GLOBAL RADIOLOGY (R STEIN-WEXLER, SECTION EDITOR)

# Ultrasound in the Limited-Resource Setting: A Systematic Qualitative Review

Molly Hallweaver  $^1\cdot Christine\ McBeth ^1\cdot Lori\ Stolz ^2\cdot Amy\ Struder ^3\cdot Michael\ Schick ^1$ 

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#### Abstract

*Purpose of Review* The purpose of this review is to summarize the most recently published literature regarding ultrasound (US) use in limited-resource settings.

*Recent Findings* The body of literature is quite heterogeneous, but several recurring themes emerged from the data. Research regarding education is burgeoning, with studies showing that low-cost training modules can effectively teach US skills to novices. Many studies reported feasibility of training non-physicians to perform US, which allows for task-shifting. Research regarding clinical application of US is broad; especially regarding Echocardiography, Infectious Disease, and OB-GYN.

*Summary* US continues to be a highly utilized tool in limited-resource settings. We identified several common themes among the recent literature: the use of educational interventions to train non-physician providers, the use of US for improved screening methods, and the expanded role of US in clinical purposes including Infectious Disease, Echocardiography, Pulmonary, and Obstetrics.

Keywords Ultrasound  $\cdot$  Resource-limited setting  $\cdot$  Lowand middle-income countries

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- <sup>1</sup> Department of Emergency Medicine, University of California Davis, Sacramento, CA, USA
- <sup>2</sup> Department of Emergency Medicine, University of Cincinnati, Cincinnati, USA
- <sup>3</sup> University of California Davis, Davis, USA

# Introduction

Ultrasound (US) is the most versatile diagnostic imaging tool in limited-resource settings. Due to its relative lowcost, portability, durability, and ease of implementation, its use throughout the world has grown rapidly. Many fields within medicine have recognized the potential for US to provide advanced imaging in settings and locations where other imaging techniques are not viable or available. Differences in availability, access, and quality of imaging affect healthcare disparities worldwide [1]. US used in a traditional radiology departmental model and as a point-ofcare (POCUS) imaging modality has the potential to address these systemic healthcare disparities. Therefore, a multitude of practitioners and researchers have explored the ability of US to fill a distinct void of imaging capabilities where other imaging modalities are not available. Many new articles are available on the topic each year. This systematic review summarizes and assesses literature published in 2018 on US in the limited-resource setting. During the review process several themes emerged including educational endeavors (such as the training of non-physician clinicians), expanded use of US for clinical care including infectious diseases, and technologic advances such as telesonography.

# Methodology

This systematic review was conducted using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [2]. A systematic search was performed for articles published in 2018 using PubMed, EMBASE, Scopus, and CAB International Global Health databases. Additional searches through Google Scholar



Michael Schick mschick@ucdavis.edu

were conducted for additional articles. The primary inclusion criteria included papers with the primary intent of studying US and its utility or feasibility in the limitedresource setting. We excluded case reports, abstracts, and studies that did not primarily focus on US, were not relevant to clinical medicine in the limited-resource setting, and that were not generalizable. Full inclusion and exclusion criteria are outlined in Table 1. Small-scale studies including case reports, conference proceedings, posters, abstracts, pilot studies, or unpublished trials were excluded as well as studies for which English language translation was not available. The search strategy used for each database was constructed using free text and MeSH terms and is outlined in its entirety in Fig. 1.

The references procured from the systematic search were managed through EndNote. Duplicates were removed. Two researchers (MS and MH) screened the titles and abstracts of identified references. The full-text version of citations identified through the screening process were assessed for eligibility using the inclusion and exclusion criteria by MS, MH, CM, and LS.

The included articles were sorted into broad categories and subcategories such as education, infectious disease and technology. Though we considered using the QUADAS tool for risk of bias assessment, many of the identified articles were qualitative in nature, thus not amenable for evaluation for diagnostic accuracy as is intended with the QUADAS tool [3, 4]. Additionally, we found significant heterogeneity among the studies making it very difficult to compare/correlate, thus we chose to defer a formal risk of bias assessment; however, we have attempted to include our assessment of overall bias of each paper when relevant in the text that follows. This article does not contain any studies by any of the authors. We received no funding for this review.

# Results

A total of 729 titles were identified through the initial search. After articles' titles and abstracts were screened, 92 full manuscripts were reviewed for potential inclusion. After full article review, 53 manuscripts were chosen for inclusion in the review and qualitative synthesis (Fig. 2).

# Discussion

A wide variety of studies were identified in many fields of medicine and with many methodologic variations. We have organized literature into three broad categories of advancement: education, clinical, and technology.

#### Education

Training programs and educational models for teaching US in the limited-resource setting vary immensely in scope and time from single-day courses to multi-year commitments. Additionally, the intended learning audience varies, with many focusing their efforts on non-physician clinicians. This is often done to "task-shift," allowing non-physician clinicians to fill a vital gap in a limited health system. The threshold required to develop competence in US acquisition and interpretation, as well as how to assess for such competence, continues to be an area of investigation. Educators saw excellent retention of knowledge and skills from physicians in Ghana after regularly spaced 10-day training courses, whereas clinicians in Kenya failed written tests consistently after repeated single-day trainings [5, 6]. However, the Kenyan's clinical skills on Objective Standardized Clinical Examinations steadily improved over time [5, 6].

Novice sonographers are playing a growing role in education, which speaks to the relative dearth of qualified teachers in limited-resource settings. Two studies describe first year medical students from the United States training

	Inclusion	Exclusion
Study type	Any prospective study, retrospective, study RCT, case series, observational study, cross-sectional surveys, systematic review	Case reports, conference proceedings, posters, abstracts, pilot studies, unpublished trials
Participants	Any	Small volume (< 10–20 participants)
Setting	Limited-resource setting, low-, or middle-income country	Developed country
Aims and outcomes	Any	Not primarily ultrasound focused, obscure
Other	Published January–December 2018	Prior to January, 2018 or after December 2018. Published in non-English language

Table 1 Inclusion and exclusion criteria

# Fig. 1 Search methodology Search Strategy: ((((("ultrasonography"[MeSHMajor Topic]) OR (ultrasound[Title] OR ultrasonography[Title] OR sonogram[Title] OR sonography[Title]))) OR (("point of care ultrasound") OR "bedside ultrasound"))) AND (((developing country) OR ((((("low resource setting"[Title/Abstract] OR "low resource settings"[Title/Abstract]))) OR (("low resource environment"[Title/Abstract] OR "low resource environments"[Title/Abstract]))) ORlmic)) OR (("global health"[MeSHTerms]) OR "global health"[Title/Abstract])) Records identified through database dentification searching (n = 801)EMBASE (n=181) PubMed (n=51) Additional records identified Scopus (n=98) through other sources CABI (n=471) (n = 1)Screening Records after duplicates removed (n = 729) **Records** screened **Records** excluded (n = 729) (n = 637) Eligibility Full-text articles assessed Full-text articles excluded for eligibility (n = 39) (n = 92) Reasons: Not generalizable or too obscure Outcome not primarily US focused Included Size (too small of a study) Studies included in Unable to access or find in qualitative synthesis English (n = 53)

Fig. 2 PRISMA flowsheet [2]

peers and healthcare providers in Africa and Central America [7, 8]. The studies concluded that these novice educators could teach peer groups, as shown by increasing test scores [7, 8]. However, the reliability of this approach requires further study. It also brings up important ethical considerations as novice educators do not have the clinical knowledge or skill set to function in a clinical environment. Learners may be left with educational insufficiencies,

misconceptions, or inflated confidence that could impact medical care decisions.

In the absence of commercial models for US procedural training, several low-cost US training models have been described and evaluated in literature. These models provide opportunities to safely practice invasive procedures. Trainees in Thailand improved their procedural time performing amniocentesis after using a low-cost training model [9]. Rate of successful amniocentesis also improved but was not statistically significant, perhaps due to low sample size [9]. A two-day course utilizing an inexpensive model for fine-needle aspiration biopsy training also greatly improved procedural skills of participants [10].

Several studies highlight barriers to employing US effectively. The main reported barriers were "the lack of US knowledge, lack of time to scan, equipment security, internet connection and technical assistance, and equipment problems" [11]. Among the papers reviewed, US-guided CVC placement was not used most commonly due to lack of training and lack of equipment [12]. Despite lack of training cited as a common perceived barrier, most respondents estimated it would be a simple procedure [13]. The data suggest that increasing access to skills workshops and equipment is crucial for widespread implementation.

# Clinical

US is a highly utilized diagnostic tool in the limited-resource setting. Of all the available resources utilized in the emergency setting in a district hospital in Uganda, 8.2% of 26,710 patients received POCUS [14]. Several studies additionally reveal the high impact of US. In rural Mexico, primary care physicians at ten clinics collected 584 US examinations over 12 months. Management and diagnosis were changed by US in 30% and 34% of cases, respectively [15]. In Tanzania, emergency physicians and trainees reported POCUS changed the diagnostic or disposition plan in 29% of cases, and when patients were scanned more than once this increased to 45% [16].

#### Abdomen

In limited-resource settings, US is frequently utilized because there is minimal access to other imaging modalities, but also despite other methods being available. When evaluating the utility of abdominal-pelvic US in Tanzania, researchers found excellent correlation between US findings and surgical confirmation for urinary tract, gastrointestinal, and hepatobiliary pathology [17]. Missed injuries were most common on focused assessment with sonography for trauma (FAST) evaluations, and gynecologic lesions were also often missed. However, the FAST exam is designed to identify free peritoneal fluid and is not intended to identify solid organ injuries. In addition, since study participants had limited access to endocavitary probes, it is not surprising that gynecologic lesions were often missed [17].

US in limited-resource settings creates opportunities to apply well established but locally novel techniques to common diseases. In Ethiopia and many other resourcelimited settings, the suspected diagnosis of intussusception has traditionally required surgery. However, US-guided hydrostatic reduction is a safe alternative. After its introduction in Ethiopia, the rate of surgery for intussusception decreased by 77% over a year at a major teaching hospital [18]. A separate study demonstrated an 88% reduction rate during a retrospective review of 100 pediatric patients, concluding that it was safe and effective. Success rate significantly decreased as diameter and length of the invaginated segment increased, which may be useful in risk-stratifying patients [19].

#### Airway Management

Emergent airway management in high-resource settings is often confirmed by end tidal capnography and chest radiography (CXR). Without these modalities, US for endotracheal tube (ETT) placement confirmation may be the best available adjunct in the limited-resource setting. A randomized, prospective single-center study in India enrolled 106 patients and demonstrated US outperformed capnography and physical exam. US confirmed proper ETT, identified esophageal and right mainstem intubations, and established the presence of traumatic injuries before intubation. Esophageal intubation was recognized after on average 18.25 s for US-guided evaluation and 177.5 s for capnography/physical exam [20].

### Carotid Artery

Carotid intima-media thickness, atherosclerosis, and plaque identification on US have been used along with traditional cardiovascular risk factors (CVRFs) for many years to risk stratify patients' cardiovascular health [21, 22]. These have been developed in well-resourced health settings, but also correlate in a sample of Nigerian patients. 162 Nigerians' CVRFs and carotid US findings were assessed, and cumulative traditional CVRF correlated with carotid US findings [23]. This suggests the need to evaluate for non-traditional CVRF in limited-resource settings.

Diarrheal disease and dehydration remain common causes of morbidity and mortality in the pediatric population. Interventions focus on prevention, early identification, and treatment. Change in carotid flow rates has been proposed as a possible indicator of response to intravenous resuscitation [24, 25]. In Bangladesh, however, carotid flow rates were found to be a poor predictor for severe dehydration in children with diarrhea [26]. This study was limited by using one static value, rather than dynamic measurements and the well-validated leg raise maneuver [26].

#### Echocardiography

There is potential for echocardiography in a limited-resource setting not only as a diagnostic tool but also for screening and determining appropriate treatment options. Non-physician providers use US more often than physicians in this setting, which creates the potential for improved screening through task-shifting. Nurses in rural Vietnam were taught to acquire and interpret features of cardiac function with a single-parasternal long-axis view [27...]. Nurses could identify significant abnormalities on echocardiogram with 83.3% sensitivity, 78.1% specificity, and 78.6% accuracy, and focused echocardiography combined with ECG captured all significant cardiac abnormalities [27••]. In Brazil, where physician-trainees were trained in screening cardiac US, the rate of appropriateness of echocardiography referral was similar to the referral rate in developed countries: 80.5% versus 85%, respectively [28]. In Rwanda, nurses received 3 months of echocardiography training and were then able to assign patients to a broad category of heart failure, which was later confirmed or corrected by a cardiologist. 264 of 288 (91.7%) echocardiograms had the correct diagnosis [29..]. The success of this program-in which nurses using basic echocardiography could accurately diagnose and initiate appropriate treatment/referrals-inspired national implementation and scaling in Rwanda and neighboring countries [29].

#### Infectious Disease

US is an important screening tool for infectious diseases and their complications. Researchers continue to expand on ways to use US to identify higher-risk patients. It has also been proposed as a tool to use serially to evaluate resolution of findings and treatment success, as well as to identify when further workup is needed.

In India, a study of 100 HIV patients demonstrated that those with severe HIV are more likely to have abnormal US findings, such as splenomegaly, hepatomegaly, and lymphadenopathy [30]. Focal hypoechoic lesions were strongly correlated with severe HIV infections (CD4 < 200), many of which required further workup and treatment [30]. Although limited by a small sample size, this study suggests US may be a good screening tool for intraabdominal pathology in those with low CD4 counts.

The global burden of tuberculosis (TB) remains high and presents great challenges to accurate diagnosis. Unfortunately, in a systematic review no conclusions could be drawn about the diagnostic accuracy of US for pulmonary TB [31]. The review identified a lack of data in literature and thus a potential area for continued research. There is value in the use of US for diagnosing extrapulmonary TB in HIV-positive versus HIV-negative patients. Prospectively, 425 patients with suspected TB were studied with a focused assessment of sonography for HIV and TB protocol (FASH), which assessed for pericardial, pleural, or abdominal fluid, hepatic or splenic microabscesses, and abdominal lymphadenopathy [32]. A positive exam was strongly correlated with a TB diagnosis for HIV-positive patients but did not significantly correlate with TB diagnosis in HIV-negative patients [32]. Of note, the US operator was trained in the study's US protocol but without formal US training, indicating this approach could readily be reproduced elsewhere.

The application of US to TB was further studied in pediatrics in South Africa, where [33] a physician with no prior US experience was taught FASH in a 4-day course and then studied 234 children with suspected pulmonary TB. The study found that children with suspected pulmonary TB were 2.6 times more likely to have positive FASH findings than those who were unlikely to have TB. A concomitant diagnosis of HIV increased the likelihood of positive findings. Findings resolved in 69% of patients after treatment. The success of this short training was confirmed by high inter-reader agreement with a radiologist blinded to the operator's interpretation [33].

US can also be used as a screening tool in areas where certain diseases such as echinococcus are asymptomatic, underdiagnosed, and undertreated. In rural villages of Bulgaria, Romania, and Turkey, a study of 24,681 people showed that the prevalence of cystic echinococcus on US studies was 0.41%. Most of these cases were first-time diagnoses [34]. The study found that other diagnostic methods underrepresent the true prevalence by as much as 700% [34]. Screening for morbidity and success of treatment associated with a disease can be just as important as diagnosing the disease. Urinary schistosomiasis is one of the most prevalent parasitic infections in the world and is associated with significant morbidity [35]. In Angolan children with schistosomiasis, the bladder was abnormal in 85.4%, ureters were dilated in 34.4%, and kidneys were abnormal in 6.3% [36]. Of those diagnosed with urinary schistosomiasis, only 15% had a normal US. When US was repeated 6-8 months after treatment, most had improved. This study suffered from high rates of non-compliance and patients lost to follow-up [37].

In many low-resource settings, there is limited, if any, access to more advanced imaging such as CT or MRI. Researchers continue to develop new uses for US in complex disease states and novel ways to improve patient care and outcomes. Transcranial Doppler (TCD) US has been identified as a potentially useful tool to evaluate neurovascular changes in cerebral malaria. In one landmark study from the Democratic Republic of Congo, daily TCD was performed on patients with cerebral malaria and a control group of children admitted for complicated malaria without cerebral malaria [38]. 76% of patients in the control group had normal cerebral blood flow velocity compared to 3% in the cerebral malaria group. Findings on TCD correlated with neurologic outcome as well. Children found to have microvascular obstruction had the highest rate of normal neurologic outcome (62%), whereas children with low-flow states had the highest incidence of death (32%). Given the variance in TCD findings in children diagnosed with cerebral malaria, these findings could lead to tailored treatment options for each phenotype, such as more aggressive fluid resuscitation in the low-flow group, or calcium channel blockers in the vasospasm group. However, multiple diseases were excluded that could affect findings, which is an important limitation of the study [38].

# Lung

Lung US has incredible potential for use in resource-limited settings, offering high accuracy and ease of use. Patel et al. assessed patients in India presenting in acute respiratory distress using the Bedside Lung US in Emergency protocol (BLUE) protocol, which assesses for COPD, pulmonary edema, pulmonary embolism, pneumonia, and pneumothorax [39]. Overall accuracy in diagnosis with US compared to other imaging was found to be 90%, which is comparable to studies done in high-resource settings [39, 40].

Many studies have addressed the difficulty of diagnosing pneumonia in limited-resource settings where radiography is not widely available. The World Health Organization (WHO) lists pneumonia as the leading cause of death in low-income countries, making this a high-yield and timely field of study. In Nepal, US was found to have a higher sensitivity for diagnosing pneumonia than CXR: 91% versus 73%, using CT scan as the gold standard for diagnosis [41]. Notably, the four pneumonias that were missed on US were also missed on CXR. In Ethiopia, the sensitivity and specificity of diagnosing pneumonia in a pediatric population by US were found to be 86% and 89%, respectively, and there was 91% agreement on the final diagnosis of pneumonia between CXR and US [42]. Similar findings have been shown in studies conducted in higher-resource settings. Bourcier et al. published a sensitivity of 0.95 for thoracic US diagnosing pneumonia compared to 0.6 for radiography [43]. Likewise, in a 2018 meta-analysis, Balk et al. concluded that lung US had significantly better sensitivity and similar specificity compared to CXR for diagnosis of pediatric pneumonia [44].

#### Obstetrics and Antenatal Ultrasound

Research in the fields of obstetrics and antenatal evaluation has focused on addressing fetal and maternal mortality using antenatal US. One of the largest, well-designed studies to date on the topic was published in 2018. This randomized cluster trial in five low- and middle-income countries compared standard antenatal care with standard antenatal care plus two US examinations and referral for identified complications [45..]. The study found that the primary endpoints of maternal mortality, maternal nearmiss mortality, still birth, and neonatal mortality were unchanged between groups. This study is consistent with studies done in high-resource countries that also demonstrate no benefit to routine antenatal screening [46, 47]. Although US may be valuable in the management of pregnancy, barriers to follow-up and the inability to address identified complications limit the utility of US in routine care [45]. A subsequent study asked the same women about barriers that may have led to the low followup at the referral center of only 71% [48]. Cost, transportation, confusion about where to present, and delays in evaluation at the referral hospital were the greatest barriers to follow-up [48].

Other papers looked at healthcare workers' views and experience with obstetric US [49, 50]. One survey-based study found that providers overwhelmingly agreed that US is decisive in pregnancy management, but that patient access to US is limited as are adequate training and number of skilled providers to perform exams [49]. Another found that midwives felt that US was necessary for good decision making in the clinical management of pregnancy, but that equipment and training were again significant barriers to care [50]. These were recurrent themes in an extensive review article [51]. This review delineated many concerns with the use of US in the resource-limited setting including poor training of providers, possible misuse/overuse of US for monetary gain without clinical need, and concerns about the use of US for fetal sex determination [51].

Researchers continue to address the lack of trained physicians using US in limited-resource settings by training other providers. One study found that a simplified antenatal US protocol performed by community health workers with handheld units compared favorably with scans performed by an obstetrician–gynecologist [52]. Another addressed the barriers to care with the use of automation of ultrasonographic measurements and described the development and testing of a computer program for automated measurements of gestational age. Their automated system was evaluated through a test set of 335 images and found to be comparable to the measurements obtained by trained sonographers [53].

Another theme of the identified literature focused on establishing local standards and references. Ali et al. determined that at their hospital, sonographers' measurements of crown-rump-length and mean sac diameter were accurate for pregnancy dating, thus establishing the accuracy of the exam in their particular resource-limited setting [54]. Another descriptive study from Kenya established the prevalence of congenital anomalies discovered on routine US examinations and described the frequency of various anomalies [55]. These studies, though limited in scope, serve to advance setting-specific standards of diagnosis and accuracy.

## Oncology

Many of the studies that are relevant to oncology in the limited-resource setting discuss palpable breast lumps and the role of US in the diagnosis of breast cancer. In Mexico, entry-level health care workers were able to use portable US to acquire satisfactory images of palpable breast lumps with minimal training [56]. Additionally, a computer triage system could assign the imaged lumps with 100% accuracy as compared to the specialist radiologist assignment [56]. Keshavarz et al. described characteristics of US findings between malignant and benign breast lesions, which could prevent unnecessary biopsies and expedite workup for more suspicious lesions [57]. Likely tele-health and artificial intelligence tools will increasingly play an important role in limited-resource settings.

# Ocular

Ocular US as an adjunct to existing exam techniques for ophthalmologic diagnosis has shown potential in literature. This is an important topic of study since blindness disproportionately affects patients in limited-resource settings [58]. In one retrospective review, patients' whose fundus could not be visualized by direct ophthalmoscopy were referred for B-scan US. The diagnosis of retinal detachment increased to 10% with US, compared to 0.8% with clinical diagnosis alone [59]. The most common reason for a non-visible fundus was found to be due to cataract. Another large retrospective study involving 1637 subjects who underwent B-scan US found that of those referred for anterior segment pathology, 22% were found to have posterior pathology, and thus would have been missed without US [60].

In a case series of 48 patients in Pakistan, the optic nerve sheath diameter (ONSD) was measured via US in the setting of pediatric head trauma. Thresholds of ONSD stratified by patient age were 100% sensitive and 60–66.7% specific for elevated intracranial pressure (ICP). In settings

where invasive monitoring is unavailable, US-measured ONSD is a good and practical screening tool for identifying increased ICP [61].

# Musculoskeletal (MSK)

Research regarding MSK US in the limited-resource setting currently remains scarce. A study using chicken bones found that US was better for long bone fracture detection than X-ray: 89% versus 75% [62]. Mogami et al. described US findings of small joint pathology in patients with normal radiographs and chronic MSK symptoms secondary to Chikungunya in Brazil [63]. Opportunities abound for research in this field, and we anticipate many future studies on the topic.

#### Technology

US equipment is inexpensive, making it highly useful in limited-resource settings. However, the relative high cost and low availability of commercial US gel can be problematic. Three studies evaluated alternatives to commercial US gel [64–66]. Cassava root flour is prevalent in many low-resource regions, and a slurry formed by heating that is inexpensive to produce: \$0.09 compared to \$15.00 for 250 ml bottle of commercial gel [64]. Cherukuri et al. studied a recipe with either guar gum or glucomannan that did not require heating and found that it was 18-33% of the cost of commercial gel and produced satisfactory images [65]. Vinograd et al. evaluated nine different gels for image quality as well as model comfort, ease of cleaning, ease of sliding, consistency, and smell [66]. All were found to produce adequate images, with xanthine gum rated the best and the two glucomannan formulas the worst when taking all characteristics into consideration [66].

Telesonography is feasible in a wide range of settings and for a wide range of indications. Diagnostic accuracy has been shown to be comparable to conventional in-person US in emergency situations. Novice operators can be guided by expert, real-time review to produce useful images, though asynchronous US image review by a remote operator may be more practical [67••].

#### Conclusion

Published studies on US in the limited-resource setting fit into three broad categories: education, clinical, and technology. Educational studies focused on non-physician clinician training programs, novice instructors, low-cost training models, and limitations to such programs. There were notable achievements in training nurses in echocardiography and rural doctors in POCUS. Novice

sonographer instructors brought up important ethical considerations. In clinical sonography, most of the literature studies focused on infectious disease, echocardiography, pulmonary pathology, and obstetrics/antenatal care, with two studies demonstrating the potentially large impact of POCUS on diagnosis and decision making. There continue to be advances in diagnostic knowledge of such diseases as TB, echinococcosis, and schistosomiasis, which disproportionately affect patients in limited-resource settings. Literature on obstetric US demonstrated no apparent mortality benefit to routine prenatal sonography in the limitedresource setting. Research on technology found multiple alternatives to regular US gel, that telesonography is a feasible tool, and that artificial intelligence may be applied to imaging in limited-resource settings. In general, increasing access to US equipment and training can lead to widespread implementation and adoption, with significant impact on health worldwide. However, while increased access to US is important, broader health system development including simultaneous access to necessary interventions and follow-up care is crucial to change outcomes.

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