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**Protocol**

# Diagnostic accuracy of pocket-size lung ultrasound for etiological definition of pneumonia and surveillance of complications in children hospitalized: a prospective diagnostic cohort study

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## ABSTRACT

**Background:** Pneumonia, the leading infectious cause of death in children worldwide, often requires a chest radiograph (CXR) for diagnosis, involving radiation exposure. Point-of-Care Ultrasound (POCUS) offers a radiation-free alternative and, specifically the pocket-size variant, enhances convenience at the patient's bedside. While evidence supports ultrasound's accuracy in detecting community-acquired pneumonia (CAP) in children comparable to CXR, few studies have explored its ability to distinguish pneumonia etiology, especially utilizing pocket-size POCUS devices.
**Methods:** In this prospective diagnostic cohort study conducted over a year in a tertiary pediatric referral center, we aim to assess the diagnostic accuracy of a pocket-size POCUS device compared to CXR for determining the etiology of CAP in pediatric patients (aged >6 months and <18 years). At least 76 participants diagnosed with CAP will undergo independent POCUS examinations at various intervals, complemented by CXRs when necessary, independently classified by a third investigator. The General Electrics Vscan AirTM®, featuring Bluetooth connectivity to smartphone/tablet, will be employed for POCUS. Data collection will include systematized POCUS and CXR descriptions, alongside sociodemographic, clinical, and therapeutic variables. Statistical analysis using SPSS® version 28 will evaluate the diagnostic accuracy of the POCUS device.
**Conclusions:** This trial's outcomes hold significant promise in unveiling unknown data about the diagnostic accuracy of pocket-size POCUS for pediatric CAP etiological diagnosis. Utilizing a device meeting technical recommendations, featuring a dual-headed probe and Bluetooth connectivity, this study has the potential to bring innovation to clinical practice, improving patient care and creating scientific value.
**Trial Registration Number:** NCT06296693.

**Keywords:** Bacterial pneumonia, Community-acquired pneumonia, Chest radiograph, Digital health, POCUS, Viral pneumonia

## INTRODUCTION

According to the World Health Organization (WHO), pneumonia is the main infectious cause of death in children worldwide. Pneumonia accounts for 14% of all children deaths under 5 years old, killing 740,180 children in 2019.[1] The high mortality rate in the least developed countries and the increasing incidence of complicated pneumonia in the developed ones highlight the importance of an early diagnosis and appropriate treatment in order to improve the prognosis.[2-4]

The diagnosis of community-acquired pneumonia (CAP) is clinical and thus chest radiograph (CXR) is not recommended in all children with typical pneumonia signs and symptoms.[5] However, British Thoracic Society Paediatric Pneumonia Audit revealed that in many cases CXR had been done to confirm the diagnosis and commonly overused during follow-up, causing unnecessary radiation exposure.[6] On the other hand, some studies showed that clinical signs and symptoms of lower respiratory tract infections are relatively non-specific and that the correlation between clinical and radiological findings in CAP is low and thus the use of imaging methods seems to be, at least somewhat, justified.[7-9]

Although CXR is inexpensive and widely available, it exposes the patient to ionizing radiation which should be avoided, particularly in young children.[10]

Lung ultrasound (LUS) emerges as an alternative method being an accessible and radiation-free technique that could also be used as a diagnostic tool in CAP.[11-14]

Eight studies that compared sensitivity and specificity of LUS vs. CXR showed that LUS can detect pneumonia in children with similar accuracy and reliability as CXR, without radiation exposure and with savings in cost and time.[15-22] Also, LUS can point towards pneumonia etiology, especially when correlated with clinical data. Despite some overlapping features, it has a higher sensitivity for bacterial pneumonia than for the viral ones (91% vs. 78.4%, respectively).[23-26]

Advances in technology enable the development of Point-of-Care Ultrasound (POCUS), an advanced diagnostic ultrasonography that is performed and interpreted at bedside, with some of the devices being pocket-size with Bluetooth connection to smartphone/tablet. Recent studies have shown a good correlation between these devices and standard ultrasound machines.[27-29] The advantages are its extreme portability, with high satisfaction scores and improvement of the patient–physician relationship, while maintaining a good image quality.[30]

To date, there are no trials that have studied pocket-size POCUS for the etiological diagnosis of CAP in paediatric ages. So, this study aims to assess, for the first time, the diagnostic accuracy of a pocket-size POCUS device for the etiological diagnosis of CAP vs. CXR, in paediatric ages. Secondarily, we intend to evaluate the correlation between CXR image vs. ultrasound, the correlation between clinical progression and ultrasound images, and the diagnostic accuracy to detect complications.

## METHODS

### *Study design*

We will conduct a prospective diagnostic cohort study in a tertiary paediatric referral centre.

The CAP diagnostic test that will be assessed is the bedside LUS performed with a pocket-sized US. CXR will be used as the reference test for CAP diagnosis.

The recruitment period will be 12 months (from April 2024 to April 2025). An explanation about the study adapted to all children and legal representative will be given, followed by the signing of a free and informed consent form.

The Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines will be used to guide our diagnostic study. This study protocol was reviewed and approved by the Ethics Committee [Committee's reference number 2023.062(051-DEFI/053-CE)].

### *Participants and sample size*

We will include, consecutively, all children aged >12 months and <18 years hospitalized to the Paediatric Department with the diagnosis of CAP on admission, based on the physician's clinical judgment, namely through clinical, analytical and/or CXR criteria. We will exclude children hospitalized with nosocomial pneumonia, with cystic fibrosis diagnosis or on long-term domiciliary ventilation.

Due to the consecutive inclusion of participants there will be no sample size determination. However, assuming an annual incidence of CAP hospitalizations of 115, a bacterial vs. viral diagnostic accuracy of 83%, and a margin of error of 5%, are required, at least, 76 participants.

### *Data collection*

All children hospitalized for CAP will be identified at the time of admission by the physicians on duty who will activate the inclusion protocol of this study. This activation implies the notification of the potential case to be included, with concealment of the aetiology of the pneumonia (viral or bacterial) for the investigators who will perform/classify the POCUS at admission and those who will classify the CXR.

Thus, after inclusion, two physicians (one pediatrician and one pediatric resident) with training and experience in POCUS will perform, independently, a POCUS at the following moments: i) admission (first 24 hours); ii) daily

during hospitalization; iii) 15 days after discharge; iv) 1 month after discharge. All children included will undergo a CXR upon admission and, whenever necessary, through the clinical judgment of the physicians, namely to assess the clinical progression and possible complications, according to the state of the art. A third investigator (radiologist) will classify the CXR independently. The 2 investigators who will classify the POCUS images at admission and the third investigator who will classify CXR images will be blinded for the aetiology of the CAP and for the results of any other exams. After the classification of the first POCUS and CXR, there will be unblinding of all the clinical data for the investigators. This unblinding is suitable, considering that, after admission, we only want to secondarily assess the performance of POCUS in the follow-up of pneumonia, specifically, in identifying possible complications.

The POCUS (index diagnostic test) will be performed in the child's inpatient room, with the child sitting on the bed. Each hemithorax will be virtually divided into 6 regions, using 2 longitudinal lines (anterior and posterior axillary line) and 2 axial lines (1 cm above the diaphragm and another 1 cm above the nipples). The lung areas are: anterior (between the sternum and the anterior axillary line), lateral (between the anterior and posterior axillary lines), and posterior (between the posterior axillary line and the vertebral column). For a comprehensive assessment, all 12 lung areas will be sequentially scanned with the ultrasound in the right-left direction, cranial-caudal to the diaphragm, and anterior-posterior. The pocket-size POCUS used will be the General Electrics Vscan AirTM®, with Bluetooth connection to smartphone/tablet.

The CXR (reference standard diagnostic test) will be preferably obtained in orthostatism, in a posteroanterior incidence, in the radiology department of our hospital.

It will be classified as bacterial CAP when the following findings in POCUS are present: i) lung consolidations (>0.5 cm), which produces a characteristic ultrasound pattern called “tissue-like”, expressing a similar density to that of tissues such as liver or spleen, ii) air bronchogram, if the bronchial structures in the area of the affected lung are patent, represented as hyperechogenic areas (foci, lines, or streaks), that could be mobile (dynamic air bronchogram) or immobile (static air bronchogram), iii) shred sign, a clear image of consolidation or simply hypoechoic, limited above by the pleural line (or the pulmonary line if there is an effusion) and below by an irregular line, as if punched out, expressing the junction with the aerated lung.[26] It is characteristic of alveolar syndrome.

Viral CAP in POCUS will be considered in the presence of at least one of the following: i) pleural abnormalities (irregularity or thickening), ii) variable number (at least three or more in the same ultrasound field) and coalescence of B-lines (perpendicular lines to the pleura, originating from it, hyperechogenic, well defined, long, reaching the end of the screen, erasing the A lines and moving with lung sliding), iii) multiple small subpleural consolidations (<0.5 cm), frequently bilateral.[26]

It will be classified as bacterial CAP in CXR when lung consolidations are present, represented as hypo-transparencies areas that tends to occur initially in the peripheral sub-pleural lung and spreads centrally. It may eventually involve the entire lobe.

Viral CAP in CXR will be considered in the presence of bilateral patchy hypotransparencies and diffuse areas of air space consolidation or interstitial lung disease.

### *Variables*

During the study, sociodemographic, clinical (signs and symptoms, complications) and therapeutic (antibiotics, supplemental oxygen therapy, inhalers) variables will be collected, in addition to those corresponding to the systematized description of POCUS and CXR. The time taken to perform POCUS, to transport and perform the CXR, the number of CXR performed and patient/caregiver satisfaction will also be considered.

### *Statistical analysis*

After data collection, statistical analysis will be performed using SPSS® version 28 (SPSS IBM, New York, NY, USA). A univariate analysis will be performed for factors associated with POCUS images, with subsequent multivariate model if relevant. The diagnostic accuracy will be evaluated by calculating the sensitivity, specificity, positive predictive value and negative predictive value for the etiological diagnosis of pneumonia. We will report a receiver operating characteristic (ROC) curve for each possible test positivity cut-off.

It will also be evaluated the concordance, using kappa statistic, between the etiological diagnosis performed by CXR vs. POCUS as well as the POCUS interoperator agreement.

## DISCUSSION

This study will determine the diagnostic accuracy of a pocket-size POCUS device vs. CXR for the etiological diagnosis of CAP, in paediatric age.

Few studies have evaluated the ability of ultrasound to distinguish the aetiology of pneumonia and none of them have used a pocket-size POCUS device. However, considering the existing studies that point to a high accuracy of ultrasound in diagnosing and differentiating between bacterial and viral pneumonia, and the good correlation between pocket-size devices and standard ultrasound machines, we can expect encouraging results.[14,25,27-29]

In order to substantially reduce possible bias, some measures will be established, namely: i) education, training and systematization of POCUS performance and classification for all physicians involved in the study, reducing a possible operator bias; ii) blinding of pneumonia aetiology from researchers reporting POCUS and CXR, eliminating classification bias.

We will use a pocket-size POCUS device that complies with the technical recommendations in the literature. It consists of a dual-headed probe, which integrates both curved and linear array transducers, and an app that can be installed on Android™ or iOS® mobile devices.

Curved array transducer is suitable for deep scanning with a frequency from 2-5 MHz and a depth up to 24 cm. Linear array transducer is used for shallow scanning with a frequency from 3-12 MHz and a depth up to 8 cm. It takes 50 minutes to a total scan time and 75 minutes to recharge the battery.

The ultrasound images are seen in real time on a smartphone/tablet screen via Bluetooth connection.

Ultrasound has gained importance in the management of lung disease. However, CXR is still the preferred exam in the imaging evaluation of children hospitalized with CAP and, in severe cases, computerized tomography (CT) scan. Those have the disadvantages of exposing the child to ionizing radiation, moving them to the Radiology Department, and, in the case of CT, it is expensive, not always available and affected by motion artifacts which impair image quality and diagnostic accuracy. On the other hand, ultrasound is a dynamic examination, not affected by movement and allowing a greater adjustment to the child. The standard ultrasound machines do not expose the patient to radiation but it is also necessary to move the patient to the Radiology Department, they are not always available and are performed only by radiologists. The pocket-size POCUS device emerges as the great innovation that combines the advantages of the previous exams and fills the gaps as it does not expose the patient to the radiation and it is not necessary to move the patient, being more comfortable for the child and parents. On the other hand, it is a simple technique that can be learned and executed by paediatricians, and is quick to perform, saving time.[31-35]

## CONCLUSION

In conclusion, this type of device will add clinical value centred on the child, will improve the patient care, will hypothetically be able to optimize therapy and reduce antimicrobial resistance (which is the 5th goal of the WHO Global Action Plan on Antimicrobial Resistanc) by properly diagnosing the aetiology of CAP. This digital mHealth technique brings innovation not only to the clinical practice but also to the scientific evidence, contributing to what could be a paradigm shift in the aetiological diagnosis of pneumonia.

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