Point-of-care ultrasound (POCUS) in the diagnosis of acute abdominal pain

A systematic review

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Table of contents

TABLE OF CONTENTS **3**
ABSTRACT (NL) **5**
ACHTERGROND 5
METHODEN 5
RESULTATEN 5
CONCLUSIE 6
ABSTRACT (EN) **7**
BACKGROUND 7
METHODS 7
RESULTS 7
CONCLUSION 8
INTRODUCTION **9**
METHODS **12**
SEARCH STRATEGY AND SELECTION CRITERIA 12
INCLUSION CRITERIA 12
EXCLUSION CRITERIA 13
QUALITY ASSESSMENT 14
DATA EXTRACTION 14
SUBSET SELECTION AND ANALYSIS 14
RESULTS **16**
STUDY POPULATION 16
RISK OF BIAS 17
DIAGNOSTIC TEST ACCURACIES 20
Acute appendicitis *20*
Acute cholecystitis *22*
Other pathologies *24*
Overall diagnostic accuracy *25*
DISCUSSION **27**
STRENGTHS 27
LIMITATIONS 28
IMPLICATIONS FOR CLINICAL PRACTICE 31
IMPLICATIONS FOR FUTURE RESEARCH 31
CONCLUSION **33**
ACKNOWLEDGMENTS **34**
CONFLICTS OF INTERESTS **35**
FUNDING **35**

REFERENCES **36**
APPENDICES **49**
Appendix 1: Protocol 49
Appendix 2: Study key characteristics 56

Abstract (NL)

Achtergrond

Acute buikpijn is een van de meest voorkomende klachten in de eerste lijn. Toch vinden huisartsen het moeilijk om te differentiëren tussen goedaardige, zelflimiterende en acute of levensbedreigende aandoeningen. Point of care echografie (POCUS) is een veilig, betaalbaar diagnostisch instrument en is beschikbaar 'aan het bed' van de patiënt. Data toont dat POCUS een waardevol instrument kan zijn in het diagnostische proces van acute buikpijn. Gegevens over zijn nauwkeurigheid zijn echter beperkt. Ons onderzoek heeft als doel de huidige literatuur te onderzoeken naar de diagnostische waarde van POCUS bij volwassenen met acute buikpijn.

Methoden

Dit onderzoek werd uitgevoerd volgens de Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). Het maakt deel uit van een systematische review over de diagnostische accuraatheid van symptomen en klinische tekenen van volwassenen met acute buikpijn. Databanken van Medline, Embase, Dare, Cinahl en Web of Science en referenties van gevonden artikels werden doorzocht.

Cross-sectionele prospectieve diagnostische accuraatheidstudies over klinische tekenen, laboratoriumonderzoek en beeldvorming bij patiënten van 18 jaar of ouder, die zich presenteerden met acute buikpijn in een ambulante zorgomgeving werden geïncludeerd. Het risico op bias werd beoordeeld met behulp van QUADAS-2. Hierna werd een subset-analyse uitgevoerd om de diagnostische accuraatheid van POCUS te onderzoeken.

Resultaten

16933 unieke artikelen werden geïdentificeerd.Hiervan werden 51 studies met een laag tot matig risico op bias geïncludeerd. Zes verschillende uitkomsten van acute abdominale pathologie werden gevonden. Een meta-analyse werd uitgevoerd voor appendicitis en cholecystitis. Gepoolde gegevens voor appendicitis toonden een sensitiviteit en

specificiteit van respectievelijk 78,7% en 90,0% voor POCUS, in vergelijking met 79,8% en 82,1% voor RADUS. Voor cholecystitis had POCUS een sensitiviteit van 92,6% en een specificiteit van 90,9%, terwijl RADUS overeenkomstige waarden vertoonde van 65,9% en 93,2%. Om de totale diagnostische nauwkeurigheid van POCUS en RADUS te vergelijken, werden de 4 studies met gepaarde gegevens opgenomen in een meta-analyse. De totale sensitiviteit en specificiteit voor POCUS waren respectievelijk 86,3% en 81,3%. Dit in vergelijking met 73,1% en 94,2% voor RADUS.

Conclusie

Deze review toonde een redelijke sensitiviteit en specificiteit voor POCUS en RADUS. De resultaten suggereren dat POCUS een nuttige bed-side beeldvormingstechniek kan zijn als ondersteuning bij de diagnose van acute buikpijn in volwassenen. Verdere onderzoeken zijn nodig om de diagnostische nauwkeurigheid van POCUS in de huisartsenpraktijk nauwkeuriger te evalueren.

Abstract (EN)

Background

Acute abdominal pain is one of the most common complaints in ambulatory care and general practitioners often struggle differentiating benign and self-limiting pathologies from acute and life-threatening. Point of care ultrasound (POCUS) is a safe and affordable diagnostic tool and could be a valuable bedside instrument in the diagnostic process of acute abdominal pain. However, data on its accuracy is limited. Our study aims to investigate the current literature on diagnostic value of POCUS for adults with acute abdominal pain.

Methods

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. It is part of a systematic review on the accuracy of signs and symptoms of adults with acute abdominal pain. Medline, Embase, Dare, Cinahl and Web of Science databases were searched using a comprehensive search strategy. Citations were searched. cross-sectional prospective diagnostic accuracy studies on clinical features, laboratory tests and imaging in patients aged 18 or older presenting with acute non-specified abdominal pain to an ambulatory care setting were included. We assessed the risk of bias using QUADAS-2. A subset analysis was performed to investigate the accuracy of POCUS.

Results

16,933 unique articles were identified and 51 studies were included with a low to moderate risk of bias. Six different outcomes of acute abdominal pathology were found. Meta-analysis was performed for appendicitis and cholecystitis. Pooled data for appendicitis yielded an overall sensitivity and specificity of 78.7% and 90.0% for POCUS, compared to 79.8% and 82.1% for RADUS, respectively. For cholecystitis, POCUS showed an overall sensitivity of 92.6% and a specificity of 90.9%, while RADUS showed corresponding values of 65.9% and 93.2%. To compare the overall diagnostic accuracy

of POCUS and RADUS, all 4 studies with paired data were included in a meta-analysis and revealed an overall sensitivity and specificity of 86.3% and 81.3% for POCUS, in comparison with 73.1% and 94.2% for RADUS, respectively.

Conclusion

This review showed reasonable sensitivity and specificity for POCUS and RADUS. These results suggest that POCUS is a useful bedside imaging technique in the workup of acute abdominal pain. Further research is needed to accurately evaluate the diagnostic accuracy of POCUS in the general practitioners setting.

Introduction

Acute abdominal pain is one of the most common complaints of patients presenting to a primary care physician or the emergency department, as it accounts for 5-10% of all presentations in this setting.[1–5] In Dutch primary care, general practitioners (GPs) see about 56 per 1000 patients with acute abdominal pain.[6] Because of its wide variety of causes, acute abdominal pain often remains difficult for clinicians to accurately identify its etiology.[7] In a substantial proportion of patients, no specific cause can be identified.[2,8] Ranging from benign and self-limiting to acute life-threatening diseases, primary care physicians must consider multiple diagnosis.[9] This remains challenging, since patients frequently present with a combination of undifferentiated, vague and psychosomatic symptoms and the symptom overlap between self-limiting and life-threatening conditions is high.[10 11] In rare but serious cases of acute abdominal pain (for example ruptured abdominal aortic aneurysm), early and accurate diagnosis is essential to provide a rapid and adequate treatment.

Diagnostic resources in primary care are limited (to e.g. clinical investigation, bloodwork and imaging via referral), so GPs often face diagnostic uncertainty whilst dealing with high patient volumes and multiple complaints per consultation. They must rule out life-threatening diseases based on simple clinical signs and diagnostic tests, which often lack good sensitivity and/or specificity.

Due to great technological advances, ultrasound devices nowadays have a good resolution, are portable, dependable and affordable. All these factors facilitate the use of ultrasound in outpatient care as well as bedside or point-of-care ultrasound (POCUS).[11]

POCUS is a clinical approach that aims to address straightforward clinical queries by confirming or excluding specific diseases or abnormalities. It demonstrates higher diagnostic accuracy when utilized to answer specific clinical questions, compared to more exploratory examinations.[12] Currently, it is widely used in hospital settings and emergency departments.[12] However, its implementation in primary care is limited, yet

appears promising in settings with limited resources. POCUS has been demonstrated to potentially reduce costs, emergency department visits, and the necessity for additional imaging in general practice.[12–14]

Previous research has indicated that GPs generally achieve satisfactory accuracy levels in their POCUS scans. The quality of these scans may vary depending on the extent of the examination and the anatomical region being examined.[15,16] Moreover, GPs are motivated to learn and apply POCUS in their practice due to self-interest and the potential to provide comprehensive patient care without referral, which enhances their job enthusiasm and professional satisfaction.[14] Patients also express high satisfaction with POCUS, finding it innovative and useful, with no reservations about undergoing it again. Notably, 66% of patients believe that POCUS should be incorporated as a routine component of physical examinations by GPs and are willing to pay additional fees for ultrasound examinations.[12,14,17]

On the other hand, there are numerous obstacles that impede the implementation of POCUS in primary care. There are no established guidelines nor training for GPs in utilizing POCUS. In addition, there are no laws governing the billing practices for POCUS services. GPs must ensure that acquired images are stored in a permanent and secure manner, and that a comprehensive report is provided, if they want to qualify for payment. This may expose GPs to legal vulnerabilities, due to incomplete documentation.[18] Because of these obstacles, it is crucial to establish clear and unambiguous regulations to promote the utilization of POCUS in primary care.[19]

POCUS could have a promising integration into primary care, as it may enhance diagnostic pathways, reduce referrals, facilitate treatment and ultimately improve patient outcomes.

Nevertheless, the implementation of POCUS in primary care faces many challenges. More knowledge about the diagnostic accuracy of POCUS is needed, particularly for each different indication and for specific diagnostic questions.

Our systematic review therefore aims to investigate the usefulness of ultrasound in the assessment of adults with acute abdominal pain in a primary care setting.

Methods

We report this study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA).[20] This study is part of a comprehensive systematic review on the accuracy of signs and symptoms of acute abdominal pain in adults (Prospero registered ID 421510). We later performed a subset analysis on this data to investigate the accuracy of ultrasound in acute abdominal pain.

Search strategy and selection criteria

Medline, Embase, Dare, Cinahl and Web of Science databases were searched for articles on the accuracy of signs, symptoms and technical investigations used in diagnosing adults with acute abdominal pain in a primary care setting from inception to December 2021. The protocol, including our search strategy with MeSH/Emtree terms and free text is shown in appendix 1. We created our search strategy around four categories: signs, symptoms and technical investigations; abdominal diseases; adults and primary care setting. Additionally, we checked references of included studies and related reviews and included relevant articles.

Selection was done by two independent reviewers in two rounds. First titles and abstracts were screened, then the full text. Primary researcher AT screened all articles and the second screening was done by the assisting researchers and authors of this manuscript (YA, ED, TS). Conflicts were resolved by a third reviewer (AB). Training of selection criteria was given to all reviewers before the start of selection. We used Covidence online software for the deduplication and study selection (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia).

Inclusion criteria

We included cross-sectional prospective diagnostic accuracy studies on clinical features, laboratory tests and imaging in patients aged 18 or older presenting with acute non-specified abdominal pain to an ambulatory care setting.

We selected studies examining the following index tests: clinical features (signs and symptoms), laboratory tests (conducted at the point-of-care or in a central laboratory) and imaging tests such as (point-of-care) ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and X-ray (RX abdomen), imaging prescribed by a primary healthcare worker (such as a GP) or at the emergency department (ED). Imaging tests that are performed during hospital admission will not be eligible.

Acute non-specified abdominal pain was defined as pain (of any intensity) the patient can feel anywhere between the chest and groin that can vary in intensity and time, existing no longer than 14 days.

Ambulatory care setting included general practice, primary care out-of-hours service, walk-in clinics, interface clinics, emergency departments and other settings in which patients were not admitted or referred to a hospital.

Exclusion criteria

We excluded retrospective studies, case-control studies, systematic reviews and meta-analyses. Systematic reviews and meta-analyses were only used as a source of references. Nested case control studies in which cases and controls were sampled from the same source population and diagnostic accuracy studies employing a stratified two-phase design were eligible. Studies including patients with known active abdominal malignancies (such as colorectal cancers) or chronic pre-existing gastrointestinal diseases (such as inflammatory bowel syndromes) were also excluded. If less than 50% of patients were aged at least 18 years or if no age demographics were specified, studies were not eligible for inclusion. Furthermore, studies with less than 50% of patients with acute pain for a maximum of 14 days or without separate data on this group were excluded. Given the low incidence of serious conditions causing acute abdominal pain, we excluded studies reporting a total sample size smaller than 50 patients because these studies would include only a few subjects with the target condition and would be prone to selection bias. We did not apply language restrictions. Inclusion of languages other than

English, French, German and Dutch will be subjected to availability of a reliable translation.

Quality assessment

All articles included in the review were assessed for the risk of bias using the QUADAS-2 items (using the Review Manager software: RevMan, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).[21] The first assessment was done by the following reviewers: YA, LB, ED, RG, TS. The second assessment was done by only two reviewers (AT, TS2), this to limit heterogeneity in the risk-assessment process. Disagreements between the first and second assessment were resolved by AT and TS2 during discussion sessions. Studies were not excluded from the review based on the risk of bias assessment, but it was used in the interpretation of the results.

Data extraction

Data was extracted by one reviewer (ED, YA, TS, AT) and afterwards double checked by the primary researcher (AT). Any discrepancies were discussed and corrected. We reconstructed two-by-two tables based on the study data.

Subset selection and analysis

After participating in the selection, quality assessment and data extraction of the above mentioned comprehensive primary systematic review, for this study, YA, ED and TS selected a subset of data from the original systematic review, to perform an analysis on the accuracy of ultrasound in adults with acute abdominal pain.

We selected all data about ultrasound (including POCUS or RADUS). All outcomes, and thus diagnosis (e.g. appendicitis, cholecystitis, …) were eligible for inclusion. All included articles were reviewed a third time in a consensus meeting (YA, ED, TS) for quality assessment and data extraction.

POCUS was defined as ultrasound performed by any investigator not specified in radiology (e.g. emergency physician, surgeon, general practitioner). RADUS was defined as ultrasound performed by a radiologist.

We calculated and analyzed measures of diagnostic accuracy, using the RevMan software.

According to our protocol, we pooled data for meta-analysis when at least four studies (without clinical heterogeneity) were available for a particular index test in a particular outcome, using a bivariate model and displaying results in a summary ROC curve. We calculated sensitivity, specificity, positive and negative likelihood ratio (LR) for each test. Confidence intervals were calculated. We considered tests to be useful in ruling out a pathology in ambulatory care if their negative likelihood ratio (LR−) was lower than 0.20; conversely diagnostic tests were considered useful as 'red flags' for pathology when their positive likelihood ratio (LR+) was 5.0 or higher.[22] For outcomes with less than four studies we had to restrict our analyses to descriptive statistics. For overall comparative analysis between POCUS and RADUS, only studies with paired data were eligible for meta-analysis.

Results

We identified 16,933 unique studies, of which 513 were selected for full text screening. Ultimately, 175 studies were included in our systematic review. 51 studies met the specific criteria for subset selection (Figure 1). Study characteristics are shown in appendix 2. The total number of included patients is 12,895. The number of participants per study ranged from 55 [23] to 1,855 [24], 4,497 patients in the POCUS group and 8,398 in the RADUS group.

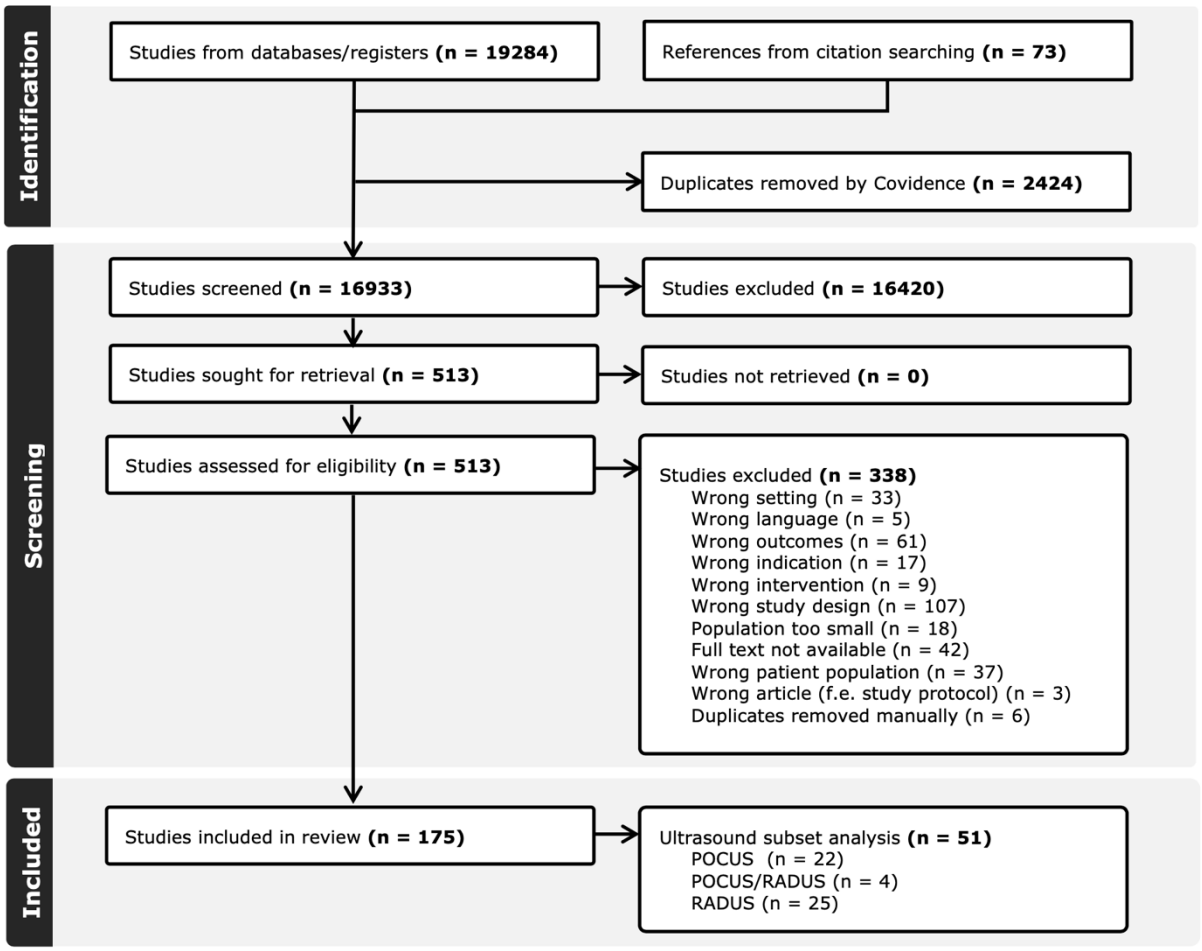


***Figure 1**: PRISMA Flow diagram for selection of studies.*

Study population

All studies were performed in an ambulatory care setting: 4 at the surgical department, 1 at the radiology department and the remaining 46 at the emergency department. Mean age across studies ranged from 19 [25] to 68 [26] years old. The proportion of women per

study ranged from 30.0% [27] to 84% [28]. Not all studies specified demographics (appendix 2). Out of the 51 studies, 22 studies reported on POCUS, 25 on RADUS and 4 on both.

The outcomes investigated were appendicitis (n = 13), cholecystitis (n = 7), diverticulitis (n = 3), small bowel obstruction (n = 2), renal colic (n = 2) and abdominal aorta aneurysm (n = 1) in the POCUS group and appendicitis (n = 25), cholecystitis (n = 4), diverticulitis (n = 2) and small bowel obstruction (n = 1) in the RADUS group.

Prevalence per pathology differed substantially between studies: for appendicitis from 14.8% [29] to 90.8% [30]; for cholecystitis 5.1% [31] to 78.0% [32]; for diverticulitis 7.1% [33] to 85.4% [23]; for SBO 6.7% [31] to 42.9% [25] and for renal colic 61.3% [26] to 77.5% [34]. This was mainly caused by differences in inclusion criteria. For example, one study with an appendicitis prevalence of 14.8% included all patients with acute abdominal pain [29], while another study with a prevalence of 90,8% [30] included only patients who already had a provisional diagnosis of appendicitis and underwent laparoscopic appendectomy. The gold standard for final diagnosis was typically based on histopathology report and clinical follow-up. Some studies also used surgical findings, review of medical charts, expert panel and multiple imaging techniques (RADUS, CT scan, …) as reference standards. Appendix 2 includes an overview of key characteristics, including the inclusion criteria and gold standard for each study.

Risk of bias

The risk of bias assessment is summarized in Figure 2. Overall, the risk of bias was low to moderate, although several studies exhibited methodological ambiguities. Specifically, 13 studies revealed issues related to patient selection, primarily stemming from inappropriate exclusion of patients who did not require surgery [35,36] or were critically ill [31,37–46]. From an ethical perspective, exclusion is justifiable since ensuring patient safety is of paramount importance. Nevertheless, exclusion of the sickest patients could lead to selection bias.

None of the studies were identified as having a high risk of bias in relation to the index test, although 15 studies were evaluated as unclear in this regard. This was primarily attributed to the blinding of the performing physicians with respect to the patients' medical records and clinical examinations being unclear. In our evaluation of the reference standard, 9 studies were deemed to have a high risk of bias. Among these, four studies compared POCUS with RADUS as the reference standard. In one study, the golden standard was based on a re-evaluation of POCUS images by a radiologist [47], while the remaining four studies relied on the decision of an expert panel that evaluated all medical records, which potentially introduced reference bias related to the index test [31,43,44,48]. Furthermore, three studies demonstrated an inadequate pattern of flow and timing due to the utilization of multiple, non-predefined reference standards [47,49,50].

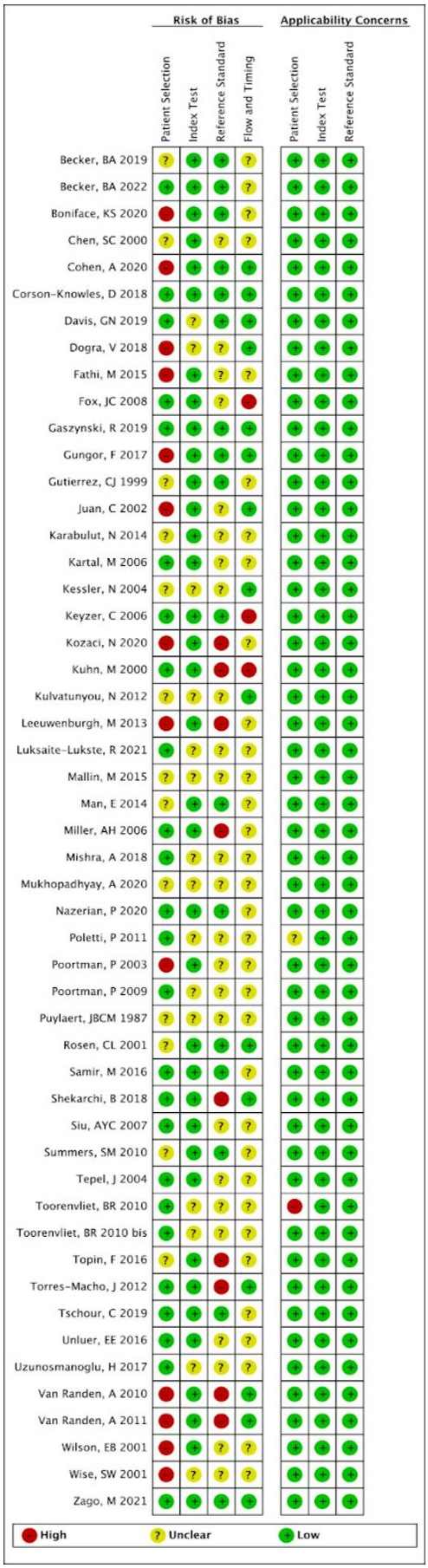


Figure 2: *QUADAS-2 risk of bias and applicability summary*

Diagnostic test accuracies

All studies are categorized based on the index test and pathology. Due to significant heterogeneity observed among the studies, subgroups were created for each pathology and results are presented according to these subgroups. A meta-analysis was conducted solely on pooled data for pathologies that had a minimum of four studies, to determine the diagnostic accuracy. To compare the overall diagnostic accuracy of POCUS and RADUS, meta-analysis was performed based on four studies that had paired data. Table 1 provides a comprehensive summary of all the results.

Index test	Pathology	Number of studies (N)	Number of cases / Total number of participants (n/N%)	Sensitivity (%)	Specificity (%)	LR+	LR-
POCUS	***Overall***	***26****	***1919/4497 (42.7%)***	*Due to heterogeneity, meta-analysis was only performed on 4 studies with paired data*			
POCUS	*Overall (paired)*	*4*	*273/604 (45.2%)*	*86.3% (78.2% to 91.8%)*	*81.3% (63.7% to 91.5%)*	*4.623 (2.089 to 10.232)*	*0.168 (0.091 to 0.312)*
POCUS	Appendicitis	13	773/1995 (38.7%)	78.7% (67.2% to 86.9%)	90.0% (83.2% to 94.3%)	7.892 (4.631 to 13.449)	0.237 (0.150 to 0.374)
POCUS	Cholecystitis	7	344/1009 (34.1%)	92.6% (89.1% to 95.0%)	90.9% (80.5% to 96.0%)	10.173 (4.547 to 22.761)	0.082 (0.054 to 0.123)
POCUS	Diverticulitis	3	426/900(47.3%)	Number of studies too small to perform meta-analysis (n<4)			
POCUS	Renal colic	2	225/307 (73.3%)				
POCUS	Small bowel obstruction	2	125/342 (36.5%)				
POCUS	Abdominal aorta aneurysm	1	26/66 (39.4%)				
RADUS	***Overall***	***29§***	***3558/8398 (42.4%)***	*Due to heterogeneity, meta-analysis was only performed on 4 studies with paired data*			
RADUS	*Overall (paired)*	*4*	*271/551 (49.2%)*	*73.1% (64.8% to 80.1%)*	*94.2% (87.3% to 97.5%)*	*12.567 (5.538 to 28.516)*	*0.285 (0.214 to 0.382)*
RADUS	Appendicitis	25	3186/7604 (41.9%)	79.8% (74.0% to 84.6%)	82.1% (67.9% to 90.8%)	4.459 (2.320 to 8.571)	0.246 (0.177 to 0.340)
RADUS	Cholecystitis	4	164/1410 (11.6%)	65.9% (48.1% to 80.1%)	93.2% (87.0% to 96.6%)	9.709 (4.588 to 20.544)	0.366 (0.224 to 0.600)
RADUS	Diverticulitis	2	140/1426 (9.8%)	Number of studies too small to perform meta-analysis (n<4)			
RADUS	Small bowel obstruction	1	68/1021 (6.7%)				

Table 1: *Summary of results*
*(*Two studies reported on two pathologies, § One study reported on four pathologies)*

Acute appendicitis

A total of 13 studies reported on the diagnostic accuracy of POCUS for appendicitis, with sensitivities ranging from 43% [51] to 96% [52] and specificities ranging from 63% [53] to 98% [51,54]. For RADUS, 26 studies were identified, with sensitivities ranging from 34% [46] to 98% [55] and specificities ranging from 0% [46] to 100%.[56]

Meta-analysis was conducted on the data from these studies, which revealed an overall prevalence for appendicitis of 38.7% in the POCUS group and 41.9% in the RADUS group. The sensitivity and specificity of POCUS for diagnosing appendicitis were found to be 78.7% and 90.0%, respectively, while for RADUS, the corresponding values were 79.8% and 82.1%, respectively. The positive likelihood ratio (LR+) of 7.892 (95%CI 4.631 to 13.449) suggests that a positive POCUS examination is a useful red flag for

diagnosing appendicitis. RADUS had a moderate LR+ of 4.459 (95%CI 2.320 to 8.571). To rule out infection, POCUS (LR- 0.237, 95%CI 0.150 to 0.374) and RADUS (LR- 0.246, 95%CI 0.177 to 0.340) both performed moderate.

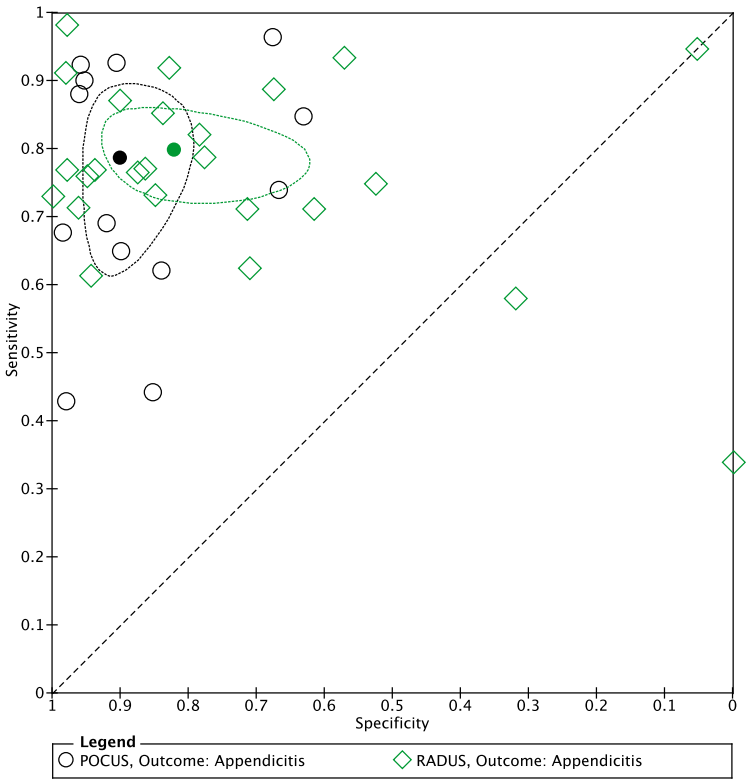


Figure 3: *SROC for POCUS and RADUS for acute appendicitis*

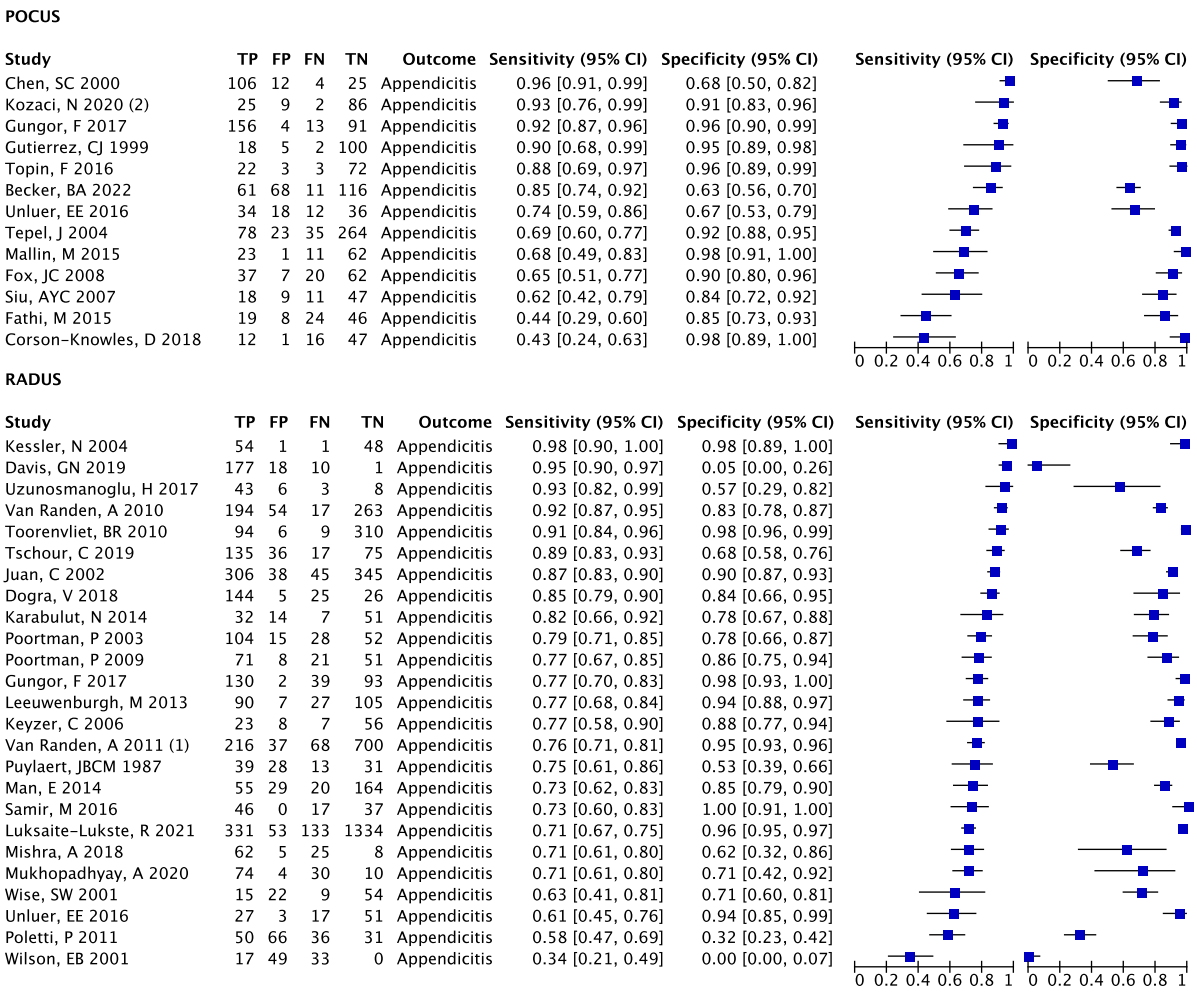


Figure 4: *Diagnostic accuracy of POCUS and RADUS for acute appendicitis*

Acute cholecystitis

7 studies reported on POCUS, with sensitivities ranging from 87% [57] to 96% [26], while the specificity ranged from 66% [58] to 100% [32]. For RADUS, a total of 4 studies were identified, with sensitivities ranging from 39% [59] to 83% [57], and specificities ranging from 86% [57] to 97% [31]. The overall prevalence of cholecystitis was found to be 34.1% in the POCUS group and 11.6% in the RADUS group.

All 11 studies were included in a meta-analysis to evaluate the diagnostic accuracy for POCUS and RADUS in diagnosing cholecystitis. The sensitivity and specificity of POCUS for diagnosing cholecystitis were determined to be 92.6% and 90.9%, respectively, whereas for RADUS, the corresponding values were 65.9% and 93.2%. Both POCUS and RADUS have high positive likelihood ratios (LR+) of 10.173 (95% CI 4.547 to 22.761)

and 9.709 (95% CI 4.588 to 20.544), respectively, indicating their usefulness as red-flag diagnostic tools for cholecystitis. In addition, POCUS demonstrated a low negative likelihood ratio (LR-) of 0.082 (95% CI 0.054 to 0.123), suggesting its potential for ruling out cholecystitis. On the other hand, RADUS had an LR- of 0.366 (95%CI 0.224 to 0.600), indicating moderate accuracy in ruling out cholecystitis.

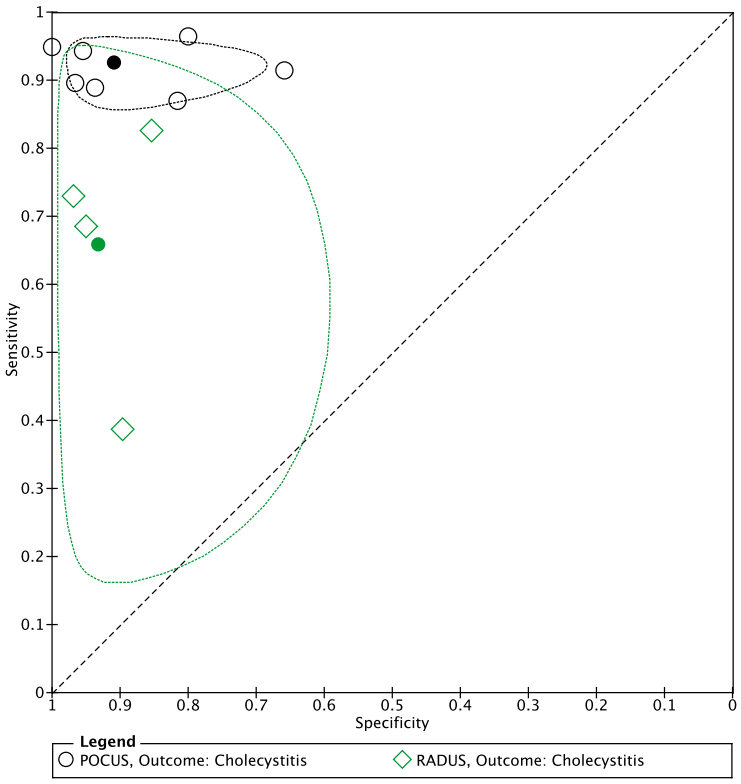
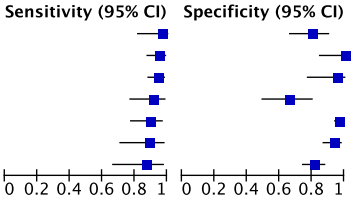


***Figure 5**: SROC of POCUS and RADUS for acute cholecystitis*

POCUS

Study	TP	FP	FN	TN	Outcome	Sensitivity (95% CI)	Specificity (95% CI)
Torres-Macho, J 2012 (1)	27	10	1	40	Cholecystitis	0.96 [0.82, 1.00]	0.80 [0.66, 0.90]
Gaszynski, R 2019	74	0	4	22	Cholecystitis	0.95 [0.87, 0.99]	1.00 [0.85, 1.00]
Miller, AH 2006	99	1	6	21	Cholecystitis	0.94 [0.88, 0.98]	0.95 [0.77, 1.00]
Rosen, CL 2001	32	14	3	27	Cholecystitis	0.91 [0.77, 0.98]	0.66 [0.49, 0.80]
Shekarchi, B 2018	43	10	5	284	Cholecystitis	0.90 [0.77, 0.97]	0.97 [0.94, 0.98]
Kozaci, N 2020	24	6	3	89	Cholecystitis	0.89 [0.71, 0.98]	0.94 [0.87, 0.98]
Summers, SM 2010	20	26	3	115	Cholecystitis	0.87 [0.66, 0.97]	0.82 [0.74, 0.88]

Sensitivity (95% CI) Specificity (95% CI)



RADUS

Study	TP	FP	FN	TN	Outcome	Sensitivity (95% CI)	Specificity (95% CI)
Summers, SM 2010	19	13	4	77	Cholecystitis	0.83 [0.61, 0.95]	0.86 [0.77, 0.92]
Van Randen, A 2011 (4)	38	29	14	940	Cholecystitis	0.73 [0.59, 0.84]	0.97 [0.96, 0.98]
Rosen, CL 2001	24	2	11	39	Cholecystitis	0.69 [0.51, 0.83]	0.95 [0.83, 0.99]
Kulvatunyou, N 2012	21	15	33	131	Cholecystitis	0.39 [0.26, 0.53]	0.90 [0.84, 0.94]

Sensitivity (95% CI) Specificity (95% CI)

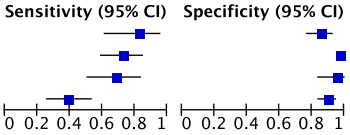


***Figure 6:** Diagnostic accuracy of POCUS and RADUS for acute cholecystitis*

Other pathologies

Additionally, our search strategy retrieved relevant but a limited number of studies on diverticulitis, small bowel obstruction, renal colic and abdominal aortic aneurysm. For each pathology, a forest plot is depicted in figure 7, 8, 9 and 10. The prevalence of these pathologies is presented in Table 2.

Acute diverticulitis

For POCUS, the sensitivity varied from 92% to 98%, while for RADUS, it ranged from 61% to 91%. As for specificity, the POCUS group ranged from 88% to 97%, while the RADUS group ranged from 99% to 100%.

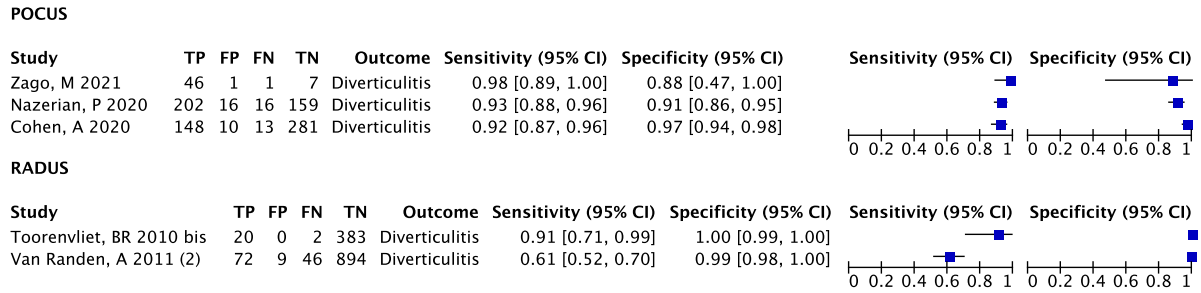


Figure 7: *Diagnostic accuracy of POCUS and RADUS for acute diverticulitis*

Small bowel obstruction

In the case of POCUS, both studies showed a sensitivity of 88%, whereas for RADUS, the only found study reported a sensitivity of 63%. Regarding specificity, the POCUS group ranged from 54% to 75%, while the RADUS study reported 99%.

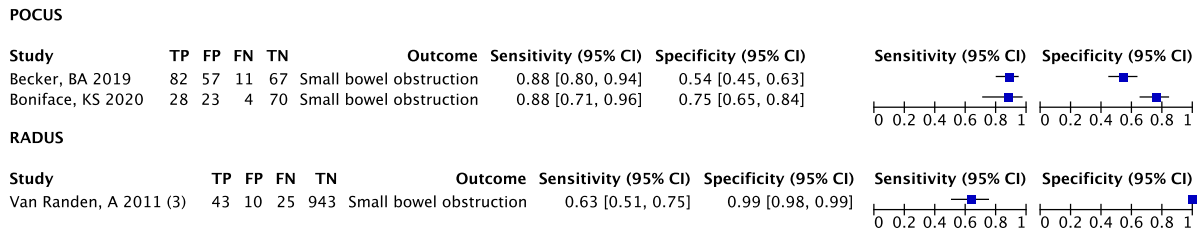


Figure 8: *Diagnostic accuracy of POCUS and RADUS for small bowel obstruction*

Renal colic

Only two studies, using POCUS as the index test, were found for renal colic. These studies demonstrated sensitivities ranging from 81% to 92% and specificities ranging from 35% to 84%.

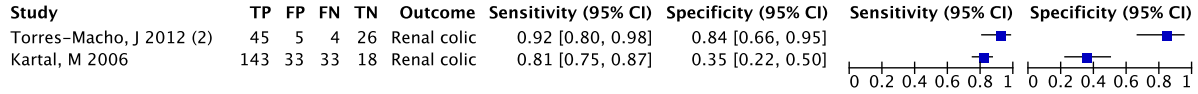


Figure 9: *Diagnostic accuracy of POCUS for renal colic*

Abdominal aortic aneurysm

One study investigated the diagnostic accuracy of POCUS on abdominal aortic aneurysm and reported a sensitivity and specificity of 100%.

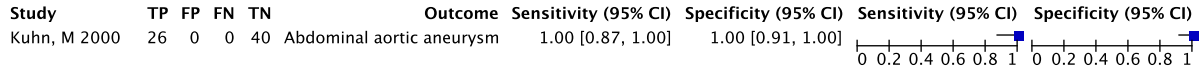


Figure 10: *Diagnostic accuracy of POCUS for abdominal aortic aneurysm*

Overall diagnostic accuracy

A meta-analysis was performed to evaluate the overall diagnostic accuracy of POCUS and RADUS. However, due to substantial heterogeneity observed among all the included studies, only studies with paired data were utilized. This heterogeneity was largely attributed to differences in patient populations and outcomes. Only 4 studies had paired data on POCUS and RADUS, two studies investigated appendicitis [41,60] and two studies investigated cholecystitis[57,58].

The sensitivity of POCUS was found to be 86.3%, while RADUS had a sensitivity of 73.1%. The specificity for POCUS was 81.3%, and for RADUS, it was 94.2%. Notably, the sensitivity favored POCUS over RADUS, whereas the specificity was higher for RADUS. The likelihood ratios further substantiate the favorable ruling-in capacities for RADUS, with LR+ of 12.567 (95%CI 5.538 to 28.516). POCUS however, had a LR+ of 4.623 (95% 2.089 to 10.232), indicating a moderate ruling-in capacity. In terms of ruling-out

capabilities, POCUS demonstrated a more reliable LR- of 0.168 (95%CI 0.091 to 0.312), whereas RADUS had a higher LR- of 0.285 (95%CI 0.214 to 0.382).

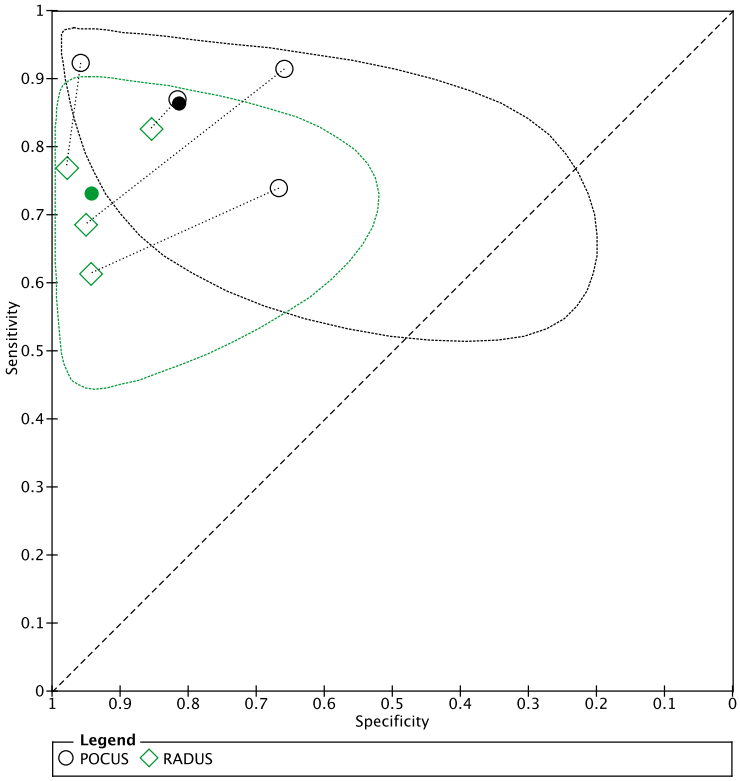


Figure 11: *SROC of POCUS and RADUS for studies with paired data*

POCUS

Study	TP	FP	FN	TN	Outcome	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gungor, F 2017	156	4	13	91	Appendicitis	0.92 [0.87, 0.96]	0.96 [0.90, 0.99]		
Rosen, CL 2001	32	14	3	27	Cholecystitis	0.91 [0.77, 0.98]	0.66 [0.49, 0.80]		
Summers, SM 2010	20	26	3	115	Cholecystitis	0.87 [0.66, 0.97]	0.82 [0.74, 0.88]		
Unluer, EE 2016	34	18	12	36	Appendicitis	0.74 [0.59, 0.86]	0.67 [0.53, 0.79]		

RADUS

Study	TP	FP	FN	TN	Outcome	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Summers, SM 2010	19	13	4	77	Cholecystitis	0.83 [0.61, 0.95]	0.86 [0.77, 0.92]		
Gungor, F 2017	130	2	39	93	Appendicitis	0.77 [0.70, 0.83]	0.98 [0.93, 1.00]		
Rosen, CL 2001	24	2	11	39	Cholecystitis	0.69 [0.51, 0.83]	0.95 [0.83, 0.99]		
Unluer, EE 2016	27	3	17	51	Appendicitis	0.61 [0.45, 0.76]	0.94 [0.85, 0.99]		

Figure 12: *Diagnostic accuracy of POCUS and RADUS for studies with paired data*

Discussion

We have identified 51 studies investigating the accuracy of POCUS and RADUS in diagnosing various abdominal pathologies in ambulatory care settings. These studies exhibited significant heterogeneity in terms of the prevalence of different pathologies, patient selection criteria, and reference standards used. The overall risk of bias in the studies was found to be low to moderate; however, some studies were at risk for selection bias, mainly due to preselection of patients with a high risk for the target disease or exclusion of critically ill patients or patients not requiring surgery.

Our meta-analysis demonstrated a good diagnostic accuracy for POCUS ruling in appendicitis and cholecystitis, as well as ruling out cholecystitis. Furthermore, based on paired data, our study indicated a good overall diagnostic accuracy for POCUS as well as RADUS, compared to histopathology, CT scan, intraoperative and clinical findings. Meta-analysis on paired data showed favorable ruling in capacities for RADUS over POCUS, whereas ruling out capacities favored POCUS over RADUS.

Therefore, POCUS appears to be a potentially valuable diagnostic tool for acute abdominal pathology in primary care settings.

These findings are supported by existing literature, a systematic review by Cho et al [61] on POCUS for appendicitis yielded a sensitivity of 91.7% and specificity of 90.9% which is even higher than our findings. On other pathologies, no systematic reviews were found and none was conducted in a general practitioners' practice.

Strengths

The primary strengths of this study lie in the elaborate search methodology, which included a systematic and comprehensive search strategy combined with a strict focus on prospective studies. In order to ensure the reliability and validity of the findings, we used stringent inclusion criteria. We deliberately restricted our search based on applicability and quality, which resulted in high applicability scores of QUADAS-2. Specifically, we

required that at least 50% of all patients included in the studies were aged 18 years or older. Moreover, we exclusively selected studies conducted in ambulatory care settings, while excluding those where participants were referred or already hospitalized. Retrospective study designs were also deliberately excluded, as they are prone to overestimating the diagnostic accuracy of the index tests.[62]

Limitations

Our study has several limitations. Typical limitations, inherent to meta-analyses, include human error, publication bias and missing relevant articles. In order to mitigate these limitations, we used a comprehensive and rigorous protocol, conducting searches in multiple databases and having articles screened by multiple investigators for inclusion, quality assessment, and data extraction. However, despite our elaborate search, we were unable to find any studies that explored the utilization of POCUS in a general practitioners' setting.

Overall, our meta-analysis suggests that POCUS may exhibit higher ruling out capabilities compared to RADUS, which is remarkable given that RADUS is a commonly used and trusted for screening our investigated target conditions. This could be due to a potential lack of blinding of the POCUS-performer to prior clinical investigations or other diagnostic test results, as the POCUS-performer in most cases is the treating physician.[41,57] In contrast, in some RADUS studies, investigators were blinded to these data, potentially resulting in lower but more reliable sensitivity results. This was demonstrated in the study of Gungor et. al [41], which directly compared POCUS and RADUS outcomes for appendicitis. POCUS yielded a sensitivity of 92% where RADUS was only 77% sensitive. The POCUS performers had prior knowledge of the patients, as their clinicians, which may have given them an advantageous position in the diagnostic process compared to radiologists who were blinded for any other patient information, while performing their routine practice.

Our meta-analysis shows that radiologists are better in ruling in various acute abdominal pathologies with a higher specificity for RADUS over POCUS. This could possibly be attributed to their extensive training and experience in comparison to emergency physicians. However, reviewing the existing literature, studies confirm that the diagnostic accuracy of POCUS approaches RADUS.[63,64] The more experienced the examiner, the better the accuracy.[65]

Moreover, our study identified heterogeneity across different areas.

Age demographics were not consistently reported and exhibited significant variation, as previously noted in the results. Some studies may have included pediatric participants but were excluded if more then 50% of all included patients were younger than 18 years.

Additionally, the ultrasounds were performed by various emergency physicians and radiologists, and the diagnostic accuracy of ultrasound is known to be influenced by user expertise. We did not account for the impact of varying levels of experience among the performers.

Besides, the effectiveness of ultrasound is also influenced by patient body habitus. For instance, in obese patients, ultrasound interpretation can be more challenging. Only Poletti et al. [66]explicitly excluded patients with a BMI above 30.

Furthermore, the quality of ultrasound is also influenced by the type of device used. For example, in the study by Puylaert et al. [67], published in 1987, the resolution of the ultrasound machine used, may not be as advanced compared to more recent studies.

Most studies included in our analysis exhibited relatively high prevalences, as reported by Chen [52], Davis [30], Dogra[39] , Gaszynski [32], and Uzunosmanoglu [68]. However, some of these high prevalences may be attributed to selection bias in certain studies. For example, in Mishra et al.[27], only patients with a high risk for complicated appendicitis were included. Likewise, in Davis et al. [30] and Kulvatunyou et al.[59], patients were only included if they

had a provisional diagnosis of appendicitis or cholecystitis, respectively, and subsequently underwent surgery.

Follow-up was frequently used as a reference standard for the non-surgery group, but this approach may have led to an underestimation of false negatives. For example, patients could have had a very early and self-limited form of appendicitis, which could have been missed at the time of investigation, as suggested by Kessler [55], Poortman [36], and Tschuor[69]. In RADUS studies, more reliable reference standards were used, such as histopathology or CT scan, whereas five POCUS studies used RADUS or review of POCUS tapes by a radiologist as a reference standard ([26,42,70,71] vs [47]).

Reviewing all studies, we identified several outliers. Upon closer investigation, we found potential explanations for these outliers. Four studies [46,51,66,67] utilized the category of "equivocal" when the ultrasound results were unclear. In Corson-Knowles et al. [51], Wilson et al. [46], and Poletti et al. [66], the indeterminate cases were considered as false negative and positive test results for the calculation of sensitivity and specificity, respectively. This approach resulted in a lower accuracy in these studies.

Kulvatunyou et al. [59] attributed the low sensitivity of RADUS in their study to the absence of verification bias. Verification bias occurs when only patients with positive RADUS results undergo surgery, leading to a falsely elevated sensitivity. In their study, patients were likely to be taken to surgery despite a negative RADUS result, potentially lowering the sensitivity.

In Uzunosmanoglu et al.[68], RADUS scored a high sensitivity, which may be attributed to selection bias as only patients who received surgery were included in the study.

Three studies conducted by Becker BA et al. [25], Fathi et al. [40], and Kartal et al. [34] were identified as outliers, but despite thorough review, no explanation was found. These studies attribute their moderate observed accuracy results to the intrinsically limited diagnostic value of ultrasound.

Kuhn et al. [47] is the only study that reports perfect diagnostic accuracy. However, despite literature supporting the good diagnostic value of ultrasound for abdominal aortic aneurysm[72], this study is suspected to have strong selection bias due to poorly defined convenience sampling. At last, also in the study conducted by Miller et al. [70] high diagnostic accuracy was observed. But upon closer investigation, Miller excluded all patients with resolved symptoms from the study. This enrichment of the population with patients who suffer severe disease may have potentially led to a falsely increased diagnostic accuracy of POCUS.

The utilization of convenience sampling in certain studies may also have introduced bias. For instance, in the study conducted by Kuhn et al.[47], it is possible that some investigators enrolled only patients whom they anticipated would be easy to scan, resulting in sample bias and inflated sensitivity and specificity estimates of 100%. Similarly, several other studies also used a convenience sampling design, leading to potentially missed subjects.[47,70]

Implications for clinical practice

In the context of diagnosing acute abdominal pain, time is of the essence. Diagnostic delay may result in poorer patient outcomes. The use of point-of-care ultrasound (POCUS) instead of radiologist-performed ultrasound (RADUS) may ensure 24/7 availability of this diagnostic tool. This systematic review demonstrates that POCUS is potentially useful in the diagnostic workup of acute abdominal pain. However, it should be noted that additional imaging or follow-up may be required to arrive at a definitive diagnosis. Furthermore, POCUS is safe, as it does not expose patients to radiation, and it is also cost-effective.

Implications for future research

The studies included in this review exhibit significant heterogeneity in terms of methods and results, indicating a need for further research in this area. Particular attention should be given to ensuring high-quality methodology and reporting. POCUS studies should use

a reliable reference standard and establish uniform ways for handling equivocal results. It is imperative that studies clearly specify the qualifications and characteristics of the individuals who performed the POCUS examinations, including whether they were blinded to previous clinical, laboratory, or imaging findings, and whether the same individuals who performed the scans also conducted the subsequent surgeries. Furthermore, future studies should aim to compare the accuracy of POCUS among different physicians, while also investigating the impact of training and experience on POCUS performance.

Most studies included in this review were conducted in the emergency department setting. Hence, additional investigation is warranted to determine the accuracy of POCUS in the context of general practitioners' practice. It is anticipated that the accuracy may be different in this setting due to the lower pre-test probability of acute abdominal pathology in primary care.

In future studies, it would be beneficial to investigate specific populations that nowadays are often excluded, such as pregnant individuals or patients with obesity. Given concerns over ionizing radiation exposure, particular attention should be given to assessing the diagnostic accuracy of ultrasound in pregnancy. Additionally, due to limited data availability, meta-analysis could not be performed for conditions such as diverticulitis, renal colic, small bowel obstruction, and abdominal aortic aneurysm. However, as more data becomes available in the future, pooled sensitivity and specificity estimates for these conditions could be calculated to further evaluate the diagnostic value of POCUS in primary care settings.

Conclusion

This is the first systematic review on the diagnostic accuracy of point-of-care ultrasound for the diagnosis of acute abdominal pain and included 51 studies. Meta-analysis showed reasonable sensitivity and specificity for POCUS and RADUS. These results suggest that POCUS is a useful initial imaging technique in the workup of acute abdominal pathology. However, ultrasound alone is not sufficient as a standalone test to definitively rule in acute abdominal pathology. In cases where patients have a high clinical suspicion but receive a negative or inconclusive US result, further evaluation is warranted.

It is important to note that included studies showed high heterogeneity. Further research is needed to validate the use point-of-care ultrasound as an effective imaging tool for diagnosis of patients with acute abdominal pain in primary care settings.

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Conflicts of interests

None

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Appendices

Appendix 1: Protocol

Title of the review	Signs, Symptoms and Test to improve diagnostic Certainty in diagnosing Patients presenting with Acute Abdominal Pain in Primary Care.
Timing	Start 2021; anticipated completion: 2023
Organizational affiliation of the review	Academic Centre for Primary Care, KU Leuven
Contact	Anouk Tans (Anouk.tans@kuleuven.be) Kapucijnenvoer 33 blok J, 3000 Leuven, Belgium
Review team members and their organizational affiliation	Dr. Anouk Tans, Academic Centre for Primary Care, KU Leuven, Leuven, Belgium Prof. dr. Ann Van den Bruel, Academic Centre for Primary Care, KU Leuven, Leuven, Belgium Dr. Yorick Asselbergh, Faculty of Medicine, KU Leuven Dr. Emmanuel Declerck, Faculty of Medicine, KU Leuven Dr. Toon Smeets, Faculty of Medicine, KU Leuven
Funding Sources/sponsors	None
Conflicts of interest	None
Collaborators if applicable	Dr. Thomas Struyf; Bio-medical master students
Background to the review	
Abdominal pain affects nearly every person at least once in their lifetime, independent from age, gender and social background.[2] As a result, it is one of the most common complaints of patients presenting to primary care or to the emergency department, accounting for 5% - 10% of all presentations.[4,73–75] In routine care, 56 per 1000 patients per year present with acute abdominal pain to Dutch general practitioners (GP).[5] Abdominal pain can be caused by a variety of conditions, ranging from acutely life-threatening to benign and self-limiting[76], including appendicitis (151 per 100 000), abdominal aorta aneurysm (4.8 to 13 per 100 000), acute pancreatitis (ranging from 4.6 to 100 per 100 000), acute biliary cholangitis (22.3 per 100 000), acute gastro-enteritis (1188 per 100 000).[77–81] In a substantial proportion of patients, even no	

specific cause can be identified. [2,8] Overall mortality rates from retrospective series vary from 2 to 13 percent and older patients with abdominal pain have a six- to eightfold increase in mortality compared to younger patients.[82] A primary care practitioner must thus consider multiple diagnoses whilst recognizing and prioritizing life-threatening conditions.[76]

Guidelines for patients with abdominal pain are mostly based on data collected at emergency departments or hospital settings. As a result, these guidelines are not adapted to primary care, where the spectrum of disease and prevalence of serious conditions is different. In addition, guidelines are dated. For example, GP guidelines concerning enteritis in Belgium date from 2011.[83] Moreover, Belgian GPs frequently use guidelines from the Dutch National GPs Association.[84] Due to a different health care organization, they are not compatible with our Belgian health care system. Therefore, new and more compatible guidelines for GPs are necessary.

Primary care physicians deal with high patient volumes and have to make decisions amid uncertainty. [85] Undifferentiated presenting features are the norm for diseases that are common in primary care, which is also the case for abdominal pain. The combination of undifferentiated symptoms, a low prevalence of serious disease, a high degree of symptom overlap between serious and benign conditions, patients with multiple complaints and psychological or social distress manifesting somatically all complicate the diagnostic process of patients with acute abdominal pain.[86]

Therefore to prevent unnecessary referrals to secondary care, to provide reassurance to patients by ruling out a serious condition and to improve clinical performance we want to assess clinical features and diagnostic tests and their diagnostic accuracy in diagnosing or ruling out serious conditions that may cause acute abdominal pain complaints in patients presenting to primary care.

Review question/Specific Objectives
What is the accuracy of clinical features (signs and symptoms), blood tests and imaging tests for diagnosing serious conditions in adults presenting with non-specified acute abdominal pain in primary care?

Search methods	
Electronic databases	MEDLINE, EMBASE, DARE, CINAHL, Web of Science
Other methods used for identifying relevant research	In addition, we will check the reference lists of included studies, systematic reviews and relevant guidelines*, and we will consult with experts. *Relevant guidelines and registers of following organizations will be checked for references: National Institute for health and Care Excellence (NICE) Infectious Diseases Society of America (IDSA) World Health Organization (WHO) U.S. National Library for Medicine: https://Clinicaltrials.gov/

	EU Clinical trials register: https://www.clinicaltrialsregister.eu/ Dutch General practitioners' society (NHG)
Criteria for including studies in the review	
Participants or population	Adults aged 18 or older presenting with acute non-specified abdominal pain to an ambulatory care setting. Acute non-specified abdominal pain is defined as pain (of any intensity) the patient can feel anywhere between the chest and groin that can vary in intensity and time, existing no longer than 14 days.
Interventions or exposures	Clinical features (signs and symptoms) such as vomiting and nausea, fever, anorexia, diarrhea, absence of flatus or constipation, peritoneal irritation, type of pain, location of pain, previous abdominal surgeries, … (list is not exhaustive) Laboratory tests either conducted at the point-of-care or in a central laboratory. Tests studied will be white blood cell count, c-reactive protein, procalcitonin, lactate, lipase/amylase, liver function tests (AST/ALT) and I-FABP. (list is not exhaustive) Imaging tests such as (POC) ultrasound, CT, MRI and Radiology (RX Abdomen). Imaging taken on referral of a primary healthcare worker (such as a GP) or at the Emergency department (ED). Imaging tests that are performed during hospital admission will not be eligible.
Comparisons or control groups	Control group not applicable Serious conditions include: Acute abdomen of any cause Acute pancreatitis Acute cholecystitis Acute appendicitis Acute diverticulitis Abdominal malignancy (colorectal neoplasms, duodenal neoplasms, pancreatic neoplasms, gastric neoplasms, esophageal neoplasms) Abdominal aortic aneurysm Bowel obstruction or perforation Mesenteric ischemia/thrombosis (bacterial) gastroenteritis This list is not exhaustive.
Setting or Context	Ambulatory care settings, which include general practice, primary care out-of-hours service, walk-in clinics, interface clinics, emergency departments and other settings in which patients are not admitted to hospital.
Types of studies to be included and selection criteria	Diagnostic accuracy studies: cross-sectional prospective cohort studies.

	Retrospective studies and case control studies will be excluded. Nested case control studies from a prospective cohort in which cases and controls are sampled from the same source population will be eligible for inclusion. Diagnostic accuracy studies employing a stratified or two-phase design will also be eligible. Systematic reviews and meta-analyses will only be used as a source of references. Given the low incidence of the target conditions, we will exclude studies reporting a total sample size smaller than 50, because these studies would include only a few subjects with the target condition and would be prone to selection bias. Consequently, case-reports will be excluded as well. Selection will be done in duplicate by two independent reviewers, in two rounds (1. Title and abstract, 2. Full text). Any discrepancies will be resolved by a third reviewer. Training of selection criteria was given to all reviewers before the start of selection; after a pilot phase of 10 selections per reviewer, the selection criteria were clarified if needed.
Primary outcome	Diagnostic accuracy for serious conditions, either as composite outcome for more than one abdominal condition or for a specific abdominal condition, of each test or clinical feature, expressed as sensitivity/specificity, predictive values, likelihood ratios and/or diagnostic odds ratios.
Secondary outcome	Multivariable prediction rules including combinations or multiple clinical features, laboratory tests and imaging tests.
Searches	
P	Adults >/= 18 years old with non-specified acute abdominal pain of a maximum of 14 days.
I	Signs and symptoms (clinical features) Laboratory tests (infection specific, White blood cell count, (POC) CRP, (POC) Lactate, Lipase/amylase) Imaging tests (radiology, (POC) ultrasound, CT, MRI)
T	(Possibly serious) abdominal diseases
S	Ambulatory care (primary care, ED)
P	*"Adult*"[Mesh] OR "Adult*"[tw] OR "Adult*"[tiab]*
I	*"Signs and Symptoms"[Mesh] OR "Signs and Symptoms, Digestive"[Mesh] OR "Diagnostic Techniques and*

	Procedures"[Mesh] OR "Clinical feature"[tw] OR "Clinical assessment*"[tw] OR "Clinical impression*"[tw] OR "Red flag*"[tw] OR "Gut feeling"[tw] OR "Intuition"[Mesh] OR "intuition"[tw] OR "C-Reactive Protein"[Mesh] OR "Signs and Symptoms"[tw] OR "diagnostic prediction rules"[tw] OR "Diagnostic Imaging"[tw] OR "Imaging"[tw] OR "ultrasound"[tw] OR "POC test*"[tw] OR "POCT"[tw] OR "Point-of-care imaging"[tw] OR "Point-of-Care Systems"[Mesh] OR "Near-patient-test*"[tw] OR "MRI"[tw] OR "CT"[tw] OR "Magnetic Resonance Imaging"[Mesh] OR "Tomography, X-Ray Computed"[Mesh] OR "Ultrasonography"[Mesh] OR "Signs"[tw] OR "Symptoms"[tw] OR "white blood cell count"[tw] OR "full blood count"[tw] OR "FBC"[tw] OR "CRP"[tw] OR "predictors"[tw] OR "technical investigations"[tw] OR "laboratory technique"[tw] OR "Clinical Laboratory Techniques"[Mesh] OR "Liver function test*"[Mesh] OR "Liver function test"[tw] OR "lipase"[tw] OR "amylase"[tw] OR "Lactic acid"[Mesh] OR "Lactic acid"[tw] OR "Lactate"[tw] OR "Fever"[tw] OR "Body temperature"[tw] OR "Melena"[tw] OR "Anorexia"[tw] OR "Vomiting"[tw] OR "Nausea"[tw] OR "Diarrhea"[tw] OR "Flatus"[tw] OR "Vital Signs"[tw] OR "Abdominal wall tenderness"[tw] "peritoneal irritation"[tw] OR "Constipation"[tw] OR "Abdominal Pain"[tw] OR "Abdominal Pain"[Mesh] OR "Abdominal tenderness"[tw] OR "right Lower-quadrant pain"[tw] OR "left lower-quadrant pain"[tw] OR "stomach pain"[tw] OR "Cramp*"[tw] OR "Pain"[tw] OR "Medical history"[tw] OR "colic pain"[tw] OR "colic"[tw] OR "Colic"[Mesh]*
T	*"Digestive System Disease*"[Mesh] OR "Abdomen"[tw] OR "nsap"[tw] OR "Acute Abdomen"[tw] OR "Peritoneal Irritation"[tw] OR "Abdominal Disease*"[tw] OR "Diverticulitis"[tw] OR "Enteritis"[tw] OR "appendicitis"[tw] OR "chron's disease"[tw] OR "Colitis"[tw] OR "Colon disease*"[tw] OR "cholecystitis"[tw] OR "gallbladder disease*"[tw] OR "pelvic inflammatory disease*"[tw] OR "pancreatitis"[tw] OR "Pancreatic diseases"[tw] OR "Aortic Abdominal Aneurysm"[tw] OR "biliary tract diseases"[tw] OR "gastritis"[tw] OR "peptic ulcer"[tw] OR "cystitis"[tw] OR "prostatitis"[tw] OR "pyelonephritis"[tw] OR "abdominal wall hernia"[tw] OR "bowel obstruction"[tw] OR "intestinal Obstruction"[tw] OR"Intestinal Volvulus"[tw] OR "aortic aneurysm"[tw] OR "torsion adnexal"[tw] OR "mesenteric ischemia"[tw] OR "intestinal perforation"[tw] OR "abdominal neoplasm*"[tw] OR "abdominal malignancy*"[tw] OR "abdominal cancer"[tw] OR "pancreatic neoplasm*"[tw] OR "colon neoplasm*"[tw] OR "duodenal neoplasm*"[tw] OR "intestinal diseas*"[tw] OR "gynaecologic disease*"[tw] OR "pelvic disease*"[tw] OR "ectopic pregnancy"[tw]*
S	*"Primary Health Care"[Mesh] OR "After-hours Care"[Mesh] OR "Emergency Service, Hospital"[Mesh] OR "Ambulatory Care"[Mesh] OR "Emergency Department*"[tw] OR "Ambulatory Care Facilities"[tw] OR "Ambulatory Health Center"[tw] OR "outpatient"[tw] OR "Out of Hours Care"[tw] OR "Out of hours primary care"[tw] OR "OOH care"[tw] OR "OOH primary care"[tw] OR "ED"[tw] OR "Family Practice"[Mesh] OR "Family practice"[tw] OR "Family medicine"[tw] OR "General*

	Practitioner"[Mesh] OR "general practitioner*"[tw] OR "General Practice"[tw] OR "GP"[tw] OR "GPs"[tw] OR "Outpatient*"[tw] OR "out-patient*"[tw] OR "Walk-in center*"[tw] OR "walk in center*"[tw] OR "Walk-in clinic*"[tw] OR "Walk in Clinic*"[tw] OR "Community health care center*"[tw]*
Criteria for excluding studies in the review	
Patients with known active abdominal malignancies and patients chronic pre-existing gastrointestinal diseases such as Crohn, Colitis or other inflammatory bowel syndromes will be excluded. Studies that include <50% of patients aged at least 18 years or do not present data for this age group separately will be excluded. Studies that include <50% of patients with acute pain for a maximum of 14 days, or do not present data for this group separately will be excluded. Case-control studies, Retrospective studies and systematic reviews or reviews will be excluded.	
Methods of review	
Data extraction	Pre-specified data extraction form by two independent reviewers. Author, year of publication Country, setting, design and year of data collection Participant characteristics: age, gender, inclusion and exclusion criteria, number of participants included, Index tests: type of test, threshold if applicable, timing if applicable Reference standard: description, threshold if applicable, timing if applicable Target condition: Abdominal disease, if defined in study
Risk of bias assessment or quality assessment	Two independent reviewers will assess risk of bias using all QUADAS-2 items. Disagreements will be resolved by discussion involving all researchers when appropriate. Studies will not be excluded from the review based on the risk of bias assessment. The results of the risk of bias assessment will be used in the interpretation of the results. In addition, specific aspects, i.e. non-consecutive inclusion and retrospective data collection, will be used in sensitivity analyses data allowing.
Strategy for data synthesis	Data for diagnostic accuracy will be displayed in two-by-two tables. Authors will be contacted if needed. Results will be reported descriptively using dumbbell plots for each (serious) abdominal disease our multiple abdominal diseases. Likelihood ratios for the presence (positive likelihood ratio) or absence (negative likelihood ratio) for the clinical features, laboratory tests and imaging tests for each (serious) abdominal

	disease outcome will be calculated. Clinical features, laboratory tests and imaging tests will be categorized based on their diagnostic value as either red flags (warning signs for an (serious) abdominal disease) or as rule-out signs for a certain (serious) abdominal disease. They are a red flag if the positive likelihood ratio is more than 5.0 and a rule-out sign if the negative likelihood ratio is less than 0.2. In addition pre-test and post-test probabilities of the possible disease outcome will be added per clinical feature, laboratory test and imaging test. Data will be pooled when at least 4 studies (without clinical heterogeneity) are available for a particular index test in a particular outcome, using bivariate model and displaying results in a hierarchical summary ROC curve for continuous test results.
Analysis of subgroups or subsets	Where possible, we will perform analyses of subsets of multiple clinical features, laboratory tests or imaging tests. Possible data on referrals and follow-up data will be collected and if possible analyzed descriptively.
Type and method of review	This is a diagnostic accuracy systematic review
Language	We will not apply any language restriction. Inclusion of languages other than English, French, German and Dutch will be subjected to availability of a reliable translation.
Country	Belgium
Dissemination plans	Results of the review will be submitted for publication in a peer-reviewed journal. In addition, results will be presented at national and/or international conferences.
Keywords	Abdominal diseases, Diagnosis, Signs and Symptoms, Laboratory tests, Imaging tests, Adults, Primary Care

Appendix 2: Study key characteristics

Study (author, year)	Design	Population (n; mean age (y); prevalence (%))	Women (%)	Index tests	Outcome	Reference standard	Setting, country	Inclusion criteria	Exclusion criteria
Becker BA, 2019[25]	Prosp, conv	217 55y 42.9%	52.5%	POCUS	Small bowel obstruction	CT scan	ED, USA	Adults with suspected small bowel obstruction	CT scan not conducted, pregnancy
Becker BA, 2022[53]	Prosp, conv	256 19y 28.1%	50.4%	POCUS	Appendicitis	Histopathology report	ED, USA	Patients with suspected appendicitis	Pregnancy, non-English speaking patients
Boniface K, 2019[37]	Prosp, conv	125 54y 25.6%	53.6%	POCUS	Small bowel obstruction	CT scan	ED, USA	Patients with suspected small bowel obstruction	CT scan not conducted, pregnancy, critically ill patients
Chen SC, 2000[52]	Prosp, conv	317 36y 74.8%	42.9%	POCUS; clinical findings	Appendicitis	Histopathology report; clinical follow-up	ED, Taiwan	Patients with right lower abdominal pain	Not specified
Cohen A, 2020[38]	Prosp, conv	425 60y 36.0%	54.0%	POCUS	Diverticulitis	CT scan	ED, USA	Adults with suspected diverticulitis	Critically ill patients, pregnancy, CT scan not conducted, recent abdominal surgery, confirmed diagnosis of diverticulitis
Corson-Knowles D, 2018[51]	Prosp, conv	76 27y 36.8%	36.8%	POCUS	Appendicitis	Histopathology report; medical chart review	ED, USA	Patients with suspected appendicitis	Missing data, prior radiological examination
Davis GN, 2019[30]	Prosp, cons	206 28y 90.8%	38.8%	RADUS; CT; Modified Alvarado; RIPASA score	Appendicitis	Histopathology report	ED, India	Adults with suspected appendicitis who underwent laparoscopic appendectomy	Pregnancy, prior radiological examination, previous trauma, right iliac fossa mass, confirmed diagnosis of urological or gynecological condition
Dogra V, 2018[39]	Prosp, ns	200 ns* 84.5%	39.0%	RADUS; Modified Alvarado score; laboratory test (WBC count)	Appendicitis	Histopathology report	SD, India	Patients with suspected appendicitis for whom surgery was planned	Critically ill patients, uncorrected coagulopathy, planned appendectomy, appendicular abscess or mass previously treated conservatively
Fathi M, 2015[40]	Prosp, conv	97 34y 44.3%	42.3%	POCUS	Appendicitis	Histopathology report; medical chart review	ED, Iran	Patients with suspected appendicitis	Pregnancy, critically ill patients, confirmed diagnosis, abdominal mass or guarding in physical examination, patients with addiction

Fox JC, 2008[49]	Prosp, conv	126 ns* 45.2%	49.2%	POCUS	Appendicitis	RADUS; CT scan; laparoscopy; surgical consultation	ED, USA	Patients with suspected appendicitis	Pregnancy
Gaszynski R, 2019[32]	Prosp, cons	100 49y 78.0%	61.0%	POCUS	Cholecystitis	Histopathology report; medical chart review	ED, Australia	Adult patients with suspected cholecystitis	Not specified
Gungor F, 2017[41]	Prosp, conv	264 30y 64.0%	42.8%	POCUS; RADUS	Appendicitis	Histopathology report; intraoperative findings; CT scan; clinical follow-up	ED, Turkey	Adult patients with abdominal pain and suspected appendicitis	Pregnancy, critically ill patients, no informed consent obtained
Gutierrez CJ, 1999[28]	Prosp, cons	125 32y 16.0%	84.0%	POCUS	Appendicitis	Histopathology report; intraoperative findings; clinical follow-up	ED, USA	Patients with atypical clinical presentation for suspected acute appendicitis	Not specified
Juan C, 2002[35]	Prosp, cons	734 34y 47.8%	50.1%	RADUS	Appendicitis	Histopathology report; clinical follow-up	ED, Taiwan	Patients with suspected acute appendicitis	Patients who didn't require surgery, patients not monitored in the hospital
Karabulut N, 2014[87]	Prosp, cons	104 27y 37.5%	51.9%	RADUS, CT scan	Appendicitis	Histopathology report; intraoperative findings; clinical follow up	ED, Turkey	Patients with suspected acute appendicitis	Not specified
Kartal M, 2006[34]	Prosp, cons	227 38y 77.5%	35.2%	POCUS; Noble algorithm; Brown algorithm	Renal colic	RADUS; clinical follow up; follow-up via phone call interviews	ED, Turkey	Patients with suspected renal colic	Patients with fever, patients < 14y, pregnancy
Kessler N, 2004[55]	Prosp, cons	125 30y 45.6%	53.6%	RADUS; laboratory tests (WBC count, CRP level)	Appendicitis	Histopathology report; intraoperative findings; clinical follow up	ED, France	Patients with suspected appendicitis	Not specified
Keyzer C, 2006[50]	Prosp, cons	94 38y 31.9%	62.8%	RADUS; CT scan	Appendicitis	Intraoperative findings; multiple diagnostic procedures (e.g. CT, colonoscopy, barium enema study, vaginal smear, lab finding); clinical follow up	ED, Belgium	Patients with suspected; age > 15y; recommended CT by emergency physician	Patients with previous appendectomy, pregnancy
Kozaci N, 2020[42]	Prosp, cons	122 42y 22.1%§	64.8%	POCUS	Appendicitis; Cholecystitis	RADUS	ED, Turkey	Adult patients with acute abdominal pain	Referred patients, patients who already received CT investigation, critically ill patients, children

Kuhn M, 2000[47]	Prosp, conv	68 ns* 38.2%	ns	POCUS	Abdominal aortic aneurysm	POCUS tape review by radiologist; multiple imaging or surgical procedures (e.g. CT, RADUS, angiography, laparotomy)	ED, Australia	Adult patients with suspected abdominal aortic aneurysm; patients age > 50y presenting with abdominal/ back pain of unclear origin or presumed renal colic	Patients with a previously diagnosed abdominal aneurysm
Kulvatunyou N, 2012[59]	Prosp, cons	192 38y 60.4%	77.5%	RADUS; clinical findings	Cholecystitis	Histopathology report; intraoperative findings	ED, USA	Patients with suspected cholecystitis who underwent laparoscopic cholecystectomy	Not specified
Leeuwenburgh M, 2013[44]	Prosp, cons	229 35y 51.3%	60.0%	RADUS; CT scan; MRI scan	Appendicitis	Expert panel (final diagnosis based on all available data, including ultrasound)	ED, The Netherlands	Adult patients with suspected appendicitis	Critically ill patients, pregnancy, patients with contraindications for MRI investigation
Luksaite-Lukste R, 2021[24]	Prosp, cons	1855 34y 28.0%	65.0%	RADUS	Appendicitis	Expert panel (final diagnosis based on all available data)	ED, Lithuania	Adult patients with suspected appendicitis	Pregnancy
Mallin M, 2015[54]	Prosp, cons	97 28y 35.0%	ns	POCUS	Appendicitis	Histopathology report; intraoperative findings	ED, USA	Patients with suspected appendicitis	Not specified
Man E, 2014[88]	Prosp, cons	268 35y 28.0%	66.9%	RADUS; Alvarado score; clinical findings	Appendicitis	Histopathology report	ED, Hungary	Patients with right lower abdominal pain with suspected appendicitis	Not specified
Miller AH, 2006[70]	Prosp, conv	132 40y 57.6%	79.5%	POCUS	Cholelithiasis	RADUS; clinical follow-up	ED, USA	Adult patients with right upper quadrant or epigastric pain with suspected biliary disease	Patients who underwent POCUS who had no laboratory result indication of biliary tract disease and whose abdominal pain resolved before RADUS was performed
Mishra A, 2018[27]	Prosp, cons	100 ns* 87.0%	30.0%	RADUS; Modified Alvarado score	Appendicitis	Histopathology report	ED, India	Patients with complicated appendicitis (e.g. perforation, abscess)	Pregnancy, patients with appendicular lump
Mukhopadhyay A, 2020[89]	Prosp, cons	118 ns* 47.5%	50.8%	RADUS; CT scan; Alvarado score	Appendicitis	Histopathology report	ED, India	Adult patients with suspected appendicitis	Patients with generalized peritonitis, palpable abdominal lumb and pre-existing intrabdominal disease, children
Nazerian P, 2020[90]	Prosp, cons	218 62y 55.5%	54.2%	POCUS	Diverticulitis	Medical chart review; clinical follow-up	ED, Italy	Adult patients with abdominal pain with suspected diverticulitis for whom CT was requested	Patients who underwent surgery in the last ten days, patients who underwent CT scan before ultrasound investigation with surgery in the last 10 days, CT scan before pocus,

Poletti P, 2011[66]	Prosp, cons	183 32y 47.0%	61.0%	RADUS; CT scan; low dose CT scan; diagnostic algorithm	Appendicitis	Intraoperative findings; medical chart review, follow-up via phone call interviews	ED, Switserland	Adult patients with suspected appendicitis	Pregnancy, patients with BMI < 18.5 or > 30.0
Poortman P, 2003[36]	Prosp, cons	199 26y 66.3%	55.3%	RADUS; CT scan	Appendicitis	Histopathology report; intraoperative findings	ED, The Netherlands	Patients with suspected appendicitis	Critically ill patients, pregnancy, patients with claustrophobia
Poortman P, 2009[91]	Prosp, cons	151 29y 60.9%	56.0%	RADUS; CT scan	Appendicitis	Intraoperative findings; clinical follow-up	ED, The Netherlands	Adult patients with suspected appendicitis	Pregnancy, patients with claustrophobia and previous appendectomy
Puylaert JBCM, 1987[67]	Prosp, cons	111 29y 46.8%	56.8%	RADUS	Appendicitis	Histopathology report; intraoperative findings; imaging en laboratory results	RD, The Netherlands	Patients with suspected appendicitis	Not specified
Rosen CL, 2001[58]	Prosp, cons	116 49y 46.1%	71.6%	POCUS; RADUS	Cholecystitis	Intraoperative findings; clinical follow-up	ED, USA	Adult patients with suspected cholecystitis	Not specified
Samir M, 2016[56]	Prosp, cons	100 26y 63.0%	57.0%	RADUS; Alvarado score	Appendicitis	Histopathology report; clinical follow-up	ED, Egypt	Patients with suspected appendicitis	Pregnancy, age < 12y or > 65y, patients with mental retardation
Shekarchi B, 2018[71]	Prosp, cons	342 54y 14.0%	63.2%	POCUS	Cholecystitis	RADUS	ED, Iran	Adult patients with suspected cholecystitis	Pregnancy, patients with a history of biliary disease or cholecystectomy, patients with jaundice, intubated patients
Siu AYC, 2007[92]	Prosp, cons	85 32y 34.1%	47.1%	POCUS	Appendicitis	Medical chart review	ED, China	Patients with suspected appendicitis	Patients with a diagnosis of urinary tract infection, ureteric colic or PID
Summers SM, 2010[57]	Prosp, conv	164 36y 14.0%	73.0%	POCUS; RADUS	Cholecystitis	Histopathology report; clinical follow-up	ED, USA	Adult patients with suspected cholecystitis	Patients who were lost to follow-up, unavailable pathology report
Tepel J, 2004[93]	Prosp, cons	400 22y 28.3%	63.0%	POCUS; laboratory tests (WBC count, CRP level); rectal temperature; Ohmann score	Appendicitis	Histopathology report; medical chart review	SD, Germany	Patients with acute abdominal pain, < 7 days	Patients with a history of appendectomy, patients with recent abdominal trauma or surgery (< 4 weeks)
Toorenvliet BR, 2010[29]	Prosp, cons	802 23y§ 14.8%	60.1%	RADUS; CT scan; clinical findings	Appendicitis	Histopathology report; clinical follow-up	ED, The Netherlands	Patients with acute abdominal pain	Patients with recent trauma, patients who underwent addition imaging prior to surgical consultation, patients who were evaluated at another hospital

Toorenvliet BR, 2010 (bis)[33]	Prosp, cons	802 60y§ 7.1%	54.5%§	RADUS; CT scan; clinical findings	Diverticulitis	Histopathology report; intraoperative findings; clinical follow-up	ED, The Netherlands	Patients with acute abdominal pain	Patients with recent trauma, patients who underwent addition imaging prior to surgical consultation, patients who were evaluated at another hospital
Topin F, 2016[48]	Prosp, cons	104 33y 24.0%	46.2%§	POCUS; laboratory tests (WBC count, CRP level)	Appendicitis	Intraoperative findings; clinical follow-up (including ultrasound results)	ED, Djibouti	Patients with suspected appendicitis	Not specified
Torres-Macho J, 2012[26]	Prosp, cons	275 68y; 61.3%§ 35.9%§	44.8%	POCUS	Hydronephrosis; Cholecystitis	RADUS	ED, Spain	Adult patients with suspected renal colic (with hydronephrosis) and/or suspected cholecystitis	Not specified
Tschour C, 2019[69]	Prosp, cons	357 31y 54.3%	53.2%	RADUS; CT scan; laboratory tests (WBC count, CRP level, PSP level); Alvarado score	Appendicitis	Histopathology report	SD, Greece and Switzerland	Adult patients with suspected appendicitis	Not specified
Unluer E, 2016[60]	Prosp, cons	100 33y 45.0%	57.0%	POCUS; RADUS; Modified Alvarado score; Alvarado score;	Appendicitis	Histopathology report; intraoperative findings; clinical follow-up	ED, Turkey	Adult patients with suspected appendicitis	Pregnancy, children, patients with a history of appendectomy, patients with flank peritonitis or neurological deficits, low POCUS image quality
Uzunosmanoglu M, 2017[68]	Prosp, cons	60 30y 76.6%	55.0%	RADUS; Doppler RADUS; CT scan	Appendicitis	Histopathology report	ED, Turkey	Adult patients with abdominal pain	Pregnancy, patients with pain > 24 hours, patients with a history of appendectomy, age < 18y or > 65y, patients who were admitted after 5PM
Van Randen A, 2010[43]	Prosp, cons	942 47y 301%	55.0%	RADUS; CT scan	Appendicitis	Expert panel (final diagnosis based on all available data)	ED, The Netherlands	Patients with acute abdominal pain	Pregnancy, children, patients with blunt or penetrating trauma, hemorrhagic shock or distinctive flank pain, patients who did not underwent imaging
Van Randen A, 2011[31]	Prosp, cons	1021 47y 27.8%§ 5.1%§ 11.6%§ 6.7%§	55.0%	RADUS; CT scan	Appendicitis; Cholecystitis; Diverticulitis; Small bowel obstruction	Expert panel (final diagnosis based on all available data)	ED, The Netherlands	Patients with acute abdominal pain	Pregnancy, children, patients with blunt or penetrating trauma, hemorrhagic shock or distinctive flank pain, patients who did not underwent imaging

Wilson EB, 2001[46]	Prosp, cons	99 27y 55.6%	49.5%	RADUS; CT scan	Appendicitis	Histopathology report; intraoperative findings; clinical follow-up	SD, USA	Patients with suspected appendicitis	Critically ill patients, pregnancy or nursing patients, patients with diffuse peritonitis
Wise SW, 2001[45]	Prosp, cons	100 38y 24.0%	74.0%	RADUS; CT scan	Appendicitis	Histopathology report; intraoperative findings; clinical follow-up	ED, USA	Patients with suspected appendicitis	Pregnancy, critically ill patients, patients with IV contrast allergy, non-English speaking patients
Zago M, 2021[23]	Prosp, cons	55 62y 85.4%	54.5%	POCUS	Diverticulitis	CT scan	ED, Italy	Adult patients with suspected diverticulitis	Patients who did not underwent imaging, patients with POCUS not performed by a contributing investigator

Table 1: *Overview of key characteristics for each study*
Abbreviations: ns: not specified; prosp: prospective; cons: consecutive; conv: convenience; ED: emergency department; SD: surgical department; RD: radiology department; CT: computed tomography scan; MRI: magnetic resonance imaging scan; WBC: white blood cell; CRP: C reactive protein; PSP: pancreatic stone protein; PID: pelvic inflammatory disease.

** At least 50% adults of total study population*

§ Represented value for relevant subgroup population

Zelfreflectie en peer-review thesis

Tijdens de Ma-na-Ma huisartsgeneeskunde maakte ik samen met twee collega HAIO's (Yorick Asselbergh en Emmanuel Declerck) een thesis over het gebruik van POCUS (= point-of-care ultrasound) voor de diagnostiek van abdominale pijn. Nu deze thesis is afgerond, is het interessant om te reflecteren over hoe de samenwerking verliep en hoe dit onderzoek bijdroeg aan mijn leerproces en evolutie als HAIO.

De thesis vergde heel wat organisatie en professionalisme. Om naast de lessen, seminaries, wachtdiensten en de stage vrije momenten te vinden, was niet altijd evident. Ook waren we gestart met achterstand, omdat het huidige onderwerp eigenlijk reeds ons derde onderwerp is. Door extreme tijden (e.g. COVID-19 pandemie; Camostat en post-COVID) en onverwachte gebeurtenissen (e.g. stop van onze initiële co-promotor) begonnen we driemaal opnieuw. Het uitvoeren van ons onderzoek vergde misschien juist daarom een goede structuur en planning, prioritering van cruciale elementen en het nauwgezet nakomen van gemaakte afspraken. Hoewel dit bij momenten zorgde voor druk en stress, gingen we hier professioneel en verantwoordelijk mee om. Er was ruimte voor ieders visie, alsook werden de ideeën en emoties van iedereen gerespecteerd.

Ook groeide ik dankzij de thesis tot een beter en meer ervaren medisch expert en wetenschapper. Met onze introductie en literatuuronderzoek leerde ik bij over (het differentieel diagnostisch landschap van) abdominale pijn, de uitdagingen die deze frequente aanmeldingsklacht met zich meebrengt en bijgevolg het nut en belang van onze studie. Ik leerde bij over de opbouw en het uitvoeren van een systematic review; m.b.v. een uitgebreide, doch gerichte zoekstrategie werd het wetenschappelijk onderzoek opgezet. De gevonden artikels werden vervolgens kritisch beoordeeld; initieel op basis van de vooraf vastgelegde in- en exclusiecriteria, nadien door een kwaliteitsanalyse met behulp van QUADAS-2. Data werd geëxtraheerd alvorens we deze verwerkten met RevMan en ShinyApps. Tijdens de studie botste ik voortdurend op blinde vlekken (e.g. uitvoeren RevMan analyse, meta-analyse via ShinyApps, etc.) waar ik steeds aan werkte. Dit deed ik zowel zelfstandig, als met de ondersteunende en sturende begeleiding van de (co-)promotor. Onze resultaten en studie in het algemeen werden in detail onderzocht; heterogeniteit, uitschieters, risico op bias, etc. Op die manier keken we verder dan enkel de resultaten door ook sterktes en limitaties te benoemen.

We beogen ook dat onze thesis een gezondheidsbevorderend effect zal hebben. Hoewel aanvullend en meer diepgaander onderzoek nodig is, zou deze studie kunnen bijdragen tot een verdere introductie van de echografie in de huisartsenpraktijk. Op die manier zouden we als huisarts over meer "tools" beschikken voor het onderzoek bij acute

abdominale pijn en dit zou kunnen leiden tot meer correcte diagnostiek en bijgevolg een beter beleid.

Het maken van de thesis vereiste een langdurige en intensieve samenwerking met twee mede HAIO's (Yorick en Emmanuel). We zijn al langdurig goede vrienden, maar zo'n complexe en uitdagende opdracht als deze voerden we nog nooit samen uit. Doordat we elkaar goed kennen, weten we hoe ieder fungeert, waarin iemand excelleert en waar we elkaar best in ondersteunen (e.g. statistiek, IT, etc.). We kennen onze valkuilen en we durven die ook constructief benoemen (e.g. perfectionistisch, last-minute werken, wat meer stressgevoelig, etc.). Omdat de thesis heel wat omvatte, verdeelden we initieel het werk een beetje. We vertrouwden elkaar hierin, omdat we weten dat iedereen punctueel en ijverig werkt. Wel controleerden we elkaar en gaven we opbouwende, doch kritische feedback. Op die manier trachtten we onze thesis naar een hoger niveau te tillen. De finale versie maakten we gezamenlijk, opdat we allen achter de uiteindelijke uiteenzetting stonden en de conclusie begrepen en ondersteunden. Iedereen was bijgevolg van elk onderdeel van de thesis op de hoogte. Tijdens het maken van de thesis waren er uiteraard ook enkele uitdagende momenten (e.g. nieuw onderwerp, foutieve berekeningen, etc.). Door elkaar te blijven aanmoedigen en motiveren, sloegen we ons hier steeds door en kwamen we er zelfs sterker uit. Als ik alleen zou gewerkt hebben, zouden deze moeilijke momenten vermoedelijk meer van mezelf gevraagd hebben. Nu konden we immers op elkaar steunen en elkaar vooruit stuwen. Verder zorgde de samenwerking voor het verenigen van verschillende visies en ideeën. Dit zorgde voor een bredere invalshoek en een meer complete thesis. Tevens bespraken we onze bevindingen met de (co-)promotor en stemden we dit met haar af. De (co-)promotor deelde haar kennis en informatie met ons, waardoor wij goed ondersteund werden en in de juiste richting konden verder werken. Terugkijkend op de voorbije maanden en jaren ben ik tevreden en voldaan over onze samenwerking. We zijn trots op ons resultaat, maar ook de manier waarop we dit onderzoek uitvoerden, maakt me gelukkig. Kort samengevat was er een opbouwende en punctuele samenwerking met aandacht voor iedereen zijn/haar visie en ideeën. We legden de lat voldoende hoog, zonder elkaar overdreven onder druk te zetten, hetgeen finaal leidde tot een mooi resultaat. De thesis bevestigde onze goede vriendschap, maar ook onze gedeelde interesse en passie voor het mooie vak "geneeskunde". Als ik opnieuw een thesis zou aanvatten, zou ik dat graag opnieuw met Yorick en Emmanuel doen.

Ook het communicatieve aspect kwam aan bod in onze thesis; in onderling overleg met Yorick en Emmanuel, alsook bij vergaderingen met onze (co-)promotor. We communiceerden open en respectvol, luisterden gefocust en we formuleerden onze

vragen to the point. Binnenkort mogen we onze thesis nog presenteren op de thesisverdediging en brengen we samen met onze co-promotor een uiteenzetting op het WONCA-congres.

Algemeen samenvattend had deze thesis een positief effect op mijn evolutie als HAIO, rekening houdend met de verschillende CanMEDS rollen. Ik leerde erg veel bij als medisch expert en wetenschapper, alsook was een goede organisatie en samenwerking fundamenteel. De samenwerking met Yorick en Emmanuel verliep erg vlot en deze droeg absoluut positief bij tot het finale resultaat van onze scriptie.