Technoleg Iechyd Cymru
Health Technology Wales

Evidence Appraisal Report [1]

Cone-beam computed tomography for breast imaging

Appraisal summary

Why did Health Technology Wales (HTW) appraise this topic?

- Breast cancer is the most common type of cancer in the UK, with over 55,000 new cases diagnosed each year. Early detection, which has been shown to reduce both breast cancer mortality and burden, is therefore essential.
- Cone-beam breast computed tomography (CBBCT) can be used to create high-resolution, three-dimensional (3D) images of each breast in approximately seven seconds, using comparable radiation to that of conventional mammography and less breast compression than mammography. It is claimed to provide more accurate results for dense breast tissue and to detect smaller lesions than two-dimensional (2D) mammography.
- Koning Vera CT (Koning Corporation; Delaware, USA) is an example of a CBBCT device that has regulatory approval. CBBCT was referred to HTW as a topic from their UK distributor (Euronoxx Medical Group; London, UK).

What evidence did HTW find?

Three systematic reviews, along with five primary studies, and one ongoing study, were identified in the clinical review section of this report. The evidence identified reported on diagnostic accuracy, radiation dose and patient comfort outcomes; however, no evidence was found for outcomes related to 1) time to diagnosis, 2) time to treatment, or 3) health-related quality of life (QoL).

Overall, the evidence suggests that CBBCT demonstrated higher sensitivity compared to 2D digital mammography; however, CBBCT had lower sensitivity when compared with magnetic resonance imaging (MRI). Digital breast tomosynthesis (DBT) had better specificity than CBBCT. However, there is a need for comparative studies to more accurately determine the diagnostic accuracy of CBBCT compared to DBT.

Regarding patient comfort, three studies reported on patient comfort experienced during CBBCT in relation to 2D digital mammography examinations. Overall, ratings of patient comfort tended to favour CBBCT, including both CBBCT modes (i.e., contrast-enhanced [CE]-CBBCT and non-contrast [NC]-CBBCT), compared to mammography. Additionally, two studies reported the body

[1] Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg
Translation of published technical HTW documents from English into Welsh

areas in which individuals experienced discomfort during the CBBCT examination, reporting the greatest discomfort levels in the neck and shoulders, followed by the ribs, arms, face, back, and hips. No evidence was identified reporting on patient comfort-related outcomes comparing CBBCT with DBT or MRI or ultrasound examinations.

Although the radiation doses for both CBBCT and digital mammography varied across studies, they were generally comparable, suggesting that both breast imaging modalities result in similar levels of patient exposure. However, DBT demonstrated lower radiation doses than CBBCT. Additionally, ultrasound imaging and MRI scans do not involve ionising radiation, highlighting their advantage in minimising patient radiation exposure.

The evidence presented was based on studies that were mostly conducted in China, while some were conducted in USA and Europe. Therefore, the studies were from countries with a diverse range of healthcare systems and population demographics, reducing the direct applicability of the evidence to the Welsh context. Additionally, the evidence involved women only, with no inclusion of men or trans individuals, limiting the generalisability of the findings and highlighting the need for future research involving a broader and more inclusive spectrum of individuals. Moreover, none of the included systematic reviews and primary studies, reported on the time to diagnosis, time to treatment, resource use, and health-related QoL outcomes. Thus, there is a need for rigorous studies that assess multiple outcomes simultaneously to better understand the broader impact of CBBCT compared with other breast imaging modalities.

No relevant economic analyses were identified which considered the cost effectiveness of CBBCT compared with standard care for the diagnosis of breast cancer. An economic model was not developed as it was concluded that the current evidence base is insufficient to support the development of a robust economic evaluation.

HTW's Patient and Public Involvement Standing Group (PPISG) recommended seeking engagement from patient organisation for this topic. Relevant organisations and charities were approached, and interest was gained from Breast Cancer Now UK, who agreed to co-produce and circulate an online survey to their patient network. Relevant PPI information was also identified during the clinical effectiveness evidence sift and included within the PPI evidence. Some evidence was also found concerning people with protected characteristics as well as other considerations for equality, diversity and inclusion. This evidence can be seen in Section 7.

What was the outcome of HTW's appraisal?

HTW is a national body working to improve quality of care in Wales. We collaborate with partners across health, social care, and industry to issue independent guidance that informs commissioning within Wales health and social care. We are supported by an Assessment Group, who ensure our work adheres to high standards of methodological and scientific rigour, and an Appraisal Panel, who consider evidence within the Welsh context and produce HTW guidance.

More details on our appraisal process, the assessment group, and the appraisal panel can be found on the HTW website.

In this case, the HTW Assessment Group considered the evidence presented in this Evidence Appraisal Report (EAR075) and concluded there was sufficient evidence for the development of guidance. Please refer to the HTW website for full guidance details. EAR075 follows below and provides full details for this topic. More comprehensive details of the HTW Guidance and HTW Appraisal Panel considerations can be found on the HTW website.

1. Purpose of the Evidence Appraisal Report

This report aims to identify and summarise evidence that addresses the following question: What is the clinical and cost effectiveness of cone-beam breast computed tomography compared to standard practice for diagnosis of breast cancer?

Evidence Appraisal Reports are based on rapid systematic literature searches, with the aim of identifying the best published evidence on the effectiveness and cost-effectiveness of health and social care technologies and models of care and support. Researchers critically evaluate this evidence. The draft Evidence Appraisal Report is reviewed by experts and by Health Technology Wales multidisciplinary advisory groups before publication.

2. Context

Breast cancer is characterised by uncontrolled growth of malignant cells in the mammary epithelial tissue (Katsura et al. 2022). Breast cancer is the most common type of cancer in the UK (NICE 2022a), with over 55,000 new cases diagnosed each year (Katsura et al. 2022). This number is projected to increase by 2% by 2035 (Cancer Research UK 2026). In Wales, more than 2,000 individuals are diagnosed with breast cancer each year (PHW 2019). While breast cancer can affect both men and women, it primarily occurs in women with the risk increasing by age (Lukong 2017, NICE 2022a, WHO 2026). More than 80% of breast cancer cases are diagnosed in women over the age of 50 (NHS Digital 2022, Katsura et al. 2022, Lukong 2017). Breast cancer constitutes the leading cause of cancer-related deaths globally, with an estimated 670,000 deaths in 2022 (WHO 2026). Early detection, which has been shown to reduce both breast cancer mortality and burden, is therefore essential (Lauby-Secretan et al. 2015, Njor et al. 2012).

Breast cancer may be suspected due to symptoms or signs but also because of an abnormal screening test. In Wales, breast screening invitations are based on how individuals are registered with their doctor (i.e., male or female, or non-specified) and their age group (PHW 2024). Individuals aged from 50 to 70 years, who are registered as female, are automatically invited for breast screening, using digital x-ray mammography, every three years (NICE 2022a, PHW 2022a). Individuals who are trans or non-binary may or may not receive invitations depending on how they registered with their doctor and whether they have breast tissue (PHW 2024). Other imaging methods may be used in selected cases, such as ultrasound imaging, DBT, and MRI scans. Suspected breast cancer is usually investigated with a triple assessment approach, including clinical examination, imaging (usually mammography and/or ultrasound), and biopsy (RCR 2025). Breast imaging typically involves full-field digital mammography, taking two x-ray images (one from above and one from the side) of each breast whilst compressed with the person usually positioned in a standing posture (NIBIB 2022a, NICE 2022a). This process takes only a few minutes, but might be uncomfortable due to compression (NHS 2025). During mammography, the radiation is directed only at the breasts and the dose received is considered very small compared to other sources of radiation (e.g., long haul flights) (PHW 2022b).

Breast ultrasound imaging uses high-frequency sound waves to produce three-dimensional (3D) real-time images of the breast tissue on a monitor (Malherbe & Tafti 2024, NIBIB 2023). The individual is positioned in a supine or oblique position, with the arm raised above the head on the side being examined (Malherbe & Tafti 2024, NIBIB 2023). Then, ultrasound gel is applied to the skin and the transducer is moved systematically over the entire breast and armpit to evaluate lymph nodes (Malherbe & Tafti 2024, NIBIB 2023). Ultrasound images can also be displayed in two-dimension and four-dimension formats (NIBIB 2023). Ultrasound imaging does not expose the individual to radiation (NIBIB 2023, Siddall et al. 2024). It is typically used as an adjunct to mammography (Malherbe & Tafti 2024, NIBIB 2023, Spear et al. 2024).

DBT constitutes an advanced form of mammography, as it uses low-dose x-rays to produce 3D breast images (NIBIB 2022a, Siddall et al. 2024, Spear et al. 2024). By obtaining multiple images from different angles around the breast at fixed intervals and then digitally reconstructing them into slices, this technique allows to examine the breast tissue layer by layer (Dhamija et al. 2021, NIBIB 2022a, Siddall et al. 2024). DBT is performed in similar breast position as full-field mammography (NIBIB 2022a). This breast screen option is approved for use in the NHS breast screening programme (BSP) in England, as an optional tool to screen detected soft tissues breast abnormalities (NHS England 2025a). It is not recommended to be routinely performed for a clinical recall, where the breast imaging is normal, and to use mammography in such cases (NHS England 2025a).

Contrast-enhanced mammography (CEM) is another advanced breast imaging modality combining a conventional mammography and an injection of iodine-based contrast dye to highlight areas of concern of the breast(s) (NICE 2022b, van Nijnatten et al. 2024). The contrast dye is injected into a vein, usually in the elbow crease or the back of the hand (Gloucestershire Hospitals NHS Foundation Trust 2024, van Nijnatten et al. 2024). The injection might cause discomfort, after which there is a short waiting period followed by conventional mammography examination (Gloucestershire Hospitals NHS Foundation Trust 2024). CEM is considered particularly valuable for downgrading false positive recalls and reducing the number of biopsies for low suspicion masses and asymmetries when no enhancement is demonstrated on CEM (NHS England 2026). In England, CEM is considered where available, particularly for individuals with dense breast tissue (NHS England 2026) and/or with inconclusive results, early symptoms or confirmed breast cancer (NICE 2022b, RCR 2025).

MRI of the breast uses strong magnetic fields and radiofrequency pulses producing 3D images of the breast tissue (Gunduru & Grigorian 2023). Intravenous administration of contrast medium (e.g., gadolinium) might be given to the individual before or during the scan to increase the brightness of the images (Gunduru & Grigorian 2023, NIBIB 2022b). During the scan, the individual is positioned prone on the MRI table, with the targeted breasts positioned into specialised coils (NIBIB 2022b). The images are taken as the table moves through the MRI scanner (Gunduru & Grigorian 2023, NIBIB 2022b). MRI scans do not use x-rays or other ionising radiation; however, MRI is more expensive than any x-ray imaging. MRI of the breast is considered as an ultimate supplementary imaging modality in addition to mammography and ultrasound in the evaluation of the breasts (Gunduru & Grigorian 2023, NIBIB 2022b, Siddall et al. 2024, Spear et al. 2024).

Experts in Wales reported that breast imaging diagnostic services are delivered through two distinct pathways: (1) symptomatic assessment, conducted within the NHS health boards, and (2) the screening pathway, performed independently by Breast Test Wales (BTW) across different sites. Experts highlighted that, although some workforce overlap exists, particularly among consultant radiologists and other trained staff, the equipment and the majority of personnel involved remain organisationally separate, reflecting distinct operational arrangements between the pathways.

3. Health technology

Cone-beam breast computed tomography (CBBCT) can be used to create high-resolution, 3D images of each breast tissue in seven seconds approximately (Siddall et al. 2024). During CBBCT, the individual is positioned prone on the imaging table, with the targeted breast suspended through an opening in the table (Siddall et al. 2024). This positioning minimizing breast compression (Siddall et al. 2024), which can often be painful for patients (O'Connell et al. 2021). A cone-shaped X-ray beam and a flat-panel detector then rotates around the breast, obtaining multiple images in a full 360-degree scan (Siddall et al. 2024).

Experts reported that CBBCT scan time ranges between five to 10 seconds per breast, with the total examination time varying depending on the CBBCT mode (i.e., NC-CBBCT and CE-CBBCT). For NC-CBBCT, the examination lasts approximately seven minutes, including completion of a patient questionnaire, patient self-positioning, and imaging acquisition, or approximately five minutes, if no questionnaire is required. For CE-CBBCT, the examination duration is approximately 10 to 15 minutes, including the patient self-positioning, contrast administration, and imaging acquisition. Furthermore, they reported that larger breasts might require additional imaging; however, no specific details were provided regarding the duration scan per breast, the number of additional images required or the technical parameters of the imaging acquisition. Thus, the potential impact of breast size on total examination time and workflow efficiency remains uncertain.

The radiation dose of CBBCT typically ranges from 5.1 to 7.5 milligray (mGy), depending on the breast size and composition (Siddall et al. 2024). This dose is generally comparable to that of conventional two-dimensional (2D) digital mammography, which ranges from 4.3 and 10 mGy (Siddall et al. 2024). It is claimed to provide more accurate results for dense breast tissue and be able to detect smaller lesions than 2D mammograms (Li et al. 2019, Siddall et al. 2024). This technology could potentially be used as a complementary or replacement imaging modality in the breast diagnostic pathway. CBBCT can be also used to facilitate other procedures required for breast cancer, such as CT-guided biopsy of breast lesions whilst the patient is in situ (prone position). Koning Vera CT is an example of a CBBCT device that has regulatory approval.

According to some experts, although diagnosis is one of the primary applications of CBBCT, it can also widely be utilised across the broader clinical pathway, including at the pre-operative stage (e.g., assessment, biopsy planning, monitoring response to neoadjuvant therapy), intra-operative stage, post-operative stage (e.g., recovery, long-term monitoring), as well as implant evaluation, dense breast tissue, small breasts, and other aspects of disease management. However, this EAR focuses on the use of CBBCT as a breast imaging diagnostic modality for individuals with suspected breast cancer and any other applications are considered beyond scope.

Although CBBCT is available in selected centres internationally, including parts of Asia (China, Thailand, United Arab Emirates, Qatar), Europe (the Netherlands), North America (Jamaica and United States: Alabama, Arkansas, California, Georgia, Florida, Illinois, Missouri, New York, Tennessee, and Texas), and Oceania (Queensland, Australia) (Koning 2025), its clinical adoption remains limited. CBBCT is not used in NHS Wales, as the current standard practice for breast imaging is mammography provided by the national BTW service (PHW 2022a). Experts further confirmed the use of CBBCT internationally but not in the UK, as described above.

4. Effectiveness

HTW researchers searched for evidence that could be used to answer the review question: What is the clinical and cost effectiveness of cone-beam breast computed tomography compared to standard practice for diagnosis of breast cancer?

For details on the methodology used to identify evidence for this report, refer to Appendix 1.

4.1 Overview

The evidence identification criteria and research question are available in Appendix 2, and the PRISMA flowchart summarising study selection is available in Appendix 4. There were three systematic reviews (Gong et al. 2023, Komolafe et al. 2022, Yang et al. 2024) identified, along with five primary studies (Li et al. 2019, O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012, Vedantham et al. 2013, Xue et al. 2025), and one ongoing study (NCT05036096). The systematic reviews and primary studies are described in Appendix 5 (Table A1 and Table A2, respectively), and below.

We identified and included evidence that compared CBBCT with the following breast imaging modalities: 2D digital mammography (Yang et al. 2024), DBT (Komolafe et al. 2022), MRI or ultrasound (Gong et al. 2023). We did not identify any evidence comparing CBBCT with CEM. There was no evidence identified on the following outcomes: 1) time to diagnosis, 2) time to treatment, or 3) health related Quality-of-Life (QoL).

Yang et al. (2024) conducted a systematic review and meta-analysis comparing the diagnostic accuracy of CBBCT and digital x-ray mammography for individuals with suspected breast cancer. Eight studies with a total of 847 individuals with suspected breast cancer were included. The studies were published between 2015 and 2022. Most of the included studies were conducted in China (6 studies, 75%), with two (25%) in Europe, specifically in Germany. All studies were comparative, involving six prospective and two retrospective studies. Across all studies, the CBCCT 1000 (Koning Corporation, USA) was used, whereas mammography was performed using a variety of systems, including the Mammomat Inspiration (Siemens Healthcare, USA), the Mo-target (Hologic, USA), the Sophie (Planmed, USA), the Selenia or Lorad Selenia (Hologic, USA) or the Senographe Essential or 2000D (General Electric Medical Systems, USA). The studies utilised CE-CBBCT and/or NC-CBBCT protocols; however, this feature was not clearly reported, and any findings related to the mode of CBBCT should be interpreted with caution. All included studies incorporated 2D digital mammography, typically acquiring craniocaudal (CC) and mediolateral oblique (MLO) views, with some mammography units involving spot compression and optional magnification views.

Komolafe et al. (2022) conducted a systematic review and meta-analysis comparing the diagnostic accuracy of CBBCT and DBT for breast cancer detection. Since there are no available studies directly comparing CBBCT and DBT for diagnostic or screening examination, they separately included comparative, prospective and retrospective studies, and interrater consensus for each breast imaging modality. For CBBCT, five studies (also included in Gong et al. (2023) and Yang et al. (2024), with a total of 407 individuals with suspected breast cancer, were included. The studies were published between 2015 and 2018. Among the five studies, two (40%) were conducted in Europe (Germany) and one (20%) in China, while the country of origin for one (20%) was not reported. Three (60%) studies were retrospective, and two (40%) were prospective studies. Across the five studies, four (80%) were comparative studies (i.e., two studies: CBBCT vs 2D digital mammography; one study: CBBCT vs MRI vs 2D digital mammography; one study: CBBCT vs 2D digital mammography vs ultrasound), while one (20%) was single arm in design. Four (80%) studies employed the CBCCT 1000 (Koning Corporation, USA), while one did not report

the CBBCT system used. For DBT, 17 studies, with a total of 126,908 individuals with suspected breast cancer, were included. The studies were published between 2015 and 2021. Among the 17 studies, seven (41.18%) were conducted in Asia (four in South Korea, and one each in China, India, and Kuwait), four (23.53%) in Europe (one each in Bosnia and Herzegovina, the Netherlands, Sweden, and one jointly conducted in Germany and the United States), and four (23.53%) solely in North America (all in the United States), and two (11.76%) in Oceania (Australia). Most of the studies (47.06%) were retrospective, while seven (41.18%) were prospective cohort studies and two (11.76%) were prospective clinical trials. Komolafe et al. (2022) reported that all DBT studies were comparative in design (e.g., DBT vs. 2D digital mammography; DBT vs. ultrasound; DBT vs. 2D digital mammography vs MRI). Across the 17 studies, four (23.53%) did not report the DBT equipment used, while the remaining 13 studies reported that DBT was performed using various systems: Selenia Dimensions, Hologic (9 studies, 52.94%), the Mammomat Inspiration, Siemens Healthcare (2 studies, 11.76%), and the Senographe Essential, General Electric Medical Systems (2 studies, 11.76%).

Gong et al. (2023) conducted a systematic review and meta-analysis on the diagnostic accuracy of CBBCT for breast cancer detection, while also comparing it with other traditional imaging modalities (i.e., digital x-ray mammography and MRI) for the diagnosis of breast lesions. Gong et al. (2023) also identified studies comparing the diagnostic accuracy of CBBCT and ultrasound; however, these studies were included only in the narrative review and the table of included studies, but they were not incorporated into the meta-analysis, and no justification was provided. Eighteen studies, with a total of 1,792 individuals with suspicious breast lesions, presented on mammography or ultrasound, were included. The studies were published between 2015 and 2022. Most of the included studies were conducted in China (11 studies, 61.11%), while two (11.11%) studies were conducted in USA and the remaining three (16.67%) in Europe and specifically in Germany. Of the 18 studies, 15 (88.33%) were of comparative design, involving six prospective and 11 retrospective studies (with one study not reporting its design), while 3 (16.67%) were single arm in design. The majority of the studies used the CBCCT 1000 (Koning Corporation, USA), while only one study used a CBBCT device invented by the University of California (San Diego), which does not have a CE-mark.

Across the five primary studies, four were comparative studies (Li et al. 2019, O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012, Vedantham et al. 2013) and one was a single-arm observational study (Xue et al. 2025).

Li et al. (2019) conducted a prospective comparative study comparing the comfort levels of CBBCT and digital mammography in 409 women. The study was conducted in two hospitals in China between October 2012 and January 2014. The mean age of individuals was 48.01 years. Individuals evaluated their comfort using an 11-point numerical scale after completing both examinations. The study used the CBCCT-1000 (Koning Corporation, USA); of the 409 women, 217 underwent the CE-CBBCT and 192 underwent NC CBBCT. Digital mammography was conducted using the 2D Selenia system (Hologic, USA) and Senographe DS system (General Electric Medical Systems, USA).

O'Connell et al. (2010) conducted a prospective comparative study evaluating the radiation dose of CBBCT and digital mammography as well as comparing the comfort levels before and during CBBCT examination relative to mammography in 23 women. The study was conducted between July 2006 and August 2008 at a hospital imaging centre in the USA. The mean age of individuals was 48.9 years. The study utilised a clinical prototype CBBCT system (Koning Corporation, USA), whereas the 2D digital mammography system was not specified. Additionally, three individuals underwent film-screen mammography instead of 2D digital mammography.

O'Connell & Kawakyu-O'Connor (2012) was a continuation of the O'Connell et al. (2010) study, but with more patients included. They conducted a pilot prospective comparative study evaluating

the radiation dose and comfort levels of CBBCT and digital mammography in 36 women. The study was conducted between August 2006 and August 2008 at a hospital imaging centre in the USA. The mean age of individuals was 56.0 years. The study utilised a clinical prototype CBBCT system (Koning Corporation, USA), where the 2D digital mammography system was not specified.

Vedantham et al. (2013) conducted a retrospective comparative study evaluating the radiation dose of CBBCT and 2D digital mammography in 132 women. The study period was not reported; however, it was conducted at two institutions in the USA. The mean age of individuals was not reported. The study utilised a clinical protype CBBCT system (Koning Corporation, USA), while the 2D digital mammography system was not reported.

Xue et al. (2025) conducted a retrospective single-arm observational study analysing 3D breast imaging data of the healthy side breast (809 left and 781 right side) from 1590 women who underwent non-enhanced CBBCT scans in different regions in China between October 2020 and November 2023. The median age of individuals was 49 years (range 19 to 84 years). The study used the CBCCT 1000 (Koning Corporation, USA).

4.2 Cone-beam breast computed tomography compared to 2D digital mammography

4.2.1 Diagnostic accuracy: sensitivity and specificity

For this outcome, Yang et al. (2024) included eight studies with 847 individuals and reported that CBBCT had a sensitivity of 0.92 (95% confidence interval [CI] 0.87 to 0.94) and specificity of 0.79 (95% CI 0.71 to 0.85), whereas mammography had a sensitivity of 0.77 (95%CI 0.69 to 0.83) and specificity of 0.75 (95% CI 0.66 to 0.82) in detecting suspected breast cancer. Yang et al. (2024) also performed Z-tests to analyse the difference in diagnostic accuracy between CBBCT and mammography for the detection of breast cancer. The sensitivity of CBBCT was better than mammography (Z-test, $p < 0.001$). However, no difference between the two imaging modalities was observed in specificity (Z-test, $p = 0.17$). The results are summarised Table 1.

Yang et al. (2024) also applied a Fagan's nomogram to evaluate how CCBCT and mammography modify the probability of breast cancer based on their diagnostic tests results. According to their analysis, a pre-test probability of 47% corresponded to post-test probabilities of 80%, following a positive CBBCT result, and 8%, following a negative CBBCT result. Therefore, among individuals undergoing CBBCT, a positive examination increased the estimated probability of breast cancer by 33%, whereas negative examination reduced the estimated probability of breast cancer by 39%. For mammography, the Fagan's nomogram indicated that the same pre-test probability of 47% corresponded to post-test probabilities of 74% for positive result and 21% for negative result. Accordingly, among individuals undergoing mammography, a positive examination increased the estimated probability of breast cancer by 27%, while a negative result decreased this probability by 26%. The results are summarised in Table 1.

Gong et al. (2023), included eighteen studies (comparative or single arm) with 1,792 individuals and reported that the overall pooled sensitivity and specificity of CBBCT in diagnosing breast cancer were 0.95 (95% CI 0.91 to 0.97) and 0.72 (95% CI 0.62 to 0.80), with high heterogeneity (88.12 and 88.36% respectively). To investigate the causes of heterogeneity, Gong et al. (2023) performed a meta-regression and found that ethnicity ($p < 0.001$ for sensitivity), study type ($p < 0.05$ for specificity) and use of contrast enhancement ($p < 0.05$ specificity) were potential causes of heterogeneity for CBBCT. The results are summarised in Table 1 and Table 2.

4.2.2 Time to diagnosis

None of the included systematic reviews and primary studies reported on this outcome.

4.2.3 Time to treatment

None of the included systematic reviews and primary studies reported on this outcome.

4.2.4 Patient acceptability and comfort

None of the included systematic reviews reported on this outcome.

Of the five primary studies, two reported on degrees of comfort experienced by individuals during CBBCT in relation to 2D digital mammography (Li et al. 2019, O'Connell & Kawakyu-O'Connor 2012), while two reported on the body areas in which individuals experienced discomfort during the CBBCT examination (Li et al. 2019, O'Connell et al. 2010).

Ratings of patient comfort tended to favour CBBCT. In Li et al. (2019) and O'Connell & Kawakyu-O'Connor (2012) studies, CBBCT was rated as more comfortable than mammography by 50% and 75% of patients respectively. CBBCT was rated as equally comfortable to mammography by 34% and 15% of patients respectively. CBBCT was rated as less comfortable than mammography by 16% and 10% of patients respectively. Additionally, Li et al. (2019) reported that CBBCT was rated as more comfortable than mammography in both CBBCT modes (i.e., NC-CBBCT and CE-CBBCT). However, the percentage of the individuals, who reported the score of CBBCT more comfortable than mammography, was 58.85% for NC-CBBCT and 41.48% for CE-CBBCT. Thus, CE-CBBCT was more likely to make patients experience discomfort.

Two studies (Li et al. 2019, O'Connell et al. 2010) provided reports of comfort on patient during CBBCT by asking patients to identify the most painful body area in which they experienced the greatest discomfort. Li et al. (2019) reported, among 177 individuals, the greatest discomfort was experienced the neck (26.65%), followed by shoulder (8.31%), ribs (6.36%), arm (1.47%), and waist (0.49%). Similarly, O'Connell et al. (2010) reported that individuals (n = 23) experienced the greatest discomfort in the neck and shoulder (39.13% each), followed by ribs (26.09%), arm (8.7%), and face, back and hip (4.35% each).

The results are summarised in Table 4.

4.2.5 Radiation dose

Yang et al. (2024) reported radiation doses for CBBCT across three studies, with two studies reporting a range of 5.8 to 24.84 mGy of radiation and one study reporting a mean (SD) dose of 8.0 (1.6) mGy of radiation. For 2D digital mammography, Yang et al. (2024) reported radiation dose from two studies, with one study reporting a dose range of 1.8 to 5.1 mGy and another study reporting a mean (SD) dose of 7 (2.1) mGy. The results are summarised in Table 3.

Of the five primary studies, four reported on radiation dose received during CBBCT. Of these, three studies reported doses for both CBBCT and 2D digital mammography (O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012, Vedantham et al. 2013), while one (single arm) study reported only the radiation dose for CBBCT (Xue et al. 2025). O'Connell et al. (2010) reported that the average glandular radiation dose for CBBCT ranged 4 to 12.8 mGy (mean [SD]: 8.2 [1.4] mGy), while the average glandular radiation dose for 2D digital mammography ranged from 2.2 to 15 mGy (mean [SD]: 6.5 [2.9] mGy). O'Connell & Kawakyu-O'Connor (2012) reported that the mean

(SD) dose for CBBCT was 9.4 (3.1) mGy, while for 2D digital mammography was 16.9 (6.9) mGy. Vedantham et al. (2013) reported that the mean (SD) glandular dose for CBBCT was 13.9 (4.6) mGy (median 12.6 mGy), while for 2D digital mammography was 12.4 (6.3) mGy (median 11.1 mGy). Xue et al. (2025) reported that the average radiation dose of CBBCT ranged from 3.9 to 5.1 mGy (median 4.9 mGy). The results are summarised in Table 3.

4.2.6 Health related Quality-of-Life (QoL)

None of the included systematic reviews and primary studies reported on this outcome.

4.2.7 Resource use

None of the included systematic reviews and primary studies reported on this outcome.

4.3 Cone-beam breast computed tomography compared to digital breast tomosynthesis

4.3.1 Diagnostic accuracy: sensitivity and specificity

Komolafe et al. (2022) reported that the overall pooled sensitivity and specificity of CBBCT in diagnosing breast cancer were 0.84 (95% CI 0.55 to 0.96) and 0.71 (95% 0.48 to 0.87), with high heterogeneity (94% for both). Komolafe et al. (2022) noted that further subgroup analysis to evaluate the potential source of heterogeneity was not performed due to the small number of included studies. For DBT, the pooled sensitivity and specificity was 0.87 (95% CI 0.80 to 0.91) and 0.87 (95% CI 0.80 to 0.92), with high heterogeneity (89% and 95%, respectively). The results are summarised Table 1.

Komolafe et al. (2022) also estimated the positive likelihood and negative likelihood ratios of CBBCT and DBT, using the MetaDiSc 1.4 software. For CBBCT, the pooled positive likelihood ratio was 2.71 (95% CI 1.39 to 5.29), while the pooled negative likelihood ratio was 0.21 (95% CI 0.07 to 0.32), which cause a slight change in the post-test probability. For DBT, the pooled positive likelihood ratio was 6.28 (95% CI 4.40 to 8.96), while the pooled negative likelihood ratio was 0.17 (95% 0.12 to 0.25). The results are summarised Table 1.

4.3.2 Time to diagnosis

Komolafe et al. (2022) did not report on this outcome.

4.3.3 Time to treatment

Komolafe et al. (2022) did not report on this outcome.

4.3.4 Patient acceptability and comfort

Komolafe et al. (2022) did not report on this outcome.

4.3.5 Radiation dose

Komolafe et al. (2022)reported radiation doses for CBBCT across four studies. Of these, three studies ranged from 5.8 to 24.84 mGy of radiation, and one study reporting a mean (SD) dose of 8.0 (1.6) mGy, consistent with Yang et al. (2024). For DBT, Komolafe et al. (2022) reported lower radiation doses for DBT, with mean doses across five studies ranging from 1.30 to 2.41 mGy (median 2.30) of radiation. It is important to note that there are no current studies directly comparing the radiation of dose of CBBCT and DBT. The results are summarised in Table 3.

4.3.6 Health related Quality-of-Life (QoL)

Komolafe et al. (2022) did not report on this outcome.

4.3.7 Resource use

Komolafe et al. (2022) did not report on this outcome.

4.4 Cone-beam breast computed tomography compared to magnetic resonance imaging

4.4.1 Diagnostic accuracy: sensitivity and specificity

Four studies with 203 patients, included in Gong et al. (2023), reported this outcome. CBBCT had a sensitivity of 0.90 (95% CI 0.79 to 0.96) and specificity of 0.79 (95% CI 0.65 to 0.88) in detecting breast cancer, while MRI had of 0.91 (95% CI 0.65 to 0.88) and specificity of 0.89 (95% CI 0.72 to 0.97) respectively. The results are summarised Table 1.

4.4.2 Time to diagnosis

Gong et al. (2023) did not report on this outcome.

4.4.3 Time to treatment

Gong et al. (2023) did not report on this outcome.

4.4.4 Patient acceptability and comfort

Gong et al. (2023) did not report on this outcome.

4.4.5 Radiation dose

Gong et al. (2023) did not report on this outcome, as MRI does not use ionising radiation.

4.4.6 Health related Quality-of-Life (QoL)

Gong et al. (2023) did not report on this outcome.

4.4.7 Resource use

Gong et al. (2023) did not report on this outcome.

4.5 Cone-beam breast computed tomography compared to ultrasound

4.5.1 Diagnostic accuracy: sensitivity and specificity

Gong et al. (2023) also identified three studies comparing CBBCT to ultrasound for the detection of breast cancer. Although these studies were included in the narrative review and listed in the table of included studies, they were not incorporated into the meta-analysis. Of these three studies, two were available only through Chinese databases/libraries, which prevented us from accessing them and extracting information directly from the primary sources.

4.5.2 Time to diagnosis

Gong et al. (2023) did not report on this outcome.

4.5.3 Time to treatment

Gong et al. (2023) did not report on this outcome.

4.5.4 Patient acceptability and comfort

Gong et al. (2023) did not report on this outcome.

4.5.5 Radiation dose

Gong et al. (2023) did not report on this outcome.

4.5.6 Health related Quality-of-Life (QoL)

Gong et al. (2023) did not report on this outcome.

4.5.7 Resource use

Gong et al. (2023) did not report on this outcome.

Table 1 – Diagnostic accuracy for CBBCT compared to 2D digital mammography, digital breast tomosynthesis, magnetic resonance imaging or ultrasound: sensitivity and specificity outcomes

Tests	Evidence source(s)	Number of studies/ patients	Population	Sensitivity (95% CI)			Specificity (95% CI)			Additional comments
				CBBCT	Comparator	Difference	CBBCT	Comparator	Difference	
CBBCT vs 2D digital mammography	Yang et al. (2024)	8 studies 847 patients	Adults with suspected breast cancer	0.92 (0.87 to 0.94)	0.77 (0.69 to 0.83)	0.15 (NR) z-value -4.83 **Favours CBBCT**	0.79 (0.71 to 0.85)	0.75 (0.66 to 0.82)	0.04 (NR) z-value -1.37 **Favours neither**	This review involves head-to-head comparative studies.
				Heterogeneity (bivariate I^2%):			Heterogeneity (bivariate I^2%):			
				10.20%, low (not affecting reliability of data)	77.70%, high (affecting reliability of data)		81.70%, high (affecting reliability of data)	69.73%, substantial (affecting reliability of data)		
CBBCT vs DBT	Komolafe et al. (2022)	CBBCT: 5 studies 407 patients DBT: 17 studies 126,908 patients	Adults with suspected breast cancer	0.84 (0.55 to 0.96)	0.87 (0.80 to 0.91)	0.3 (NR) p = 0.7622 **Favours neither**	0.71 (0.48 to 0.87)	0.87 (0.80 to 0.92)	0.16 (NR) p = 0.0622 **Favours DBT**	Since there are no available studies directly comparing CBBCT vs DBT, this review included (1) prospective and retrospective studies, and (2) interrater consensus for each imaging modality separately.
				Heterogeneity (bivariate I^2%):			Heterogeneity (bivariate I^2%):			
				94%, high (affecting reliability of data)	89%, high (affecting reliability of data)		94%, high (affecting reliability of data)	95%, substantial (affecting reliability of data)		

Tests	Evidence source(s)	Number of studies/ patients	Population	Sensitivity (95% CI)			Specificity (95% CI)			Additional comments
				CBBCT	Comparator	Difference	CBBCT	Comparator	Difference	
CBBCT vs MRI	Gong et al. (2023)	4 studies 203 patients	Adults with suspicious breast lesions (presented on mammography or ultrasound)	0.90 (0.79 to 0.96)	0.91 (0.79 to 0.97)	-0.01 (NR) **Favours MRI**	0.79 (0.65 to 0.88)	0.89 (0.72 to 0.97)	-0.10 (NR) **Favours neither**	This review involves head-to-head comparative studies.
				Heterogeneity (univariate I^2%)			Heterogeneity (univariate I^2%)			
				79.64% (high) (affecting reliability of data)	83.18% (high) (affecting reliability of data)		0.00% (low) (not affecting reliability of data)	66.45% (substantial) (affecting reliability of data)		
CBBCT vs ultrasound	Gong et al. (2023)	3 studies 537 patients	Adults with suspicious breast lesions (presented on mammography or ultrasound)	NR	NR	NR	NR	NR	NR	These studies were included in the narrative review and listed in the table of included studies but were not incorporated into the meta-analysis. No justifications were provided.
				Heterogeneity (bivariate I^2%):			Heterogeneity (bivariate I^2%):			
				NR	NR		NR	NR		

Abbreviations: CBBCT, cone-beam breast computed tomography; CI, confidence interval; DBT, digital breast tomosynthesis; MRI, magnetic resonance imaging; NR, not reported; p, probability; z, z-score; 2D, two-dimensional

Table 2 – Subgroup analysis of diagnostic performance of CBBCT: age, ethnicity, study type, and type of CBBCT

Subgroup	Evidence source(s)	Number of studies	Sensitivity (95% CI)	p-value of sensitivity	Specificity (95% CI)	p-value specificity	Additional comments
Overall pooled analysis							
	Gong et al. (2023)	18 studies	0.95 (0.91 to 0.97)	NA	0.72 (0.62 to 0.80)	NA	15/18 were comparative and 3/18 single-arm in design; total n of patients = 1,792 Heterogeneity (univariate I^2%): Sensitivity: 88.12%, high (affecting data reliability) Specificity: 88.36%, high (affecting data reliability)
Age							
>50 years	Gong et al. (2023)	5 studies	0.96 (0.94 to 0.99)	p = 0.64	0.72 (0.60 to 0.85)	p = 0.30	One of the studies used a non-CE mark CBBCT device.
≤50 years		11 studies	0.89 (0.80 to 0.97)		0.75 (0.58 to 0.92)		
Ethnicity							
Asian	Gong et al. (2023)	11 studies	0.96 (0.94 to 0.99)	p <0.001	0.72 (0.60 to 0.85)	p = 0.53	
Any other ethnicity		5 studies	0.89 (0.80 to 0.97)		0.75 (0.58 to 0.92)		One of the studies used a non-CE mark CBBCT device.
Study design							
Retrospective	Gong et al. (2023)	11 studies	0.96 (0.93 to 0.99)	p = 0.23	0.67 (0.55 to 0.80)	p =0.02	
Prospective		6 studies	0.91 (0.85 to 0.98)		0.81 (0.70 to 0.93)		One of the studies used a non-CE mark CBBCT device.
Type of CBBCT [1]							
NC-CBBCT	Gong et al. (2023)	13 studies	0.89 (0.79 to 0.99)	p = 0.63	0.70 (0.49 to 0.90)	p = 0.64	The total n of CBBCT modes is unclear; findings should be interpreted with caution.
CE-CBBCT		4 studies	0.95 (0.92 to 0.98)		0.72 (0.61 to 0.84)		One of the studies uses a non-CE marked CBBCT device.

Subgroup	Evidence source(s)	Number of studies	Sensitivity (95% CI)	p-value of sensitivity	Specificity (95% CI)	p-value specificity	Additional comments
[1] Reported study numbers for the CE-CBBCT vs NC-CBBCT comparison in do not correspond to study characteristics reported elsewhere in the paper. Abbreviations: CBBCT, cone-beam breast computed tomography; CE, Conformité Européenne; CE-CBBCT, contrast-enhanced cone-beam breast computed tomography; CI, confidence interval; n, number; NC-CBBCT, non-contrast cone-beam breast computed tomography; p, probability							

Table 3 – Radiation dose for CBBCT, digital mammography (2D), digital breast tomosynthesis: systematic reviews and primary studies

Tests	Evidence source(s)	Study design	Number of studies/patients/breasts	Radiation dose (range or mean (SD) or median)	Additional comments
Systematic reviews (n = 2)					
CBCCT vs 2D digital mammography	Yang et al. (2024)	Systematic review and meta-analysis	**CBBCT:** 3 studies, 336 patients **2D digital mammography:** 2 studies, 271 patients	**CBBCT:** range: 5.8 to 24.84 mGy (2 studies) mean (SD): 8.0 (1.6) mGy (1 study) median: NR mGy **2D digital mammography:** range: 1.8 to 5.1 mGy (1 study) mean (SD): 7 (2.1) mGy (1 study) median: NR mGy	
CBBCT vs DBT	Komolafe et al. (2022)	Systematic review and meta-analysis	**CBBCT:** 4 studies, 377 patients **DBT:** 5 studies, 15,835 patients	**CBBCT:** range: 5.8 to 24.84 mGy (3 studies) mean (SD): 8.0 (1.6) mGy (1 study) median: NR mGy **DBT:** range: 1.30 to 2.41 mGy (5 studies, means) mean (SD): NR mGy median: 2.30 mGy (5 studies)	
Primary studies (n = 4)					
CBCCT vs 2D digital mammography	O'Connell et al. (2010)	prospective comparative study	**Total n of patients:** 23 **Total n of breasts:** 40	**CBBCT:** range: 4 to 12.8 mGy mean (SD): 8.2 (1.4) mGy median: NR mGy **2D digital mammography:** range: 2.2 to 15 mGy mean (SD): 6.5 (2.9) mGy median: NR mGy	Imaging reviewed side by side
CBCCT vs	O'Connell & Kawakyu-O'Connor (2012)	prospective comparative study	**Total n of patients:** 35 **Total n of breasts:**	**CBBCT:** range: NR mGy mean (SD): 9.4 (3.1) median: NR mGy	Imaging reviewed side by side.

Tests	Evidence source(s)	Study design	Number of studies/patients/breasts	Radiation dose (range or mean (SD) or median)	Additional comments
2D digital mammography			37	**2D digital mammography:** range: NR mGy mean (SD): 16.9 (6.9) median: NR mGy	This study is a continuation of the O'Connell et al. (2010) study, but with more patients included.
CBCCT vs 2D digital mammography	Vedantham et al. (2013)	retrospective comparative study	**Total n of patients:** 132 **Total n of breasts:** 133	**CBBCT:** range: NR mGy mean (SD): 13.9 (4.6) mGy median: 12.6 mGy **2D digital mammography:** range: NR mGy mean (SD): 12.4 (6.3) mGy median: 11.1 mGy	
CBCCT	Xue et al. (2025)	retrospective single-arm observational study	**Total n of patients:** 1590 **Total n of breasts:** 1590 (images of the healthy side of the breast - 809 left and 781 right side)	**CBBCT:** range: 3.9 to 5.1 mGy mean (SD): NR mGy median: 4.9 mGy	Outcomes stratified by regions in China

Abbreviations: CBBCT, cone-beam breast computed tomography; DBT, digital breast tomosynthesis; mGy, milligray; n, number; SD, standard deviation; 2D: two-dimensional

Table 4 – Patient comfort for CBBCT and 2D digital mammography: primary studies

<table>
<tr><th>Tests</th><th>Evidence source</th><th>Study design</th><th>Total number of patients</th><th>Comfort (Patient comfort questionnaire)</th><th>Additional comments</th></tr>
<tr>
<td>CBCCT

vs

2D digital mammography</td>
<td>Li et al. (2019)</td>
<td>Prospective comparative study</td>
<td>409</td>
<td>Reports of discomfort on patient during CBBCT and choosing the most painful parts of the body (n = 177):
<table>
<tr><th>Areas of discomfort</th><th>n (%) reports</th></tr>
<tr><td>Neck</td><td>109 (26.65%)</td></tr>
<tr><td>Shoulder</td><td>34 (8.31%)</td></tr>
<tr><td>Ribs</td><td>26 (6.36%)</td></tr>
<tr><td>Arm</td><td>6 (1.47%)</td></tr>
<tr><td>Waist</td><td>2 (0.49%)</td></tr>
</table>
Degrees of comfort during CBBCT examination relative to 2D digital mammography (n = 409):
<table>
<tr><th>Rating</th><th>CBBCT/mammography, n</th><th>%</th></tr>
<tr><td>Better</td><td>203/409</td><td>50</td></tr>
<tr><td>Equal</td><td>140/409</td><td>34</td></tr>
<tr><td>Worse</td><td>66/409</td><td>16</td></tr>
</table>
Degrees of comfort during CBBCT examination relative to 2D digital mammography, based on scan mode (i.e., CE-CBBCT or NC-CBBCT):
<table>
<tr><th rowspan="2">Rating</th><th colspan="2">CBBCT/mammography, n (%)</th></tr>
<tr><th>CE-CBBCT</th><th>NC-BBCT</th></tr>
<tr><td>Better</td><td>90/217 (41.48%)</td><td>113/192 (58.85%)</td></tr>
<tr><td>Equal</td><td>86/217 (39.63%)</td><td>54/192 (39.63%)</td></tr>
<tr><td>Worse</td><td>41/217 (18.89%)</td><td>25/192 (13.02%)</td></tr>
</table>
</td>
<td>An 11-point numerical rating (NRS-11) scale was used:

0 ('no pain') to 10 ('the worst pain').

The lower the score was, the more comfortable the examination modality was.</td>
</tr>
</table>

<table>
<tr><th>Tests</th><th>Evidence source</th><th>Study design</th><th>Total number of patients</th><th>Comfort (Patient comfort questionnaire)</th><th>Additional comments</th></tr>
<tr><td>CBBCT

vs

2D digital mammography</td><td>O'Connell et al. (2010)</td><td>Prospective comparative study</td><td>23</td><td>Reports of discomfort on patient during CBBCT and choosing the most painful parts of the body (n = 23):

<table><tr><th>Areas of discomfort</th><th>n (%) reports</th></tr><tr><td>Face</td><td>1 (4.35%)</td></tr><tr><td>Neck</td><td>9 (39.13%)</td></tr><tr><td>Shoulder</td><td>9 (39.13%)</td></tr><tr><td>Ribs</td><td>6 (26.09%)</td></tr><tr><td>Back</td><td>1 (4.35%)</td></tr><tr><td>Hip</td><td>1 (4.35%)</td></tr><tr><td>Arm</td><td>2 (8.7%)</td></tr></table></td><td>An eight-question survey, along with an upper body map from chin to abdomen to mark any pressure points or areas of discomfort during the CBBCT examination, were used.</td></tr>
<tr><td>CBCCT

vs

2D digital mammography</td><td>O'Connell & Kawakyu-O'Connor (2012)</td><td>Prospective comparative study</td><td>40</td><td>Degrees of comfort before and during CBBCT examination relative to 2D digital mammography:

<table><tr><th>Rating</th><th>CBBCT/mammography</th><th>%</th></tr><tr><td>Better</td><td>30/40</td><td>75</td></tr><tr><td>Equal</td><td>6/40</td><td>15</td></tr><tr><td>Worse</td><td>4/40</td><td>10</td></tr></table></td><td>A brief paper questionnaire requesting to choose a single best response for 'Comfort of Exam vs. Mammogram' by marking one of the following options 'better', 'equal', or 'Worse', was used.

Response rate was 100%.

This study is a continuation of the O'Connell et al. (2010) study, but with more patients included.</td></tr>
<tr><td colspan="6">Abbreviations: CBBCT, cone-beam breast computed tomography; CE-CBBCT, contrast-enhanced cone-beam breast computed tomography; n, number; NC-CBBCT, non-contrast cone-beam breast computed tomography; 2D, two-dimensional</td></tr>
</table>

4.6 Ongoing studies

We identified one relevant ongoing study, which is summarised in Table 5 below.

Table 5 – Summary of ongoing primary studies

Study information	Status	Research question and outcome measures
Registration: NCT05036096 **Country:** United States (Koning Corporation) **Target recruitment (estimated)**: 1,024 participants **Follow-up:** 3 months	Active, not recruiting **Last updated:** 05 February 2026 **Study completion (estimated):** 30 December 2026	**Title:** Cone Beam Breast CT for Breast Cancer Screening Comparison of CBBCT and digital mammography across two groups: screening and diagnostic. **Population:** **Screening group:** women who are 40 years or older and any ethnicity and scheduled for a routine screening mammography exam within four weeks. **Diagnostic group:** women who are 30 years or older and any ethnicity and have an abnormality detected by BSE, or CBE, or have an abnormality detected by an imaging modality or will undergo diagnostic mammography, prior to breast biopsy (if needed). **Intervention:** CBBCT of both breasts, only one breast will be scanned in case of mastectomy (for both groups) **Comparison:** digital mammography standard views of both breasts, only one breast in case of mastectomy (for both groups) **Primary Outcome Measure:** (1) radiation dose, and (2) recall rates. **Secondary Outcome Measure:** NR

Abbreviations: BSE, Breast Self-Exam; CBBCT, cone-beam breast computed tomography; CT, computed tomography; CBE, Clinical Breast Exam; NR, not reported

4.7 Certainty of the evidence

- All the included systematic reviews and primary studies included exclusively in women, with no inclusion of men or trans individuals. This lack of diversity limits the generalisability of the findings and highlights the need for future research involving broader and more inclusive patient populations.

- Overall, across the included systematic review, several studies were conducted in China, and were available through Chinese databases, which prevented direct access to those studies and evaluation of their data. Building on this, one of the systematic reviews (Gong et al. 2023) was poorly reported, and although it included three studies comparing CBBCT vs ultrasound, it did not report their diagnostic accuracy, and the inaccessibility of the original articles further limited our reporting on these outcomes. Additionally, Gong et al. (2023) found that ethnicity ($p < 0.001$ for sensitivity), particularly Chinese ethnicity, was a potential cause of heterogeneity for CBBCT. Another example of inconsistent reporting in Gong et al. (2023), was the numbers for the CE-CBBCT vs NC-CBBCT comparison, since they did not correspond to the

study characteristics reported elsewhere in the paper. Thus, interpretation of findings regarding the different CBBCT modes, should be interpreted with caution. This highlights the need for better reporting standards and future research conducted in the United Kingdom, especially in Wales, as well as rigorously designed comparative studies evaluating the diagnostic accuracy between CBBCT and ultrasound.

- All included systematic reviews and primary studies comparing CBBCT with any other breast imaging modalities (i.e., 2D digital mammography, DBT, MRI or ultrasound) were mostly conducted internationally, and mainly in China, while some were conducted in USA and Europe. Thus, the studies were from countries with a diverse range of healthcare systems and population demographics, reducing the direct applicability of the evidence to the Welsh context.

- Some included studies (O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012, Vedantham et al. 2013) were dated and used an early clinical prototype of CBBCT technology, which might not represent the performance standards of currently available CBBCT scans.

- There are currently no available studies directly comparing CBBCT with DBT. Consequently, we included a systematic review and meta-analysis (Komolafe et al. 2022) that synthesised evidence from studies reporting on CBBCT and those reporting on DBT separately, providing independent estimates of sensitivity and specificity for each imaging modality. While this approach allowed for an indirect comparison, the absence of direct comparative data highlights the need for future rigorously designed comparative studies, especially in Wales, to more accurately determine the diagnostic accuracy of CBBCT compared to DBT.

- None of the studies included in the secondary and primary evidence compared CBBCT with other breast imaging modalities considering different age groups, ethnicity, and breast density.

- None of the included systematic reviews and primary studies, reported on the following outcomes: 1) time to diagnosis, 2) time to treatment, 3) resource use, and 4) health-related QoL. These gaps highlight the need for rigorous studies that assess multiple outcomes simultaneously to provide a deeper understanding of the broader impact of CBBCT compared with other breast imaging modalities.

5. Cost effectiveness

5.1 Economic literature review

Appendix 4 summarises the selection of articles for inclusion in the evidence review. The titles and abstracts of 1,178 records identified in the search for this research question were screened but no relevant economic studies were identified.

5.2 HTW cost utility analysis

The potential for developing an economic analysis to estimate the cost effectiveness of CBBCT compared with standard care for the diagnosis of breast cancer was discussed with the HTW Assessment Group. It was concluded that the current evidence base is insufficient to support the development of a robust economic evaluation.

5.3 Estimated unit costs

Based on correspondence with the manufacturer, the base system price for the Koning Vera system is approximately £875,000, with final pricing varying depending on configuration, service level, and local market factors. A fully configured Koning Vera system with integrated biopsy capability is estimated to cost £1,050,000. This includes the Core Vera 3D Breast CT system, biopsy module (image-guided intervention capability) and clinical and technical training. This cost estimation excludes the cost of shipping and logistics, site preparation and installation, taxes, import duties, and any local compliance costs. The cost includes an initial 12-month warranty. The cost of extended warranty/service contracts range between 8-12% of the system cost per annum, depending on coverage level.

The manufacturer also provided an indicative cost per scan estimate of £400 for a bilateral scan. However, it should be noted that this figure is an approximation based on global benchmarking. The true cost would depend on utilisation, staffing and the operational model within the UK market.

The cost per use for other imaging modalities were estimated from an NHS perspective using the most recently available prices. The costs associated with an MRI scan or ultrasound imaging were based on 2024/25 NHS National Cost Collection Data (NHS England 2025b). The cost of a 2D digital mammography was not available within NHS National Cost Collection Data but was estimated as part of Medtech Innovation Briefing (MIB) 242 on 'Artificial intelligence in Mammography' by the National Institute for Health and Care Excellence (NICE 2021). The cost of DBT was sourced from a study which estimated an additional cost of €8.10 (£9.54) for DBT in comparison to 2D digital mammography (Moger et al. 2022).

Table 6 – Estimated unit costs for each diagnostic approach

Diagnostic approach	Cost	Source
CBBCT	£400	Indicative cost per scan for the UK market based on correspondence with the manufacturer.
2D digital mammography	£204†	Estimated total cost, including interpretation of results and an outpatient appointment from NICE MIB242 on 'Artificial intelligence in Mammography'. Inflated to UK 2024 prices (NICE 2021).
DBT	£214‡	Based on cost of 2D digital mammography above plus an estimated additional cost for DBT from (Moger et al. 2022). Converted and inflated to UK 2024 prices.
MRI scan of one area without contrast	£184	Outpatient imaging cost of an 'MRI scan of one area without contrast, 19 years and over' from NHS National Cost Collection Data. (NHS England 2025b)
MRI scan of one area with contrast	£241	Outpatient imaging cost of an 'MRI scan of one area with post-contrast, 19 years and over' from NHS National Cost Collection Data (NHS England 2025b).
MRI scan of two or three areas without contrast	£193	Outpatient imaging cost of an 'MRI scan of two or three areas without contrast' from NHS National Cost Collection Data (NHS England 2025b).
MRI scan of two or three areas with contrast	£252	Outpatient imaging cost of an 'MRI scan of two or three areas with contrast' from NHS National Cost Collection Data (NHS England 2025b).
Ultrasound imaging without contrast	£79	Outpatient imaging cost of an 'ultrasound scan with duration of less than 20 minutes, without contrast' from NHS National Cost Collection Data (NHS England 2025b).
Ultrasound imaging with contrast	£61	Outpatient imaging cost of an 'ultrasound scan with duration of less than 20 minutes, with contrast' from NHS National Cost Collection Data (NHS England 2025b).

Abbreviations: CBBCT, cone-beam breast computed tomography; DBT, digital breast tomosynthesis; MRI, magnetic resonance imaging

† Original cost of £170 has been inflated to UK 2024 prices using the NHS cost inflation index (NHSCII) from the Personal Social Services Research Unit (PSSRU) 2025 (Jones et al. 2025).
‡ The estimated additional cost of €8.10 for DBT from Moger et al. (2022) was converted to UK pound sterling using purchasing power parities (OECD 2024) for the price year of the study. Cost was inflated to 2024 prices (£9.54) using the NHSCII from the PSSRU 2025 (Jones et al. 2025).

6. Organisational considerations

CBBCT is not currently used in Wales, and consequently its implementation would require additional organisational considerations. These could include training staff in CBBCT operation and interpretation, developing and validating clinical protocols, and investing in the necessary CBBCT scanners to equip NHS Wales sites. This would also involve planning equipment maintenance, and quality assurance to ensure its safety. However, other standard breast imaging modalities are routinely provided through the BTW programme across multiple health boards, such as digital mammography to women aged between 50 to 70 years olds every three years (PHW 2019, PHW 2022a).

As highlighted previously, experts in Wales reported that breast imaging diagnostic services are delivered through two distinct pathways: (1) symptomatic assessment, carried out within the NHS health boards, and (2) the screening pathway performed independently by BTW across different sites. Experts highlighted that, although some workforce overlap exists, particularly among consultant radiologists and other trained staff, the equipment and the most personnel involved remain organisationally separate.

Most experts suggested that CBBCT should be introduced as an adjunct to current national standard practice, rather than as a replacement, across different contexts: (1) diagnostic and screening pathways, (2) an alternative to MRI in selected cases (e.g., individuals with implants, intolerance to MRI), and (3) supporting post-, intra- and pre-operative planning. Experts based in Wales considered CBBCT unsuitable to be part of the initial screening pathway due to organisational changes and time constrains, however they suggested that it may be better implemented within assessment clinic settings (i.e., health boards and BTW clinics). One expert suggested introducing CBBCT as an adjunct breast imaging modality initially, with the potential to evolve into an alternative to one or more existing imaging options in selected clinical contexts, as staff expertise with its imaging characteristics increases. Another expert highlighted that if CBBCT is not adopted across screening settings, its use might be limited to private settings, where service users are responsible for the full cost of the examination.

Experts in Wales reported that the implementation of CBBCT in Wales would require purchase of new equipment, substantial staff training, as well as re-organisation of current pathways and processes, at significant cost, including capital investment considerations and maintenance costs relative to existing imaging infrastructure. Additionally, some experts highlighted that radiology departments in the UK generally have a fixed footprint with multiple breast imaging modalities and minimal space for additions, and therefore additional costs for building works and installations (e.g., dedicated space, shielding) might be required. Experts also reported that the CBBCT will require Picture Archiving and Communication System (PACS) integration connecting the images with the Radiology Information System (RIS), Electronic Health Record (HER) and other hospital platforms to streamline workflows, and obtain accurate data, as well as governance and quality assurance oversight, considerations comparable to previous breasting imaging modality introductions. Some experts, however suggested that the CBBCT equipment quality assurance is simpler than digital mammography units. Furthermore, some experts also noted that the use of AI is being adopted for the interpretation of mammograms, a feature that could also be used for the interpretation of CBBCT images.

Regarding training, experts reported that radiologists, radiographers and other allied healthcare professional would require training in CBBCT usage, imaging acquisition and interpretation. Some experts reported that this might be challenging as the staff might be reluctant to change. On the contrary, other experts supported that CBBCT training is minimal as patient positioning is self-positioned and requires no skill set from the radiographer, while radiologists can be trained in approximately the same time as for digital mammography. Furthermore, some experts

emphasised that it is unclear if the CBBCT examination will be performed by mammographers or CT trained staff.

In terms of ethical considerations for CBBCT, one expert reported that no additional ethical concerns beyond standard imaging governance are anticipated, considering that radiation exposure and informed consent processes are appropriately managed.

Some experts raised concerns about CBBCT usage potential implication on healthcare equity and inclusivity. According to experts, elderly individuals and those with limited mobility (e.g., wheelchair users, mobility aid users) may experience difficulties accessing the CBBCT table and positioning themselves on the table. Specifically, it was reported that the design of the CBBCT unit requires the individual to position themselves on their hands and knees and lower themselves onto the CBBCT table (essentially performing a push-up motion), which limits its use for people who are unable to adopt or maintain this posture. Experts in Wales reported that mammography can be adapted to a seated position, enabling accessible examination for people with limited mobility.

7. Patient, carer and family considerations

Patients can be reluctant to undergo mammography due to the prospect of experiencing pain during the examination. Pain is most often associated with the compression of the breast tissue when images are being taken. Patients in the UK are advised to consider several preparations before undergoing a mammogram, including timing the appointment according to their menstrual cycle, taking action to reduce anxiety and stress, breathing exercises, reducing salty foods and caffeine intake and taking pain medication (Coles 2023).

HTW sought to understand the experience of breast cancer diagnosis for patients, including how the pain and discomfort experienced can impact them, and why efforts to reduce this pain and discomfort are important for people who are facing a possible and/or confirmed breast cancer diagnosis.

HTW collaborated with Breast Cancer Now UK to run an online survey of patients, who have undergone breast cancer diagnosis. The survey ran from 24/11/2026 to the 09/01/2026. Thirty-three responses were collected. These are summarised in section 7.1.

Additionally, three papers (Li et al. 2019, O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012), reporting on patient comfort during CBBCT in relation to 2D digital mammography examination, were found during the clinical effectiveness evidence sift. This is summarised in section 7.2.

7.1 Collaboration with Breast Cancer Now

The respondents to the online survey were all breast cancer survivors. Dates of diagnosis ranged, with the oldest diagnosis taking place in 1997 to the most recent in 2025. Twenty-one respondents were diagnosed from 2020-2025, making their experiences with breast diagnosis in the UK recent. HTW did not collect information, such as age, ethnicity, background etc in accordance with GDPR, and as such cannot pass comment on the impacts of these variables on patient's experiences.

7.1.1 Impacts of breast cancer

Facing a breast cancer diagnosis has a profound impact on patient's lives. Respondents were unanimous in pressing both the severity and the totality of the effect the diagnosis has. Describing it as a 'devastating, life changing' experience, respondents' responses reflected themes of fear and shock, exhaustion (physical, emotional and psychological), various forms of loss, a changed life and facing mortality, with most respondents recalling similar reactions. As respondents were recalling their full experiences with breast cancer, some of the impacts they describe are not only about the point of investigation or diagnosis. While this EAR is concerned on breast cancer diagnosis, the further impacts of a breast cancer diagnosis (including treatment and through to recovery) are included in this section. It is important to understand the complete picture of what patients go through, as breast cancer is not experienced as a series of single events (i.e., diagnosis, treatment and recovery), but as a singular whole event.

Fear and shock

"*I've never been so scared in my life.*"

Respondent quote

Respondents report an initial shock and fear response both during investigation and once breast cancer was confirmed, describing it as 'a scary place' to be. For those with family members, who had breast cancer, and for those who had a recurrence years later, the fear was coupled with the knowledge of what may be in store. For those who had no experience to draw on, the fear was that of the unknown. Respondents also described a 'constant fear of recurrence' and fear for the future. Shock seemed to impact both patients who did, or did not, have previous experiences with breast cancer, either themselves or within families.

"It rocked my world, I was scared of the treatment I'd need and its potential side effects"

"This time I was terrified, as I had lived experience of breast cancer and had more idea of what was coming"

"It was a shock initially because I had previously been told I didn't have breast cancer"

"It was shocking, upsetting, unsettling"

"A huge shock. Sudden news of a mastectomy in the following few weeks completely threw me. It occupied every thought of every day"

"Devastated and completely taken by surprise"

"However, on an emotional level I was quite stunned that I actually had cancer. I had always been fit and considered myself to have low risk factors so wasn't expecting such a diagnosis."

Respondent quotes

Exhaustion

"The immediate impact was practical and physical - undergoing tests, appointments and treatments while holding down a full time job"

Respondent quote

Respondents described the process of undergoing breast diagnosis as exhausting physically, emotionally, and psychologically.

> *"I felt like I was going mad. I felt trapped and without any choices. I wanted to run away and die with it."*
>
> *"It negatively impacted my mental health and wellbeing on a daily basis. It continues to impact me two and a half years on"*
>
> Respondent quote

Exhaustion was most often recalled in the process of going from diagnosis to treatment. Appointments for diagnosis and appointments for treatment were recalled as very demanding, both physically and psychologically. It appeared to be the combined effect of having to attend multiple appointments for various uncomfortable tests and treatments that caused the exhaustion patients experienced.

Loss and a changed life

Respondents described experiencing different kinds of loss. Respondents talked about losing their jobs, their relationships, their connection to their own bodies, and a loss of normality and the future. The impacts of these losses were profound, and many were not recovered from even after cancer treatment, particularly those concerning relationships and the respondents' relationship with their own body and self-image. These losses contribute to an overall changed picture of what life is for the respondents. Why mostly negative, some respondents felt that the changes to their lives helped them to shift perspectives and priorities for the better.

> *"I was off work in the end for 18 mths which was very tough financially, as well as managing the treatment."*

> *"took my confidence and self esteem, changed my relationship which ultimately ended in divorce"*

> *"loss of closeness to some friends , lost my job , 18 months of not going abroad and daily life completely differed"*

> *"My life was great at the point of diagnosis and suddenly it felt as though everything was slipping away from me and the life I had been planning /hoping for vanished."*

> *"My life was changed completely. I ended up taking retirement. It has huge impacts on one's family and puts a strain on relationships."*

"However, this [hair loss] affected me emotionally more than any other part of my treatments I was terrified of losing my hair. I've never felt able to have it bleached again since my breast cancer, and this has affected my self image long term as I had blonde hair for years and it was part of who I saw when I looked in the mirror……It has had permanent effects on me emotionally, with anxiety and PTSD in particular, and also physical after effects have been very long term for me. I never fully regained my previous levels of energy…..the brain fog I suffered from severely during chemotherapy still has after effects now. My body is fragile and I feel old before my time"

"Breast cancer now hangs over me every single day……I have no hair and likely never will again. My relationship broke down and I feel that I'll never have a partner again. I managed to work and remain relatively normal for 2 years but now I'm off sick from work, Ultimately this illness will cut my life short and has stopped me from leading a life free of worry and limitations. Breast cancer has wrecked my life and will kill me."

"Changed not just my life but that of mine and my husband's life. I've had to accept that I'm not going to be the same as I was before and how to live with the ongoing side effects"

"I left my job (I worked at a cancer charity and I didn't want my entire life to be consumed by cancer), and as such lost a part of me. I've needed counselling to help deal with the diagnosis, both during and after treatment But cancer helped me to reassess my priorities - work, friendships, personal wellbeing) and although I have changed and am no longer the person I was before I was diagnosed, I like to think it's changed me for the better"

"Huge impact on my marriage, I have since divorced."

It changed everything in my life and still is, I'm not the same as I used to be. I feel 20 years older than I am, I'm having to worry about physical symptoms someone in their 50/60s worries about."

"The whole process was overwhelming and turned the lives of my family upside down. Me, my husband and my two children have been irrevocably changed since my diagnosis"

Respondent quotes

Facing mortality

Respondents advised that their diagnosis forced them to confront their mortality, and the impacts of this were difficult.

"I felt my mortality, and have never since being able to take for granted that my body will carry on working. My mental health was affected severely, and the anxiety I have suffered from for years became a lot worse"

"It rocked my world, I was scared of the treatment I'd need and its potential side effects. I was made so aware of my mortality and that frightened me. I didn't want my children and family to see me suffer."

"The first thing I thought was I was going to die as everyone I knew in my family had died from cancer."

Respondent quotes

7.1.2 Experiences with breast cancer diagnosis

Respondents were asked to recall their experiences attending a mammogram or ultrasound appointment. They recalled waiting for periods from one to three weeks for an appointment, with the exception being those who were diagnosed during routine breast imaging screening. For those who waited, little information was provided for them, while they were preparing for their appointment. A few respondents mentioned they were given a letter describing what to expect at the mammogram. The type and amount of information and help offered varied, with those who sought help independently receiving the most support. Information was provided by leaflets, and most respondents were put in touch with a breast cancer nurse. Respondents spoke positively of breast cancer clinics and breast cancer nurses, with only a few recalling that these resources were too busy to always meet their needs. Many respondents reached out independently to charity and support groups.

When recalling a mammogram, only a few respondents described it as 'fine' and 'no problem'. Most of the respondents who experienced mammogram described it as 'painful', 'uncomfortable', 'embarrassing' and as 'putting people off'. However, there was a sense that the discomfort involved is worth 'putting up with' to reach a diagnosis.

Conversely, respondents described getting an ultrasound as 'not as problem at all'.

"Mammograms are not comfortable and I think that puts people off. But both of my cancers were diagnosed from mammograms, so I always tell people that 5 mins discomfort is far better than 1yr of cancer treatment. Ultrasound no problem at all.."

"I turned down several regular screening mammograms pre diagnosis to avoid the pain."

"OK with ultrasound. The mammogram hurt a lot. I am a small woman with small breasts. I had to be manhandled a lot. It was very painful."

"Mammogram was painful. Recall was depersonalising, having to wear horrid little cape, standing beside a machine while a radiographer explained why the recall"

"Scared, embarrassed, vulnerable and the process was painful."

"Physically uncomfortable and scary but not embarrassing"

"Mammograms didn't bother me. Yes, they were uncomfortable, but I expected that. But when they said something about magnifying plates I began to suspect something was wrong. The ultrasound for the biopsies was okay, as ultrasounds go."

"The mammogram was fine. I was a little embarrassed as you need to strip off the top half of your clothing. It did not hurt me."

Respondent quotes

Respondents were also asked about their experiences with biopsy. Some confirmed that they had a biopsy at the same time as their ultrasound appointment. However, others reported waiting between a week and a month for a biopsy from the time of their mammogram appointment. Results took between two and three weeks following biopsy. Respondents described the period of waiting, both between appointments and for results, as particularly difficult.

"The waiting was a very anxious time as I suspected from the radiologist approach that she knew I had cancer from the imaging."

"it is nerve wracking to wait and makes sleeping hard"

"It was a worrying wait but it wasn't too long."

"The waiting and not knowing was the worst thing."

"Waiting for results from multiple procedures is emotionally and psychologically very difficult"

Respondent quotes

7.1.3 Opinions on CBBCT

As this technology is not currently available in the UK, none of the respondents had any experiences with using it. Instead, they were given a description of how the technology works and the differences between CBBCT and standard mammography or ultrasound and then asked for their thoughts and opinions.

When asked what benefits they thought CBBCT could provide for patients, responses included less pain or discomfort, better accuracy, increased confidence in test results and the hope that, with these improvements, more people would be encouraged and less reluctant to attend breast imaging appointments. Respondents spoke about turning down screening opportunities before, eventually, their diagnosis, due to worries about the pain and discomfort involved.

"Less uncomfortable, more accurate especially with younger women, more confidence in the results"

"Less discomfort and removes worry of the compression of mammogram making things worse"

"Game changing I would think. More people willing to be tested as less uncomfortable. For me would depend on whether it gives quicker and more accurate results and reduced waiting time and hence anxiety."

"As I have dense breasts I imagine it would be more accurate. If it uses x-rays and not ionising radiation then it would be lower risk. No squeezing of the breast tissue. n.b. I turned down several regular screening mammograms pre diagnosis to avoid the pain."

"It's sounds more accurate and could avoid needing to rescan and create unnecessary anxiety. It also sounds more comfortable which would encourage people to attend for their mammogram"

"I have dense breasts.my cancer was missed with a normal mammogram -it was not until i had a 3D mammogram that it was picked up incidentally Whilst checking for something else that turned out to be benign. Cone imaging may have picked this up initially much earlier for me requiring less treatment as I had no lumps or any idea I had cancer"

"It would be less painful - physically and emotionally. I finished treatment in January and had a follow up mammogram in March and it was possibly one of the most painful things I've ever experienced. It also caused me to have flashbacks to my clinic appointment where I was told I probably had cancer - this was incredibly upsetting and felt like a huge set back in moving on after treatment. Also as a younger patient with dense breasts, I'm always worried that my follow up mammograms might have missed something so this more accurate diagnostic tool would help relieve some of that worry."

"It sounds as though it would be less painful. Although my mammograms have gradually become less painful over the years, for the first couple of years they were absolutely agonising."

"If it is not uncomfortable I can see some people going for screening who don't do it now because they're afraid of the discomfort. Of course speed and better detection would benefit everyone. But I think some people feel pain or discomfort, and there are plenty of stories of mammograms about. If they could be assured it didn't hurt they'd be more likely to have the screening done"

"I think it sounds amazing. Lots of women have dense breasts, and if this imaginary can detect better than a mammogram, then its a must. Also, I believe lots of women suffer pain, and possibly don't turn up for the next mammogram, better life saving results hopefully, and less burden on the NHS."

"I welcome this and think it's a fantastic advance. Especially as I have dense breasts and for larger women less painful. Less like being on a butchers block"

"This would be excellent as it doesn't require breast compression. I have really struggled with my annual check up mammograms as my breast is still painful from the treatment I received. It is really painful for my breast to be compressed so anything that avoids that would be excellent"

Respondent quotes

When asked, all respondents advised that they would be happy to undergo breast imaging examination using the CBBCT technology. Lastly, respondents were asked what they want researchers and decision makers to understand about breast cancer diagnosis. All respondents emphasised that going through breast cancer is very difficult, and that anything that potentially could improve any part of it would be very welcome. Respondents placed emphasis on the importance of 'being seen as person', and not just as a 'breast under investigation' and that their personal experience, namely the anxiety, pain, discomfort, fear, and shock, is as important to manage as their cancer. They called for more empathy and more information sharing as well as quicker, more accurate results.

"My own experience with the heath service was exemplary but there is the need to cut waiting times and anxiety for others and to understand that it can change people's lives for good "

"It felt at times like I was on a non stop rollor [sic] coaster of appointments, tests, surgery, radiation, medications. Whilst knowing they were all to help me it felt rushed and the only concern was my breast, not me as a person"

"The waiting and delays are stressful. A technique that is quicker and more accurate would help reduce this"

"I don't feel we are seen as people and there is often a lack of empathy and understanding. We are just another number"

"Mammograms are not accurate enough for dense breasts and we are not informed we have dense breasts when screened so I had no idea of my increased risks."

"The importance of the patient feeling in control of the process as much as possible (and as much as the patient would like). To be given full and accurate information to make an informed decision about treatments, including possible long term effects"

"I'm wondering if this new imaging would be useful for people in wheelchairs. It must be very difficult for someone who can't stand to get a normal mammogram"

"The impact of the devastation on the person/family/employment/finances. The better the technology, the better the outcome of this devastating disease."

Respondent quotes

7.2 Patient experiences literature

7.2.1 Patient experiences with CBBCT

Li et al. (2019) conducted a comparison of comfort between CBBCT and digital mammography in breast cancer patients in China. They found that CBBCT was superior to digital mammography for comfort of breast tissue and pain during the examination. However, some patients experienced discomfort or pain in other areas during CBBCT, such as the neck, shoulder, ribs, arm and waist. A small number of patients found CBBCT to be more painful than digital mammography. They found that CE-CBBCT was more likely to make patients feel uncomfortable than scans that did not include contrast. The authors found that the age of the patient was also a contributor, with older patients experiencing more discomfort than younger patients and younger patients reporting lager differences in comfort level between CBBCT and digital mammography favouring CBBCT. They also found that patients who were underweight were more likely to feel uncomfortable undergoing CBBCT than those who were not, and that CBBCT was more comfortable than digital mammography for all weight classes. Lastly, breast tissue type was also found to be a contributing factor, with patients who had fatty or dense tissue experiencing higher levels of comfort during CBBCT than compared to digital mammogram.

Most experts supported that patients might be more willing to attend breast imaging if CBBCT was available, largely due to perceived improvement in comfort during examination. However, experts in Wales highlighted that there is an uncertainty as to whether patient perception of less CBBCT compression and increased comfort would encourage breast imaging attendance. It was noted that individuals who attend screening or symptomatic assessment do so on the basis that they are watching out for their health, irrespective of comfort or discomfort.

7.2.2 Mammography pain and its impacts

Three studies (Mathers et al. 2013, Nelson et al. 2020, Whelehan et al. 2013) were found considering the impacts of mammography pain on patient participation in screening programs and in ongoing appointments for diagnosis and treatment. While screening is outside of this EARs scope, pain and its influence over attendance at mammography appointments is the same experience for patients whether the appointment be part of a screening program or for diagnosis after symptom presentation, and as such they are included in this section.

Nelson et al. (2020) considered pain experienced during successive mammography examinations in the UK. They found that multiple factors can influence the pain that is

experienced during mammography, including equipment design, practitioner technique and factors unique to the individual patient, but that compression of breast tissue was not a large influencing factor. They saw that pain can result in a failure to attend subsequent mammography examinations. They also saw that that patient's with a family history of breast cancer may be more susceptible to mammography-related pain, and pose that improving mammographic experiences for patients will increase uptake translating into earlier diagnosis and increased survival.

Mathers et al. (2013) considered the breast imagining experiences of women with a diagnosis of breast cancer in the UK. They found that many women feel pain during all the imaging procedures they describe, but the degree of pain is very personal. Participants described mammography as being an uncomfortable to extremely painful process that had the potential to deter them from future attendance but placed emphasis on the attitudes of staff as something that makes a difference. They spoke of being expected to stay in the same uncomfortable position for a long time as the procedure was repeated to get the required samples for diagnosis and a lack of information prior to appointments. The patients advised that they were consistently anxious when attending their follow up mammograms after their diagnosis and treatment and this did not diminish over time. However, this anxiety did not keep them from attending appointments. Post-treatment, they spoke of breast tissue tenderness, scaring and worried that this would affect their ability to stand still during the scans. Despite the pain and their negative experiences, patients were still keen to encourage others to attend appointments.

> *"I'd been through the process with the benign breast lump. my first experience of mammograms really put me off. I think because of that I was putting off going to get another mammogram. (The machinery). really seemed to squeeze me, more than I thought, I thought my breast was going to explode, but subsequently it hasn't been so bad. I got the feeling with the first one, she was a bit forceful. Whereas the last time I had a really nice person, I don't know if she put me at my ease and I felt I could trust her because you do sort of have to expose yourself. Although you would think having the first experience I would tense up even more for the second one but that didn't seem to happen. I just felt that it was the person."*
>
> Patient quote from Mathers et al. (2013)

Whelehan et al. (2013) conducted a systematic review into the role of mammography pain on participation in breast cancer screening. The authors note that barriers to testing are complex, but that decisions to re-attend are primarily based on past experiences. From their analysis, 25% to 46% of UK patients chose not to re-attend an appointment due to mammography pain, which in 2011 equated to 47,000 to 77,000 women in the UK. They also found that a higher proportion of women who do report pain at mammography will choose not to re-attend for future breast screening than of those who do not report any pain, but do not re-attend. They conclude that the extent to which painful mammography influences screening behaviour is dependent on the individual, as pain is subjective, but that a key principle of testing is that the test should be acceptable to the population and they acknowledge that there are an important percentage of the breast cancer population to whom mammography may not be acceptable. They pose improving the experiences of people as a possible route to increase attendance.

7.3 Equality, diversity and equity considerations

Li et al. (2019) found that age, weight and breast type all contribute to a patient's level of comfort when undergoing diagnosis via CBBCT and digital mammogram. One respondent in the online survey questioned if the technology would be easier for wheelchair users or others who may have difficulty standing for the duration of a traditional mammogram.

Whelehan et al. (2013) saw that population characteristics, such as psychosocial and socio-demographic factors, can also affect reattendance for mammography. They also saw that certain subpopulations, such as people who have physical disabilities, experience more pain than others during mammography.

Some experts also raised concerns about equitable access during CBBCT examination, considering that elderly individuals and those with limited mobility may experience difficulties getting onto and positioning themselves on the CBBCT table. Additionally, experts in Wales supported that the current breast imaging modalities available constitute equitable and inclusive options.

8. Conclusions

This evidence review summarised evidence on the clinical and cost effectiveness of CBBCT compared to standard practice for the diagnosis of breast cancer.

The literature search identified three systematic reviews (Gong et al. 2023, Komolafe et al. 2022, Yang et al. 2024), five primary studies (Li et al. 2019, O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012, Vedantham et al. 2013, Xue et al. 2025), and one ongoing study. Yang et al. (2024) compared the diagnostic accuracy of CBBCT and 2D digital mammography for individuals with suspected breast cancer. Gong et al. (2023) reported on the diagnostic accuracy of CBBCT for breast cancer detection, while also comparing it with other traditional imaging modalities (i.e., digital mammography and MRI) for the diagnosis of breast lesions. Gong et al. (2023) also identified studies comparing the diagnostic accuracy of CBBCT and ultrasound; however, these studies were included only in the review and were not incorporated into the meta-analysis and no justification was provided. Komolafe et al. (2022) compared the diagnostic accuracy of CBBCT and DBT for breast cancer detection. Since there are no available literature directly comparing CBBCT and DBT for diagnostic or screening examination, Komolafe et al. (2022) separately included comparative, prospective and retrospective studies, and interrater consensus for each breast imaging modality. Across the three reviews, the Koning Vera CBBCT system was used; in addition, one study included in Gong et al. (2023) used a CBCCT system developed by the University of California (San Diego), which is not CE-marked.

Across the five primary studies, four were two-arm observational (Li et al. 2019, O'Connell et al. 2010, O'Connell & Kawakyu-O'Connor 2012, Vedantham et al. 2013) and one reported single-arm observational studies (Xue et al. 2025). All four comparative studies compared CBBCT with 2D digital mammography, reporting on the radiation dose of both CBBCT and digital mammography; two of these studies also reported on patient comfort (Li et al. 2019, O'Connell & Kawakyu-O'Connor 2012). Xue et al. (2025) reported only on the radiation dose of CBBCT.

Regarding diagnostic accuracy, Yang et al. (2024) reported that CBBCT exhibited higher sensitivity than 2D digital mammography. Similarly, Gong et al. (2023) also reported that CBBCT demonstrated higher sensitivity compared to 2D digital mammography; however, CBBCT had lower sensitivity than MRI. Additionally, Komolafe et al. (2022) demonstrated that DBT had better specificity than CBBCT. However, there is a need for comparative studies to more accurately determine the diagnostic accuracy of CBBCT compared to DBT.

Ratings of patient comfort tended to favour CBBCT, including both CE-CBBCT and NC-CBBCT, compared to mammography. However, the percentage of the individuals, who reported the score of CBBCT more comfortable than mammography, was 58.85% for NC-CBBCT and 41.48% for CE-CBBCT. Individuals reported that the greatest discomfort during CBBCT examination was experienced in the neck and shoulder, followed by rib, arm, face, back and hip. Moreover, no evidence was identified reporting on patient comfort or experience during CBBCT compared with DBT or MRI or ultrasound examinations.

Radiation doses for both CBBCT and digital mammography varied across studies, but they were generally comparable, suggesting that both breast imaging modalities result into similar levels of patient exposure. In contrast, DBT demonstrated lower radiation doses than CBBCT, while ultrasound imaging and MRI scans do not involve ionising radiation, highlighting their advantage in eliminating the risk of patient radiation exposure.

The evidence presented was based on studies that were mostly conducted in China, while some were conducted in USA and only two in Europe (both in Germany). Thus, the studies were from countries with a diverse range of healthcare systems and population demographics, reducing the direct applicability of the evidence to the Welsh context. This shows that there is a need for studies conducted in the United Kingdom, especially in Wales, assessing the diagnostic

accuracy of CBBCT compared with current breast imaging modalities, providing locally relevant evidence and generate findings that are transferable to NHS Wales practice. Moreover, the evidence involved women only, with no inclusion of men or trans individuals, limiting the generalisability of the findings and emphasizing the need for future research involving a broader and more inclusive spectrum of individuals. Additionally, inconsistency in reporting of certain findings were identified. For instance, the numbers for the CE-CBBCT vs NC-CBBCT comparison did not correspond to the study characteristics reported elsewhere in Gong et al. (2023) study. Therefore, interpretation of findings regarding the different CBBCT modes, should be interpreted with caution. Currently, there are no available studies directly comparing CBBCT with DBT, highlighting the need for future rigorously designed comparative studies to more accurately determine the diagnostic accuracy of CBBCT compared to DBT. In addition to this, none of the included systematic reviews and primary studies, reported on the time to diagnosis, time to treatment, resource use, and health-related QoL outcomes. Therefore, there is a need for rigorous studies that assess multiple outcomes simultaneously to gain a better understanding of the broader impact of CBBCT compared with other breast imaging modalities.

No relevant economic analyses were identified which considered the cost effectiveness of CBBCT compared with standard care for the diagnosis of breast cancer. An economic model was not developed as it was concluded that the current evidence base is insufficient to support the development of a robust economic evaluation.

9. Contributors

This topic was proposed by Dr Amandeep Goma, Co-founder and Chief Executive Officer, Euronoxx Medical Group.

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The HTW Assessment Group advised on methodology throughout the scoping and development of the report.

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Subject experts contributed to this appraisal by commenting on a draft of this report, and in some cases providing other advice to HTW's staff and decision-making groups. All contributions from reviewers were considered by HTW's Assessment Group and actioned accordingly. However, subject experts had no role in authorship or editorial control, and the views expressed are those of Health Technology Wales.

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Appendix 1 – Evidence review methods

We searched for evidence that could be used to answer the review question: What is the clinical and cost effectiveness of cone-beam breast computed tomography compared to standard practice for diagnosis of breast cancer?

The criteria used to select evidence for the appraisal are outlined in Appendix 2. These criteria were developed following comments from the Health Technology Wales (HTW) Assessment Group and UK experts.

The systematic search followed HTW's standard rapid review methodology. A search was undertaken of Medline, Embase, CINAHL, KSR Evidence, Cochrane Library, and the International Network of Agencies for Health Technology Assessment (INAHTA) HTA database. Additionally, searches were conducted of key websites and clinical trials registries. The searches were carried out 18-24 September 2025, with an update search of Medline, Embase, CINAHL, KSR Evidence, Cochrane Library, and the INAHTA HTA database conducted on 6 March 2026. At the same time as the update search, forward citation searching of the included studies used within this review was conducted in Scopus.

Appendix 3 gives details of the search strategy used for Medline. Search strategies for other databases are available on request.

Appendix 4 summarises the selection of articles for inclusion in the review.

Appendix 2 – Inclusion and exclusion criteria for evidence included in the review

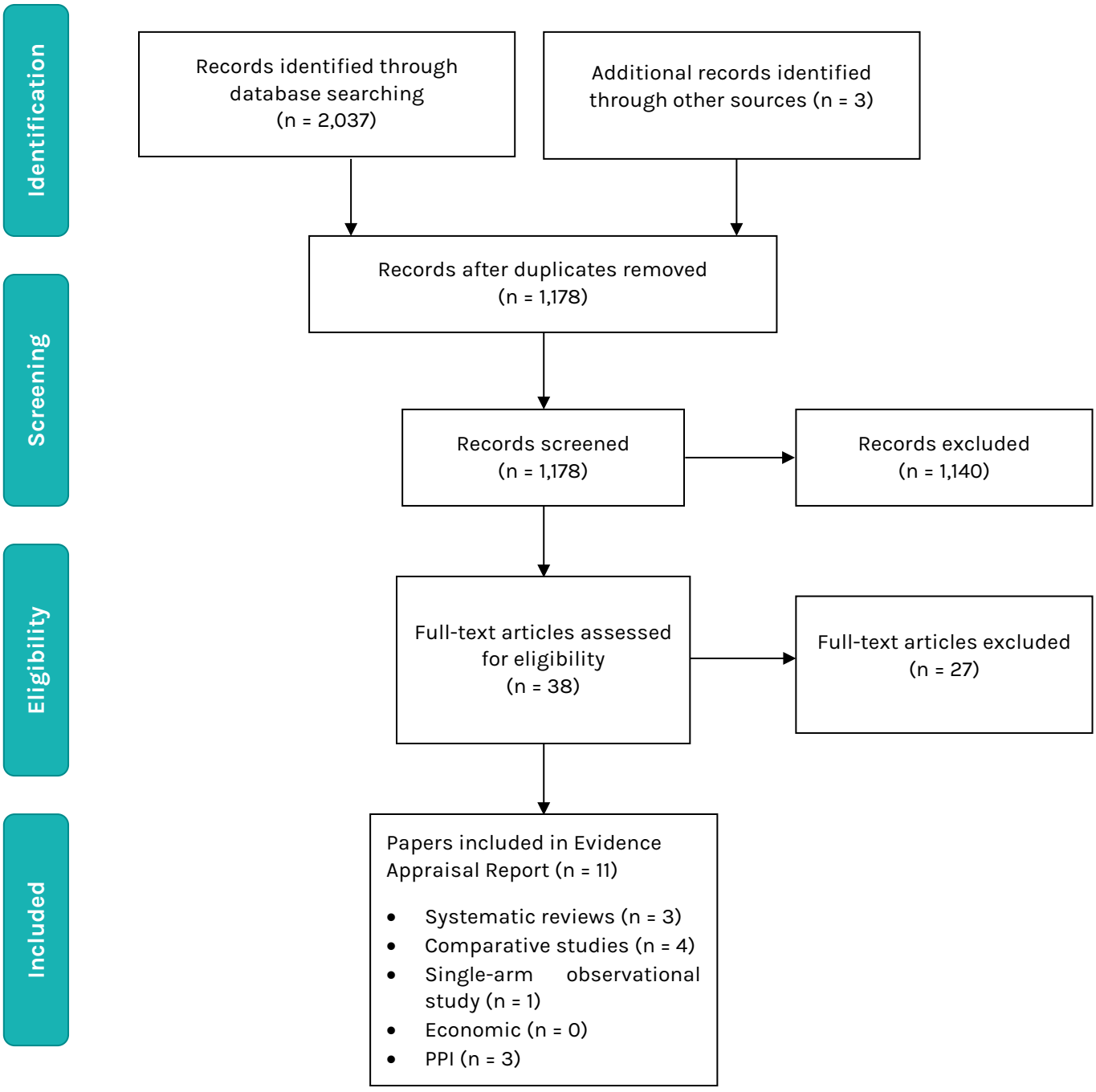
	Inclusion criteria	Exclusion criteria
Population	Individuals with suspected breast cancer, including screening recall, second opinion, patient with symptoms	Individuals undergoing breast cancer screening Individuals with known breast cancer
Intervention	Cone-beam breast computed tomography	
Comparison/ Comparators	Standard practice of breast imaging modalities: • X-ray mammography • Digital breast tomosynthesis (DBT) • Magnetic Resonance Imaging (MRI) • Ultrasound imaging	
Outcome measures	• Diagnostic accuracy including sensitivity, specificity, positive predictive value, negative predictive value (reference standard: combination of imaging, biopsy and clinical examination) • Time to diagnosis • Time to treatment • Patient acceptability and comfort • Radiation dose • Health-related Quality-of-Life (QoL) • Resource use • Economic outcomes	
Study design	We will prioritise the following study types, in the order listed: • Systematic reviews of randomised controlled trials or diagnostic test accuracy studies • Randomised controlled trials. • Diagnostic test accuracy studies • Non-randomised comparative trials. We will only include evidence from "lower priority" sources where this is not reported by a "higher priority" source. This could be because higher priority evidence: • Does not cover all relevant populations • Does not compare the technology of interest to all relevant comparators • Does not cover all outcomes of interest • Reports over short-term follow up periods, and longer follow up data is required to facilitate decision making. Where relevant and well-conducted systematic reviews exist, we will use these by: • Reporting or adapting their reported outcome measures where these are fully relevant to the scope of our review, and appropriate synthesis methods have been used	

	Inclusion criteria	Exclusion criteria
	• Using these reviews as a source of potentially relevant studies where the review cannot be used as a source of outcome data. We will prioritise systematic reviews in terms of the sources of evidence they include, using the order described above.	
Search limits	No date limits apply	
Language limits	English language only	
Publications status	We will include evidence from studies that are published in full. We will only include evidence from conference abstracts if there are critical gaps in the fully published evidence. We will include details of any ongoing trials that have a planned completion or reporting date within 24 months of the date searches are carried out. We will only include trials of a design that is likely to add to the existing evidence in terms of certainty; for example, if we report evidence from randomised controlled trials in the EAR, we will only report details of ongoing trials if they also use a randomised design.	
Subgroup analysis	Where the evidence allows, we will report outcomes separately according to list any factors identified as potentially influential on outcomes, such as: • Demographics (e.g., age) • Breast tissue density.	

Appendix 3 – Medline strategy

Ovid MEDLINE(R) ALL <1946 to March 05, 2026>		
cone-beam CT (intervention)		
1	exp Cone-Beam Computed Tomography/	18181
2	((cone beam or cone-beam or conebeam) adj3 (CT or "comput* tomog*" or "comput* mamm*" or cat or imag*)).tw,kf.	25080
3	((cone beam or cone-beam or conebeam) adj4 tomog*).tw,kf.	21050
4	((cone beam or cone-beam or conebeam) adj3 (tomosynthes* or tomo-synthes*)).tw,kf.	32
5	(CBCT or CB-CT).tw,kf.	19632
6	(cone beam or cone-beam or conebeam).kf.	8301
7	or/1-6	30546
breast (population)		
8	exp Breast/	56718
9	(breast* or mammar*).tw,kf.	695639
10	exp Breast Neoplasms/	379516
11	or/8-10	740226
cone-beam breast CT		
12	7 and 11	596
13	(CBBCT or CB-BCT or CBB-CT or CB-B-CT).tw,kf.	64
14	(CBCTB or CB-CTB or CB-CT-B).tw,kf.	1
15	(CBCTBI or CB-CTBI or CBCT-BI or CB-CT-BI).tw,kf.	1
16	(CECBBCT or CE-CBBCT or CE-CB-BCT or CE-CBB-CT or CE-CB-B-CT).tw,kf.	21
17	(dedicated breast adj1 (CT or comput* tomog* or imag*)).tw,kf.	217
18	or/13-17	283
19	12 or 18	782
breast imaging		
20	Breast/dg [Diagnostic Imaging]	5799
21	exp Breast Neoplasms/dg [Diagnostic Imaging]	33385
22	((breast* and mammar*) adj3 imag*).tw,kf.	864
23	exp Mammography/	35717
24	mammog*.tw,kf.	41538
25	digital breast tomosynthesis.tw,kf.	1724
26	((breast* or mammar*) adj3 (tomosynthes* or tomo-synthes*)).tw,kf.	1939
27	or/20-26	68307
28	7 and 27	297
set combination		
29	19 or 28	800
manufacturer		
30	(Koning and breast CT).tw,kf.	5
31	"CBCT 1000".tw,kf.	1
32	izoview.tw,kf.	0
33	or/30-32	6
set combination & limits		
34	29 or 33	802
35	limit 34 to english language	786
36	exp animals/ not humans/	5427987
37	Disease Models, Animal/	448729
38	(baboon*1 or bovine*1 or canine*1 or chimpanzee*1 or cow*1 or dog*1 or feline*1 or goat*1 or hens or macque*1 or mice or monkey*1 or (mouse adj2 model*1) or murine*1 or ovine or pig*1 or porcine or (non-human adj2 primate*1) or sheep or rabbit*1 or rat or rats or rattus or rhesus or rodent*1 or zebrafish).ti.	2234389
39	or/36-38	5983693
final set		
40	35 not 39	778

Appendix 4 – Flow diagram outlining selection of relevant evidence sources



Appendix 5 – Full sources of evidence and outcome data

Table A1 – Included systematic reviews: design and characteristics

Review	Design, search period	Eligibility criteria	Study/patient characteristics	Outcome measures	Comments
Yang et al. (2024)	Systematic review and meta-analysis **Search date:** inception to March 2023 **PROSPERO registration:** CRD42023439157	**Inclusion criteria:** (1) patients with suspected breast cancer and admitted to hospital due to discovery of breast cancer (2) diagnostic performance of CBBCT and DMG for primary cancer breast (i.e., initial diagnosis of invasive breast cancer excluding cases of recurrence or metastasis) (3) minimum 20 patients or lesions (4) CBBCT and DMG performed before treatment (5) reference standard: histological pathology or follow-up imaging (6) study design: prospective or retrospective. **Exclusion criteria:** (1) Publication status: review, case reports, meeting abstracts, and articles beyond review scope (2) Lack of data on true positive, false positives, true negatives, or false negatives.	**Number of studies:** 8 **Total number of patients:** 847 **Age (median, IQR):** NR (33.24 to 86.6) years **Population:** adults with suspected breast cancer **Study design:** • Prospective (n = 6) • Retrospective (n = 2) **Study type:** • Comparative (n = 8) **Intervention:** • CBCCT-1000 (Koning Corporation, USA) (n = 8) **Comparator (DMG):** • Mo-target (Hologic, USA) (n = 1) • Sophie (Planmed, USA) (n = 1) • Lorad Selenia (Hologic, USA) (n = 1) • Senographe 2000D (General Electric Medical Systems, USA) (n = 1) • Senographe 2000D (General Electric Medical Systems, USA) or Selenia (Hologic, USA) (n = 1)	Diagnostic accuracy of CBBCT and DMG for the diagnosis of primary breast cancer, including sensitivity and specificity, as well as the Fagan nomogram (positive predictive and negative predictive value).	5 studies were based on lesion analysis and 1 on patient analysis 5 studies reported breast density, and 4 presented data on the proportion of breast lesions with microcalcification

Review	Design, search period	Eligibility criteria	Study/patient characteristics	Outcome measures	Comments
			• Senographe DS (General Electric Medical Systems, USA) (n = 1) • Mammomat Inspiration (Siemens Healthcare, USA) or Senographe Essential (General Electric Medical Systems, USA) (n = 1) • NR (n = 1) **Reference standard:** • Histopathology (n = 5) • Histopathology and/or follow-up imaging (n = 3) **Location:** • China (n = 5) • Germany (n = 2) • USA (n = 1)		
Komolafe et al. (2022)	Systematic review and meta-analysis **Search date:** From January 2015 up to and including December 2021 **PROSPERO registration:** CRD42020180192	**Inclusion criteria:** (1) studies utilised dedicated CBBCT and DBT to detect breast cancer, with at least the sensitivity and specificity reported. breast (i.e., initial diagnosis of invasive breast cancer excluding cases of recurrence or metastasis) (2) study design: prospective RCTs, or prospective or retrospective comparative or observer performance studies **Exclusion criteria:** (1) publication status: reviews (2) phantom or simulation studies (3) other radiation studies of CBBCT and DBT (e.g., radiotherapy)	**Total number of studies:** 22 studies (DBT = 17, CBBCT = 5) **Total number of patients:** 127,315 **CBBCT (n = 5)** **Total number of patients:** 407 **Age (weighted mean):** 50.2 years **Population:** individuals with suspected breast cancer **Study design:** • Prospective (n = 2) • Retrospective (n = 3) **Study type:**	Diagnostic accuracy of CBBCT and DBT of suspected breast cancer, including sensitivity and specificity, as well as positive predictive and negative predictive value.	Although the studies for each modality included comparative study types, none of them directly compared CBBCT to DBT.

Review	Design, search period	Eligibility criteria	Study/patient characteristics	Outcome measures	Comments
		(4) studies involving computer-aided detection (i.e., machine and deep learning applications in breast cancer diagnostic accuracy) (5) studies reporting two or more hybrid modalities (i.e., DBT with DMG or CE-CBBCT with NC-CBBCT)	• Comparative (n = 4) • Single-arm (n = 1) **Intervention:** • CBCCT-1000 (Koning Corporation, USA) (n = 4) • NR (n = 1) **Reference standard:** • Histopathology (n = NR) • Histopathology and follow-up imaging (n = NR) • Follow-up imaging (n = NR) **Location:** • China (n = 1) • Germany (n = 2) • USA (n = 1) • NR (n = 1) **DBT (n = 17)** **Total n of patients:** 126,908 **Age (weighted mean):** 54.5 years **Population:** individuals with suspected breast cancer **Study design:** • Prospective (n = 9; 7 cohort studies and 2 clinical trials) • Retrospective (n = 8) **Study type:** • Comparative (n = 17)		

Review	Design, search period	Eligibility criteria	Study/patient characteristics	Outcome measures	Comments
			Intervention: • Selenia Dimensions (Hologic, USA) (n = 9) • Mammomat Inspiration (Siemens Healthcare, USA) (n = 2) • Senographe Essential (General Electric Medical Systems, USA) (n = 2) • NR (n = 4) **Reference standard:** • Histopathology (n = NR) • Histopathology and follow-up imaging (n = NR) • Follow-up imaging (n = NR) **Location:** • Australia (n = 2) • Bosnia and Herzegovina (n = 1) • China (n = 1) • Germany/ USA (n = 1) • India (n = 1) • Kuwait (n = 1) • South Korea (n = 4) • Sweden (n = 1) • the Netherlands (n = 1) • USA (n = 4)		
Gong et al. (2023)	Systematic review and meta-analysis **Search date:** inception to August 2023 **PROSPERO registration**: CRD42022358161	**Inclusion criteria:** (1) diagnostic clinical trials using CBBCT to assess the malignancy of breast tumours (2) sufficient data to calculate sensitivity and specificity. **Exclusion criteria:** (1) duplicated articles (2) abstracts, irrelevant titles and abstracts (3) unavailable data	**Number of studies:** 18 **Total number of patients:** 1,792 **Age (median, IQR):** NR (44.6 to 67.8) years **Population:**	Diagnostic accuracy of CBBCT, DMG, MRI and/or US of suspicious breast lesions, including sensitivity and specificity.	Out of the 18 included studies, one does not hold CE mark (i.e., USCBT). 3 CBBCT studies were single arm in design.

Review	Design, search period	Eligibility criteria	Study/patient characteristics	Outcome measures	Comments
		(4) phantom or simulation studies (5) other radiation studies of CBBCT (e.g., radiotherapy) (6) studies involving computer-aided detection (i.e., machine and deep learning applications in breast cancer diagnostic accuracy)	adults presenting suspicious breast lesions on mammography or ultrasound **Study design:** • Prospective (n = 6) • Retrospective (n = 11) • NR (n = 1) **Study type:** • Comparative (n = 15) • Single-arm (n = 3) **Intervention:** • CBCCT-1000 (Koning Corporation, USA) (n = 17) • USCBT (n = 1) **Reference standard:** • Histopathology (n = NR) • Histopathology and follow-up imaging (n = NR) • Follow-up imaging (n = NR) **Comparator (MRI; n = 4):** • Signa HDX (GE Healthcare, USA) or Magnetom Sonata (Siemens, USA) (n = 1) • NR (n = 3) **Comparator (US; n = 3):** • iU22 xMATRIX (Phillips, Netherlands) (n = 1) • NR (n = 2) **Location:** • China (n = 11) • Germany (n = 3) • USA (n = 2) • NR (n = 2)		Reported n of studies for the CE-CBBCT and NC-CBBCT subgroups do not match the study characteristics presented elsewhere in the paper. *Experts highlighted that breast MRI is inherently contrast-enhanced; thus, evaluations should focus on CE-CBBCT only. Pooling CE-CBBCT and NC-CBBCT may obscure diagnostic performance differences.*

Review	Design, search period	Eligibility criteria	Study/patient characteristics	Outcome measures	Comments
Abbreviations: CBBCT, cone-beam breast computed tomography; CE, Conformité Européenne; CE-CBBCT, contrast-enhanced cone-beam breast computed tomography; DBT, digital breast tomosynthesis; DMG, digital mammography; IQR, interquartile range; MRI, magnetic resonance imaging; n, number; NC-CBBCT, non-contrast cone-beam breast computed tomography; NR, not reported; RCTs, randomised controlled trials; US, ultrasound.					

Table A2 – Comparative and observational studies: design and characteristics

Study reference	Methods, setting	Patient characteristics	Intervention and Comparison	Outcome(s)	Comments
Li et al. (2019)	**Design:** Prospective comparative study **Setting:** 2 hospitals **Country:** China **Study period:** October 2012 to January 2014	**Total n of patients:** 409 **Total n of breasts:** NR **Age (mean, SD):** 48.01 (8.085) years (range 35 to 89 years) **Sex:** 100% women	**Intervention:** NC-CBBCT (n = 192) or CE-CBBCT (n = 217) (CBCCT 1000, Koning Corporation, USA) **Comparison:** 2D digital mammography (Selenia, Hologic, USA and Senographe DS, General Electric Medical Systems, USA)	• Patient-reported comfort rating after completing both examinations. • Patient-reported discomfort in body areas during CBBCT examination.	
O'Connell et al. (2010)	**Design:** Prospective comparative study **Setting:** 1 hospital breast imaging centre **Country:** USA **Study period:** July 2006 to August 2008	**Total n of patients:** 23 Toal n of breasts: 40 **Age (mean, SD):** 48.9 (5.7) years (range 40 to 61 yeas) **Sex:** 100% women	**Intervention:** clinical prototype system (Koning Corporation, USA) **Comparison:** 2D digital mammography (NR)	• Radiation dose • Patient discomfort on the body areas during CBBCT examination.	This is a clinical protype system of CBBCT and findings should be interpreted with caution. Individuals were recruited if they had normal or benign mammographic findings within 6-months. Justification was based on the BI-RADS guidelines (ACR 2003 cited in O'Connell et al. 2010) suggesting that benign findings are not expected to change over a 6-month interval. Three individuals underwent film screen mammography rather than 2D digital mammography.
O'Connell & Kawakyu-O'Connor (2012)	**Design:** Prospective comparative study	**Total n of patients:** 36 **Total n of breasts:**	**Intervention:** clinical prototype system (Koning Corporation, USA)	• Radiation dose • Patient-reported comfort rating after completing	This is a clinical protype system of CBBCT and findings should be interpreted with caution.

Study reference	Methods, setting	Patient characteristics	Intervention and Comparison	Outcome(s)	Comments
	Setting: 1 hospital breast imaging centre **Country:** USA **Study period:** July 2006 to August 2008	37 **Age (mean, SD):** 56.0 (9.8) years (range 41 to 77 years) **Sex:** 100% women	**Comparison:** 2D digital mammography (NR)	the CBBCT examination.	
Vedantham et al. (2013)	**Design:** Retrospective comparative study **Setting:** 2 institutions (university medical school and hospital breast imaging centre) **Country:** USA **Study period:** NR	**Total n of patients:** 132 **Total n of breasts:** 133 **Age (mean, SD):** NR years **Sex:** 100% women	**Intervention:** clinical prototype system (Koning Corporation, USA) **Comparison:** 2D digital mammography (NR)	• Radiation dose	This is a clinical protype system of CBBCT and findings should be interpreted with caution.
Xue et al. (2025)	**Design:** Retrospective single-arm observational study **Setting:** 4 hospitals **Country:** China	**Total n of patients:** 1590 **Total n of breasts:** 1590 (health side breast: 809 left side and 781 right side) **Age (median):** 49 years (range 19 to 84 years)	**Intervention:** NC-CBBCT (CBCCT 1000, Koning Corporation, USA)	• Radiation dose	The outcomes were stratified by regions in China.

Study reference	Methods, setting	Patient characteristics	Intervention and Comparison	Outcome(s)	Comments
	Study period: October 2020 to November 2023	**Sex:** 100% women			

Abbreviations: BI-RADS, Breast Imaging Reporting and Data System; CBBCT, cone-beam breast computed tomography; CE-CBBCT, contrast-enhanced cone-beam breast computed tomography; n, number; NC-CBBCT, non-contrast cone-beam breast computed tomography; NR, not reported; SD, standard deviation; 2D: two-dimensional