number of variables that could be included in multivariable analysis. As a result, some potentially relevant clinical or radiological predictors may not have reached statistical significance despite possible clinical importance. In addition, patients managed with surveillance alone were excluded from the upgrade analysis, which may introduce selection bias toward surgically excised lesions. Nevertheless, within these limitations, the study provides robust institutional data that support risk-adapted management of papillary breast lesions and are consistent with current international literature.

Conclusions

Our findings support a selective excision strategy in which patients with atypical papillomas, age >50 years, particularly age >70 years, radiological-pathological discordance, or suspicious imaging features should undergo diagnostic excision. The low upgrade rates observed in younger patients without atypia warrant future studies evaluating the safety of surveillance in a similarly large cohort.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Osama Shakil, Muhammad Haris Mirza, Wardah Jabeen

Acquisition, analysis, or interpretation of data: Osama Shakil, Muhammad Haris Mirza, Wardah Jabeen, Shona Tormey, Chwanrow Baban, Anne Merrigan, Juliette Buckley, Marie Lavelle

Drafting of the manuscript: Osama Shakil, Muhammad Haris Mirza, Wardah Jabeen, Shona Tormey, Chwanrow Baban, Anne Merrigan, Juliette Buckley, Marie Lavelle

Critical review of the manuscript for important intellectual content: Osama Shakil, Muhammad Haris Mirza, Wardah Jabeen, Shona Tormey, Chwanrow Baban, Anne Merrigan, Juliette Buckley, Marie Lavelle

Supervision: Shona Tormey, Chwanrow Baban, Anne Merrigan, Juliette Buckley, Marie Lavelle

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Ethical Review Board Of University Hospital Limerick issued approval 0394. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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