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# Asymptomatic pulmonary nodules in the paediatric population – a literature review

## Bezobjawowe guzki płuc w populacji pediatrycznej – przegląd piśmiennictwa

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## Abstract

Pulmonary nodules are mostly solitary focal opacities typically round or oval in shape, with a diameter of less than 3 cm. They are surrounded by aerated lung parenchyma or located subpleurally, and are not associated with abnormalities, such as lymphadenopathy or atelectasis. Pulmonary nodules are found in up to one-third of computed tomography scans taken in adults, whereas they are significantly less common in children. In adult patients, incidentally detected pulmonary nodules are more frequently associated with neoplastic processes, while they are primarily related to congenital disorders or inflammatory conditions in paediatric populations. The identification of single or multiple pulmonary nodules should always prompt an attempt to determine the likely aetiology. The so-called idiopathic nodules, for which no definitive cause can be established, are a particular subgroup. Although the majority of these lesions are benign in children, some may represent an early stage of malignancy. Due to the lack of standardised management guidelines for the paediatric population, clinical decisions regarding follow-up and further diagnostic workup are often challenging. This literature review outlines the potential causes of incidentally detected paediatric pulmonary nodules, from malignant tumours to other diseases that can present in this form, and discusses methods for assessing the malignant risk of pulmonary nodules in paediatric patients. Finally, a management strategy is proposed for asymptomatic pulmonary nodules detected on imaging, computed tomography in particular.

**Keywords:** children, incidental finding, multiple pulmonary nodules, solitary pulmonary nodule

## Streszczenie

Guzek płuca (*pulmonary nodule*) to cień ogniskowy [często pojedynczy (*solitary*)], zwykle okrągły lub owalny, o średnicy <3 cm, otoczony upowietrznionym miąższem płuca lub leżący podopłucnowo, bez towarzyszących nieprawidłowości potencjalnie związanych ze zmianą, takich jak powiększenie węzłów chłonnych lub niedodma. U dorosłych bywa stwierdzany nawet w jednej trzeciej tomografii komputerowych, natomiast u dzieci – znacznie rzadziej. Guzki płuc wykrywane w badaniach obrazowych u dorosłych częściej wiążą się z chorobami nowotworowymi, podczas gdy u dzieci występują głównie w kontekście chorób wrodzonych lub stanów zapalnych. Stwierdzenie pojedynczego guzka lub guzków mnogich płuc zawsze wymaga podjęcia próby ustalenia prawdopodobnej etiologii. Szczególną kategorię stanowią guzki idiopatyczne, których etiologii nie udało się ustalić. U dzieci charakter większości z nich jest łagodny, jednak istnieje ryzyko, że niektóre mogą stanowić wczesny etap rozwoju nowotworu. W populacji pediatrycznej ze względu na brak jednoznacznych kryteriów postępowania decyzje dotyczące dalszego monitorowania i diagnostyki są trudne. W niniejszej pracy dokonano przeglądu piśmiennictwa, omówiono charakter przypadkowo wykrytych guzków płuc u dzieci, od nowotworów po przykłady innych chorób, i metody oceny ryzyka

nowotworowego guzków płucnych w populacji pediatrycznej oraz zaproponowano strategię postępowania w przypadku wykrycia bezobjawowych guzków płuc w badaniach obrazowych, szczególnie w tomografii komputerowej.

**Słowa kluczowe:** dzieci, przypadkowe znalezisko, mnogie guzki płuc, pojedynczy guzek płuca

## INTRODUCTION

Pulmonary nodules (PNs) are defined as solitary or multiple focal opacities, typically round or oval in shape, measuring less than 3 cm in diameter, and surrounded by aerated lung parenchyma or located subpleurally. PNs are not associated with abnormalities, such as lymphadenopathy or atelectasis. PNs identified on imaging in adults are often associated with malignancies, whereas they are predominantly related to congenital or inflammatory disorders in children. Samim et al. reported that nodules were detected in up to 38% of children undergoing chest computed tomography (CT) following trauma[1]. These lesions were generally small, with a mean diameter of 3.2 mm, and their number reached a maximum of five in a single patient (an average of two nodules per child). Children are more likely to present with PNs in the interlobular region. Furthermore, the incidence of nodules increases with age, particularly after the age of 15 years, which is associated with a higher risk of potential malignancy. Although the majority of incidentally detected paediatric PNs are benign, it is important to recognise that some may represent early stages of malignant tumours. Idiopathic PNs, which are characterised by the absence of an identifiable cause or associated disease, are a distinct category of PNs. They are of particular interest because of the diagnostic challenges they pose, given their potential malignancy despite the absence of symptoms and a clearly identifiable aetiology. The Fleischner Society criteria[2] have been proposed for individuals over 35 years of age, classifying nodules based on their size (<6 mm, 6–8 mm, or >8 mm), number (solitary or multiple), and radiological findings (e.g. ground-glass opacities). Based on these criteria, specific follow-up intervals are recommended; however, no additional follow-up is advised for the smallest and lowest-risk lesions. Nonetheless, these guidelines cannot be directly applied to the paediatric population. As noted by Liang et al., clear criteria for the management of PNs have not yet been established due to the limited number of publications and the challenges in distinguishing benign from malignant nodules in children[3].

## METHODS

The aim of this literature review was to identify the morphological and clinical features that may aid in distinguishing benign from malignant PNs in children and to determine the disease entities with which these lesions may be associated. Additionally, based on the available data, preliminary algorithms for diagnostic and therapeutic management were proposed considering specific clinical contexts. Clinical case reports, as well as review and original papers addressing incidentally detected PNs in children were analysed. The PubMed database was used for the literature search, and papers published between 1974 and 2024 were included. The following keywords were used: "solitary pulmonary nodule", "multiple pulmonary nodules", "children" and "incidental finding". Based on this analysis, we identified features indicative of the malignant nature of a nodule, as well as those that exclude malignancy with high probability. This formed the basis for proposing a management algorithm for specific clinical scenarios. Additionally, we described conditions that may be accompanied by asymptomatic PNs along with their radiological characteristics (Fig. 1).

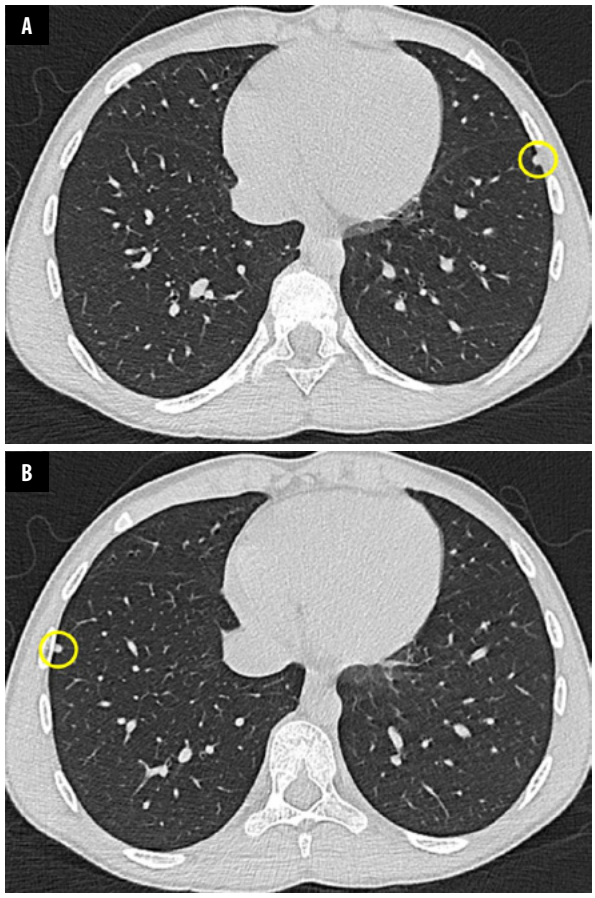


*Fig. 1 A, B. Asymptomatic incidentally detected PNs in a 13-year-old boy, archives of the National Tuberculosis and Lung Diseases Institute in Rabka-Zdrój*



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## RESULTS

### How common are PNs in children and how often are they cancerous?

A literature review has shown that although asymptomatic, PNs may be incidentally found in the paediatric population, and the risk of their malignancy remains relatively low[4–6]. In their study, Breen et al. assessed a cohort of 5,234 children who underwent abdominal CT, of whom 62 were found to have incidentally detected PNs located at the lung bases. Further diagnostic evaluation revealed that the lesions were neoplastic in only two cases, and both children had a prior cancer diagnosis[7]. In their review, Westra et al. emphasised that reports of asymptomatic, malignant PNs incidentally detected in children are rare[8]. In cases of neoplastic involvement of the lung parenchyma, they typically produce clinical symptoms at CT. Incidentally detected PNs are suspected of malignancy far more frequently in adults than in children, as primary lung cancer (LC) represents one of the most common malignancies in the adult population[9].

### On what basis is the risk of a cancerous nodule assessed?

Given their extreme rarity yet potential for malignancy, the question arises as to how higher-risk nodules can be distinguished from those with a low risk. The criteria used for this differentiation are outlined below.

#### Size and number of PNs

Nodule size is the most commonly emphasized risk factor. Breen et al. proposed that a diameter of ≥7 mm is associated with a high probability of malignancy. In their analysis, the mean size of malignant nodules was 11.5 ± 6.4 mm, compared with 4.7 ± 3.0 mm for benign nodules ($p = 0.003$)[7]. However, in their literature review, Westra et al. referred to McCarville et al., who assessed a small cohort of 41 children, demonstrating that nodule size was not a reliable predictor of malignancy[8,10]. Two other studies involving 30 and 111 children, respectively, showed that the risk of malignancy increased in cases where nodules >5 mm in diameter[11,12]. Similar findings were reported by Grampp et al., who analysed data from 74 children with confirmed extrapulmonary solid malignancies and observed that solitary PNs <5 mm typically remained stable on follow-up CT, whereas larger nodules (multiple in particular) were most likely to be malignant[13]. Furthermore, in a study involving 1,341 children, Dilimulati et al. demonstrated a statistically significant correlation between larger nodule size and an increased risk of malignancy ($p < 0.001$). Children with malignant tumours were more likely to present with multiple nodules (particularly bilateral), as well as with larger nodules compared to those without malignancies[9].

These findings suggest that, although a clear threshold distinguishing nodules suspected of malignancy from those considered benign has not been established, the malignant potential of any nodule increases with its size.

#### History of cancer

Personal or family history of cancer is another indicator of the malignant nature of nodules[14]. Most PNs that are ultimately found to be malignant occur in children with a prior history of cancer. In the aforementioned study by Breen et al., only nodules detected in children with a history of cancer were found to be malignant[7]. Similarly, Dilimulati et al. reported that, in a cohort of 209 paediatric patients with PNs, the majority of lesions classified as malignant (114 patients) represented metastases, and 91% of the children with malignant nodules had a prior history of cancer[9]. Lim et al. reported a case of a child who was incidentally found to have a PN. Sclerosing pneumocytoma, a rare benign tumour with a potential for malignant transformation, was diagnosed. The patient had no personal history of cancer; however, there was a positive family history, as his 9-year-old sister had been diagnosed with anaplastic large cell lymphoma[15].

#### PN morphology and location

Morphology, including shape, blurring of margins, calcifications, cavitation, and attenuation, is another factor contributing to the malignant potential of PNs. However, Breen et al. found no statistically significant correlation between these features and the differentiation between malignant vs. benign nodules[7]. Grampp et al. observed that nodules with irregular margins generally remained stable on follow-up CT, whereas those with smooth, well-defined outlines were more likely to be malignant[13]. As pointed out by Westra et al. in their review, true primary LC typically presents in children as a solid mass with a perihilar growth pattern, appearing either as a mixed cystic-solid lesion or as a fully cystic mass. Ground-glass nodules are rarely malignant in children[8].

#### Location

Dilimulati et al. reported that, in addition to a history of malignancy and nodule diameter, nodule location is another important potential predictor of malignancy. Specifically, nodules (whether solitary or multiple) located in the upper or middle lobe of the right lung were more likely to exhibit malignant potential[9].

#### Other factors

Westra et al. emphasised that, in addition to a history of cancer, other aspects of the patient's medical history are also important in assessing the risk of malignancy. These include the presence of clinical symptoms (e.g. pneumonia or obstructive manifestations), recent travel, immunodeficiency, exposure to tuberculosis (TB), and congenital lung malformations such as cystic fibrosis. In the absence of these risk factors, ground-glass opacities on imaging warrant particular attention. In such cases, they should be carefully



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| | Potentially cancerous | Potentially non-cancerous |
|---|---|---|
| **Size** | >5 mm | <5 mm |
| **Personal or family history of cancer** | Yes | No |
| **Appearance** | • Multiple<br>• Well defined | • Solitary<br>• Poorly defined |
| **Location** | Upper or middle lobe of the right lung | Left lung or lower lobe of the right lung |
| **Other factors** | • Accompanying symptoms such as pneumonia or obstruction<br>• Immunodeficiency<br>• Travels or exposure to TB<br>• Congenital cystic lung disease | |

*Tab. 1. Differentiation of PNs into cancerous and non-cancerous*

differentiated from inflammatory processes, microatelectasis, or fibrotic scarring[14].

Although asymptomatic PNs incidentally detected in children are rarely malignant, they should not be completely ignored. Appropriate diagnostic vigilance remains necessary, as cases of pulmonary malignancies in children have been reported by Dosanjh, Niitu et al., and Ohye et al., each involving patients aged ≤15 years with incidentally detected PNs that were ultimately found to be malignant[16–18] (Tab. 1).

## What other conditions, besides cancer, could account for a random lesion in the lung?

Given the low malignant potential of incidentally detected PNs, the question arises as to their possible aetiologies and their radiological features that may suggest specific diseases. Toma et al. described nodule-like lesions of fungal origin[19]. For instance, invasive pulmonary aspergillosis may manifest as single or multiple nodules, areas of consolidation, ground-glass opacities, or cavitary lesions[20]. Mycetoma, described as a mass composed of interwoven fungal hyphae bound together with mucus, fibrin, and cellular debris that colonizes pre-existing pulmonary cavities, may be caused not only by *Aspergillus* species but also by *Streptomyces*, *Coccidioides*, and *Phycomycetes*. It is most commonly found in residual TB cavities, although any pre-existing pulmonary cavity constitutes a predisposing condition. The presence of a round, mobile, mass within a cavity, surrounded by a ring of air (the so-called air crescent sign) is a characteristic radiological finding[19,21]. *Pneumocystis* pneumonia caused by *Pneumocystis jirovecii* typically presents as bilateral, confluent interstitial infiltrates with a predominantly perihilar distribution. Unilateral findings, areas of consolidation, nodules, and cavities may also be present, and in some cases, imaging findings may even appear normal. The radiological presentation of *Cryptococcus neoformans* infection is highly variable, ranging from the absence of detectable changes to miliary or solitary nodules, alveolar infiltrates, and lymphadenopathy. In pulmonary histoplasmosis, miliary nodules accompanied by hilar and mediastinal lymphadenopathy may be observed, closely resembling the pattern seen in miliary tuberculosis.

Arkoudis et al. emphasised that lymph node enlargement, most commonly involving the hilar (often right-sided) and paratracheal regions, is a characteristic radiological feature of tuberculous lesions[21]. Primary TB typically manifests as an area of consolidation and, less commonly, as a well-defined tuberculoma. When accompanied by previously mentioned lymphadenopathy, it may form a Ranke complex, a structure composed of a healed, often calcified Ghon focus (a focus of caseous necrosis within the lung parenchyma) and enlarged, calcified hilar or mediastinal lymph nodes. On contrast-enhanced CT, the affected lymph nodes typically demonstrate low-attenuation centres corresponding to necrotic areas, with peripheral rim enhancement. Calcifications are observed in up to 11% of children[22] and may develop over time within areas of previously formed TB lesions[23]. While calcifications often suggest a benign process in adults, they may be associated with malignancy, particularly in cases of osteosarcoma, in children.

Other incidentally detected lesions that should be distinguished from incidental, asymptomatic PNs include bronchopulmonary sequestrations[21]. This rare congenital anomaly of the lower respiratory tract consists of a non-functioning mass of lung tissue that lacks normal communication with the bronchial tree and receives its arterial blood supply from the systemic circulation[24]. Congenital pulmonary airway malformation (CPAM), where, unlike in pulmonary sequestration, the affected lung parenchyma maintains communication with the bronchial tree and is supplied by the pulmonary circulation is another example. According to the established pathogenesis, CPAM arises from the disrupted development and branching of the respiratory tract during morphogenesis, resulting in cyst formation[21,25]. Arkoudis et al. also identified other potential causes of PNs, including bronchial cysts, congenital bronchial atresia, congenital lobar emphysema, and hydatidosis (also known as hydatid disease, or cystic echinococcosis), and outlined the radiological features that facilitate differentiation of these conditions[21].

Of particular importance are inflammatory lesions that may present as round pneumonia, inflammatory pseudotumors, or abscesses. Round pneumonia mostly occurs in children under 8 years of age. At this developmental stage, the collateral ventilation pathways (the canals of Lambert and the pores of Kohn) are insufficiently developed, limiting the spread of infection within the lung parenchyma and thereby promoting the formation of round-shaped lesions. *Streptococcus pneumoniae* the most common etiologic agent[21,26]. In contrast, an inflammatory pseudotumor of the lung is a benign mass of uncertain aetiology that may mimic a malignant tumour. Most researchers consider this clinical entity to be a variant of the inflammatory repair process resulting from either acute or chronic inflammation; clinically, it is most often asymptomatic[21,27].



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## What treatment is recommended for children with asymptomatic PNs?

Barber et al. found no underlying disease in 94% of 88 otherwise healthy children with solitary PNs. Moreover, follow-up imaging showed spontaneous resolution of the nodulus in nearly half of the children. Non-invasive laboratory workup was performed in 41 children presenting with solitary or multiple nodules, with or without concomitant systemic disease. The obtained findings indicated active infections caused by *Mycoplasma*, *Histoplasma*, *Aspergillus*, *Coccidioides*, *Mycobacteria*, or Epstein–Barr virus, as well as positive Fungitell tests (suggestive of fungal infection) in nine children. Bronchoalveolar lavage (BAL) was performed in seven of these children; nontuberculous mycobacteriosis was confirmed in one child with cystic fibrosis, while a clinically active inflammatory process was diagnosed in four children, without identification of a specific aetiologic agent. The nodules were suspected to be secondary to systemic disease in eight of the 41 children assessed; however, this was not confirmed by laboratory testing. The diagnosis remained undetermined in 15 children (37%). Follow-up imaging was performed in 32 children (78%), with regression of the lesions observed in 12 cases[28]. Similarly, in their study in 36 children and adolescents aged 5–20 years (median age: 15 years), Assefa et al. demonstrated that incidentally detected PNs were frequently stable on follow-up CT scans and, in some cases, even showed regression[4]. This suggests that the detection of PNs in a child does not necessarily indicate disease but rather warrants careful observation. Nevertheless, it remains important to run basic laboratory tests, including sputum analysis, and BAL. The need for repeated imaging studies, particularly CT scans, should be carefully assessed in light of the potential risks associated with radiation exposure at a young age. A reasonable approach may involve monitoring the progression of subpleural PNs using ultrasound, similar to the follow-up of inflammatory lesions[29] or even pulmonary embolism[30]. However, reports on the efficacy of this method for monitoring idiopathic PNs remain limited.

As previously noted, Westra et al. proposed a simplified model for assessing cancer risk for PNs <3 cm in children, based on a comprehensive literature review. In the absence of clinical symptoms and risk factors, such as a history of cancer, immunodeficiency, travel, TB exposure, or congenital cystic lung disease, special attention should be paid to ground-glass lesions. In such cases, infections, inflammation, scarring, and microatelectasis should be ruled out. The authors emphasise that, regardless of the presumed risk, each case should be managed individually. Current guidelines, including the Fleischner criteria, were developed for adult populations and therefore should not be directly applied to paediatric patients[14]. A more detailed diagnostic algorithm was proposed by Dilimulati et al. In this

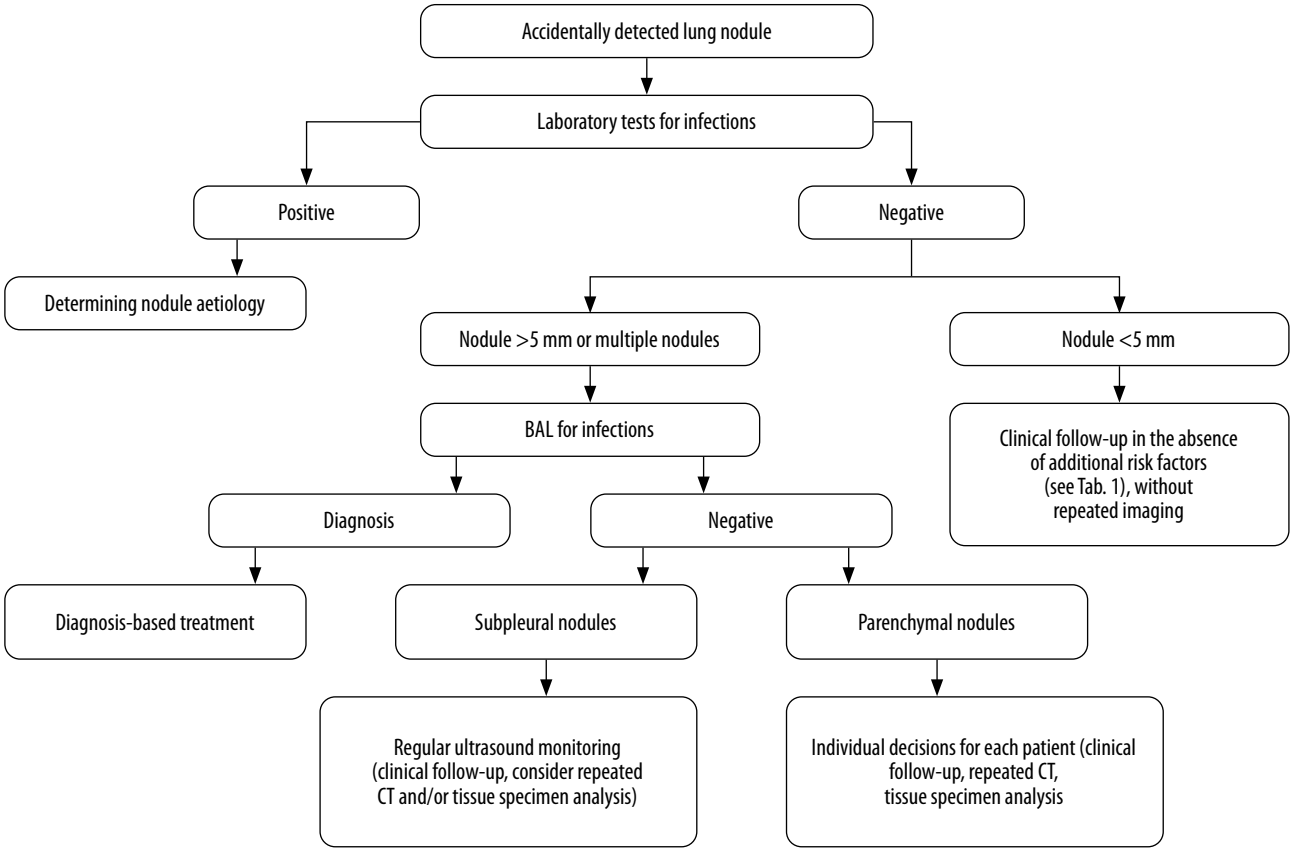


*Fig. 2. Proposed algorithm for pulmonary nodule detection in children*



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approach, a nodule in a child without a history of malignancy is generally considered likely benign. However, in the case of prior cancer history, a lesion ≥5 mm in diameter should be considered potentially malignant. Smaller lesions (<5 mm) are evaluated based on their location and number. Solitary nodules located in the middle or upper lobe of the right lung, as well as multiple nodules present bilaterally or confined to the right lung, are considered more suggestive of malignancy[9] (Fig. 2).

## CONCLUSIONS

PNs incidentally detected in the paediatric population are rarely associated with malignancy. In children, these lesions are typically benign and most commonly arise from inflammatory processes, such as fungal infections, post-inflammatory changes, or scarring, or from other non-neoplastic causes. Lung cancer is extremely rare in children, particularly for nodules <5 mm in diameter. When assessing the potential causes of a PN, several key aspects should be carefully considered:

- Nodule size and morphology – larger PNs may raise greater suspicion for malignancy, particularly those well-defined and multiple. Smaller nodules, especially those with benign features, typically remain stable over time.
- PNs in children with a prior history of malignancy may indicate the possibility of metastatic disease or tumour recurrence.
- Other conditions – PNs may also arise from fungal infections (e.g. aspergillosis), TB, or certain congenital anomalies. Radiographic findings associated with these conditions may include areas of consolidation, ground-glass opacities, cavitations, or lesions confined to specific pulmonary regions.

At present, there is no universally accepted standard of care for children with incidentally detected PNs, asymptomatic cases in particular. Although several diagnostic algorithms have been proposed, the absence of consensus prevents these approaches from being recognised as established standards of care until they are formally endorsed by official respiratory societies.

### Conflict of interest

*The authors do not report any financial or personal associations with other persons or organisations that might affect the content of this publication of claim any rights hereto.*

### Author contribution

*Original concept of study: NMS. Collection, recording and/or compilation of data: NMS, JKR, KC, ES, KG. Analysis and interpretation of data: NMS, JKR, AAG, MM, JM. Writing of manuscript: NMS, JKR, KC, ES, MM, KG, JM. Critical review of manuscript; final approval of manuscript: HM.*

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