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The impact of legislation mandating breast density notification – review of the evidence

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Abstract

Breast density (BD) is an independent risk factor for breast cancer and reduces the sensitivity of mammography. The enactment of BD legislation in a majority of states in the USA mandating notification of risks associated with BD directly to women undergoing mammography has catapulted interest in BD among women, physicians, and policymakers. We therefore report a descriptive review of the evidence on the impact of enactment of BD legislation. Based on 22 eligible studies, we identified four broad themes of research: studies of the impact on screening rates, most showing increased utilisation of supplemental screening; studies exploring the effect on women, radiologists, or primary physicians (reporting heterogeneous effects on knowledge, awareness, perceptions, attitudes and behaviour; and changes in practice); few studies assessing the population impact (effect on screening outcomes or breast cancer stage); and studies of costs highlighting the economic burden from supplemental screening. Given that many of the studies were retrospective single institution studies (comparing pre- and post-legislation) or small surveys with a paucity of population-level studies, we highlight areas meriting additional research. The information described in this review can inform research priorities where BD legislation has been introduced and can be used to guide world-wide policy or practice decisions where BD legislation may be under debate or contemplation.

Keywords

breast cancer; breast density; legislation; mammography; population screening

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Introduction

Contemporary issues regarding breast density

A large body of research has been dedicated to breast density (BD) over the past 40 years, from elucidating its role as a risk factor for breast cancer (1, 2) to screening trials using density categorisation to triage women for supplemental screening (3, 4). However, this decade's unprecedented enactment of legislation in some parts of the USA mandating notification of risks associated with BD directly to women undergoing mammography has catapulted interest in (and discussion of) BD among women, physicians, and policymakers (5–10). While more than 70% of all states in the USA now have density reporting laws enacted (5, 7, 11, 12), resorting to legislative measures in the routine breast cancer screening setting is likely to have broader implications beyond the USA. For example, Australia does not have BD-specific legislation and Australia's national breast screening program (BreastScreen) does not routinely provide BD information to women having screening. However, in 2018, the Australian Government's Department of Health commissioned a public survey to inform discussion of whether BreastScreen's position statement on BD requires modification (13). Although there are no published reports on whether BD legislation is being considered or is in the process of being enacted in countries other than the USA, it seems likely that the ripple effect of enactment of BD legislation in the USA may have world-wide reach.

Scientific issues on breast density and the detection capability of supplemental screening

Mammographic BD is an independent risk factor for breast cancer (1, 2), and separate from this inherent risk, high BD also increases the risk of having a cancer missed on screening mammography (ie, increases the risk of an interval cancer in screened women) (14). Box 1 summarises some of the key scientific facts regarding BD. Early evidence suggests that supplemental (adjunct) screening in women with dense breasts detects additional breast cancers not detected on mammography (4, 15, 16). Specifically, there is early evidence that breast ultrasound and digital breast tomosynthesis detect additional cancers following 'negative' mammography screening; estimates of increased cancer detection and the associated increase or decrease in recall rates from supplemental imaging for women with dense breasts varies by imaging modality as summarised in systematic reviews (4, 16). The variability in estimated additional cancer detection from supplemental imaging is in the broad range of an additional 1.4 to 28.6 cancers per 1000 screens in dense breasts (4), and is partly driven by selection of study populations, with studies often including women with risk factors other than high BD due to clustering of risk factors in some women. Of equal importance is acknowledgement that routine supplemental screening for women with dense breasts has not been sufficiently evaluated to allow any conclusions about long-term health benefit. Therefore, recommendations about supplemental screening for women with dense breasts build on an assumption that additional cancer detection (above that from mammography) will transfer into additional clinical benefit and assume that the potential benefit outweighs the potential harms from supplemental screening.

Aims of this review

In this complex and evolving landscape of BD legislation, we undertook a review of the evidence to describe and summarise evidence on the impact of enactment of legislation mandating notification of BD information to women. Insights into the impact or potential impact of BD legislation is needed to guide the path forward with research and evaluation where BD legislation has been introduced (or is in the process of being enacted), and to inform world-wide policy or practice decisions where BD legislation may be under debate or contemplation.

Methods

Literature search and eligible studies

A literature search was performed (June 2018) as shown in online Appendix 1. This review does not attempt to address the broader literature on the detection capability of supplemental screening in women with dense breast tissue on mammography, which has been covered in systematic reviews and meta-analyses (4, 15, 16). The present review focuses on describing and summarising the evidence related to the impact of introducing or enacting BD legislation, and aims to identify a broad scope of research themes. Eligible studies were those that (a) stated that a purpose of the study was to assess or report on the impact of BD legislation, and (b) reported any quantitative information on the observed, perceived, or estimated effect of the enactment or potential enactment of BD legislation. The literature search consisted of a Medline search (exploded “breast neoplasm”, combined with “density” and “legisla\$” or “mandatory” or “notification” in the title; repeat search using “laws” instead of “legisla\$”), searching reference lists of eligible studies, and contact with content experts. Literature searching and identifying relevant studies was performed by both co-investigators: selection of eligible studies is shown in a flow-chart (online Appendix 1).

Extracted information

Information was extracted into an evidence table to summarise the scope of research evidence on the impact of BD legislation, as follows: purpose of the study, design and methods, source population or subjects, and the main findings. Extraction from eligible studies was performed by both investigators (NH, CL), using discussion and consensus to collate the information and to resolve disagreement. The information collated in the evidence table was used to define the main themes of research that have emerged in response to BD legislation and to summarise their findings.

Results

There were 22 primary studies (17–38) meeting eligibility criteria; the majority of other citations identified in the literature search were review articles, viewpoints, or group (expert panel) BD-related recommendations (details in online Appendix 1). All eligible studies are described, and their main findings summarised in Table 1. Studies were retrospective studies of medical or imaging records (18, 20, 27, 30, 34, 35, 37, 38), retrospective studies using sourced population datasets (26, 28), survey (or interview-based) studies (17, 19, 21–25, 29, 31, 32), and studies using micro-simulation modelling (33, 36).

Many studies undertook comparisons using a ‘before/after’ methodology, that is comparing outcomes of interest pre- and post-legislation (20, 28, 30, 34, 35, 38) or compared radiologists’ (or radiology facilities’) practices or states with versus without enacted BD legislation (24, 26, 29); one study integrated both forms of comparisons (26). On the other hand, several studies solely described or explored factors (such as women’s or health practitioners’ knowledge) post-enactment of BD legislation (17, 19, 22, 23, 25, 32), or described post-legislation test performance or utilisation (18, 27, 37). The two studies based on established simulation models used several sources of data to estimate comparative effectiveness and cost-effectiveness of supplemental screening for women with dense breasts (33, 36). Survey-based studies generally had modest response rates (17, 19, 21–25, 29, 32).

Using the evidence presented in Table 1, we identified 4 broad themes of research on the impact of BD legislation: (a) studies of the impact on screening and testing rates or utilisation (18, 20, 29, 30, 34, 35) or describing the performance of supplementary screening (27, 37, 38); (b) studies exploring the effect on women, radiologists or radiological practices, or primary physicians (shown as two subgroups in Table 1 depending on whether the study focused on women or health providers) (17, 19, 21–25, 28, 29, 31, 32); (c) studies assessing the population impact (screening effectiveness and health outcomes) (26, 33, 36); and (d) studies of cost-effectiveness or costs (33, 35, 36). These studies reported on various observed outcomes (18, 20, 26–30, 34, 35, 37, 38), perceived or expressed behavioural measures (17, 19, 21–25, 31, 32), or modelled outcomes (33, 36): study-specific results are detailed in Table 1. The group of studies exploring the effect of BD legislation on women, radiologists or physicians, reported on various domains such as knowledge, awareness, perceptions, attitudes and behaviour; or changes in practice or density reporting. The above-described research themes were not mutually exclusive; for example, studies may have examined screening rates as well as changes in services provided (29, 34) or may have examined health outcomes as well as costs (33, 36).

Despite heterogeneity in the types of studies assessing the impact of BD legislation and variability in their findings as outlined in the study-specific summaries (Table 1), some key themes emerged from the tabulated information:

- Supplemental screening: the introduction of BD legislation was followed by increases in supplemental screening rates (ultrasound, MRI) (18, 20, 27, 29, 30, 34, 35, 37, 38), and a suggestion of a decrease in mammography rates in two (relatively large) studies evaluating that outcome (20, 30); several studies of supplemental screening also documented additional cancer detection in the range of 1.8 to 3.2 cancers per 1000 supplemental screens (27, 35, 37).
- Effect on women: variable findings across studies on parameters such as concern about risk from BD, knowledge or awareness of BD, response to (or recall of) BD notification message, and intention to screen or interact with the health system (17, 18, 21, 22, 25); overall, these suggest that BD information or notification to women needs to be both specific in content and carefully crafted, and that the relatively modest proportion of women with dense breasts taking up supplementary screening (18, 35) may vary based on communication method (18).

- Effect on health professionals: primary care physicians have unmet training and support needs to enable them to address BD-related issues and to provide informed recommendations to patients (19, 23, 32); BD legislation did not have a consistent nor sustained effect on radiologists' reporting (classification) of BD (28, 31) or on the provision of formal risk assessment (29); however, there exists uncertainty amongst radiologists about the 'best approach' to manage BD legislation and supplemental imaging recommendations (21, 24, 28, 29, 34).
- Population impact: one study showed that BD legislation was associated with an increase in the proportion of women with localized invasive breast cancer at diagnosis but no evidence of a statistical reduction in the proportion with regional or metastatic disease (26); and, based on a modelling approach, there was limited additional health benefit (above that for mammography alone screening) from adding supplemental ultrasound for dense breasts (36) but a possible benefit from adding DBT achieved largely through reductions in false-positive screens (33).
- Economic impact: BD legislation directly (or potentially) leads to a substantial economic burden to the health system and/or the community based on the costs of supplemental screening for women with dense breasts, whether estimated through direct costing (35, 37) or through modelling (with the latter indicating that DBT is more cost-effective than ultrasound per QALY gained) (33, 36).

Discussion

Health legislation, inclusive of mandatory notifications of some diseases, has been in existence for over two centuries to protect and improve the health of populations in diverse areas, from the control of infectious diseases to environmental health and biosecurity laws. A multitude of factors, however, render the enactment of BD legislation somewhat unique – not only is mammographic density nested within the setting of breast cancer screening, complexifying the debate on its benefits and harms and how these might be altered by supplemental screening, but the anticipated health gains from BD legislation in the general population of women with dense breasts are far from clear (5–10, 39). Legislation mandating BD notification was largely progressed in response to consumer advocacy (5–8, 10), complemented by the growing movement of informed decision-making in health practice. Yet, the practice of notifying women of their BD is not supported by evidence of health benefit, nor is there a defined strategy to effectively manage the process and consequences of such notification. Many would argue that the benefit of notifying women of their BD classification is that women would then have an opportunity to undergo supplemental screening, which has been shown to enhance cancer detection in those with dense breasts as described earlier in this review. However, whether a further layer of screening and testing in women solely based on BD information confers health benefit is a highly debated issue (4, 5, 8, 36). The additional cancer detection from supplemental screening and the estimated incremental screening benefit (33, 36) may not outweigh the associated adverse outcomes, such as false-positives, substantial costs, and the possibility of overdiagnosis. All the above-described issues surrounding mandatory BD notification makes

it critical to understand what has been evaluated to date on the impact or potential effect of enactment of BD notification laws. Our work addresses this timely issue by collating and describing emerging evidence on the impact of BD legislation, to inform those who practice in settings where such legislation is enacted, to guide research directions, and to inform policy formulation in regions where BD legislation may be under discussion, be it in the USA or other nations.

While the evidence shown in Table 1 highlights a mix of study-specific findings, the key messages summarised at the results section of this review indicate that BD legislation has increased supplemental screening rates, with some studies also reporting additional cancer detection rates from supplemental screening (mostly ultrasound) in women with dense breasts, and some suggesting an accompanying modest decrease in mammography rates (18, 20, 27, 29, 30, 34, 35, 37, 38). Although the decrease in mammography rates has been reported in only two studies (both reporting around a 6% reduction)(20, 30), these studies were based on relatively larger imaging datasets than other studies of screening utilisation (Table 1) – this raises concern that some women maybe opting to undergo ultrasound (with unproven health benefit) for primary screening and foregoing mammography. Thus, future studies of supplemental screening, in the setting of enacted BD notification, should also monitor the effect on mammography screening rates rather than merely reporting supplemental screening rates.

The above-described studies of supplementary screening outcomes were mostly institution-based retrospective studies; we identified only one study that investigated population-level impact of BD legislation, finding an association with an increase in the proportion of women with localized invasive breast cancer at diagnosis but no concomitant change in the proportion with late-stage disease (26). As noted by the authors of the study, an effect on the proportion of women with late-stage disease at diagnosis may require longer follow-up time (26). Comparative effectiveness of supplementary screening for women with dense breasts was shown to be imaging modality-dependent, based on two modelling studies (33, 36): each of DBT and ultrasound were estimated to confer marginal benefit in terms of cancer deaths averted when used to screen women with negative mammography and dense breasts; however, adding DBT also had the effect of reducing false-positive screens. Hence, whilst we make no recommendations about whether supplemental screening should or should not be done routinely for dense breasts, supplemental DBT in this setting had a more favourable trade-off between incremental benefit and harms (33, 36).

An emerging area of research on the impact of BD legislation comprises qualitative and quantitative studies that explore the effect of BD notification on women (17, 18, 21, 22, 25), primary care and other physicians (19, 23, 32), and radiologists (21, 24, 28, 29, 31, 34). While some of these studies are limited to small or selected samples or surveys with modest responses, they highlight areas of uncertainty (for example, lack of consensus amongst health professionals on the most appropriate approach for managing women with dense breasts), and unmet knowledge and support needs amongst women receiving notifications, as well as amongst health providers. They also flag the potential for BD notification to have unintended consequences, such as misinterpretation of BD information and concern amongst women who receive notification (17), and expressed (25) or perceived anxiety (21).

Although few studies in our review examined women's responses, these were consistent in showing that around 50% of women experience some anxiety in response to BD notification or express concern from knowing that BD increases their risk of breast cancer (17, 25). This should be placed in the context that BD has limited utility as stand-alone risk factor and that a woman's risk of developing breast cancer is multi-factorial (5, 40). The challenge regarding management of BD is reflected in findings from studies of the effect of BD legislation on health providers, which indicate uncertainty and variability (amongst radiologists and primary physicians) on whether to recommend risk-based strategies or offer supplemental screening (19, 21, 23, 24, 29, 32). These issues are at the core of the controversy relating to mandating BD notification, and underscore the need for collaboration between all stakeholders to define effective strategies for future breast screening – ideally, these would incorporate but would not be solely driven by BD. For example, future research can evaluate supplemental screening targeted to women at risk of experiencing an interval breast cancer following mammography screening based on their risk profile and their BD, underpinned by the work from Kerlikowske and colleagues (41).

Additional adverse or unintended consequences may emerge from enacting BD legislation, some of which are related to the scope and framing of the laws used and the processes associated with implementation of legislation. State-level density reporting laws in the USA require inclusion of specific language dictated by individual laws into patient lay results letters; the notification letters are issued by the mammography provider or facility. However, the actual language varies widely across states. Most laws dictate language pertaining to the increased risk of missed cancers due to dense breasts, while a handful also detail an additional inherent risk of breast cancer associated with high breast density. Most states require this additional language only for women with heterogeneously or extremely dense breasts while others send out the additional language to all women. Dehkordy and Carlos highlight differences in the language of the BD laws in the USA and the variable recommendations for supplemental testing which is often unaccompanied by provisions for insurance coverage (7, 11). From a public health perspective, the latter raises the concern that BD notification legislation without consideration of the economic burden it imposes on women will contribute to inequity in access to additional testing (assuming supplementary imaging has potential benefits that outweigh harms). This concern, along with other issues discussed earlier in this review, underscore the importance of formulating recommendations on BD notification based on unequivocal evidence of benefit, and not merely based on knowledge of BD as a risk factor, to ensure that legislation (if, and when, introduced) minimises the potential economic burden on the community, and does not add to widening health disparities.

Current evidence regarding the impact of enacting BD legislation, outlined in this review, is predominantly from retrospective single institution studies (comparing pre- and post-legislation) or small surveys, with a paucity of population-level studies. Overall, there is little evidence supporting a health benefit from enactment of BD legislation, or identifying what has occurred pre- versus post-legislation in terms of supplemental screening and its outcomes at a state or broader level, and little is known about the factors driving recommendations beyond state-specific laws. Further, research on the effect of enacted BD laws to date has not considered the confounding effect of generally improved awareness of

BD, and the variability in insurance coverage for supplemental screening (with few states in the USA requiring insurance coverage as part of BD legislation) (7, 11). Future policies suggesting that women with dense breasts may benefit from supplemental screening or mandating BD notification should incorporate strategies to assess the implications (in terms of clinical and economic outcomes) of such recommendations, for example by prospectively implementing data collection to enable evaluation of impact as part of notification laws. It is also clear from the work highlighted in our review that informing women about BD (risk, and supplemental screening) is an area requiring additional research to ensure that women are accurately informed and enabled to make decisions about supplemental screening, and that information materials or decision aids are rigorously developed and tested using established methods before wider implementation (42).

Our work also suggests that the introduction of BD legislation should be preceded by training of health practitioners to ensure that they are provided with the necessary education and support systems to allow them to manage patients' information and clinical needs related to enacted BD notification laws, more so given the uncertainty about effective management of BD. We suggest that future screening efforts should be directed towards integrating BD as part of the woman's overall risk profile (for example, using risk models) and directing augmented screening to those not only at increased risk of breast cancer but at risk of experiencing an interval cancer at mammography screening, based on their risk profile inclusive of BD. The paucity of studies assessing population-level impact of BD notification highlights another research priority, and merits further review in a future update of the evidence on the effect of BD legislation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Box 1: Current Evidence Regarding Breast Density as a Risk Factor

More than 40% of the screening population have dense breasts (heterogeneously or extremely dense) (43), making it one of the most common breast cancer risk factors

Breast density is subjectively categorized into four groups by radiologists (with significant inter-reader and intra-reader variability) (44), with the top two groups considered to have dense breasts

The relative risk for developing breast cancer when comparing women with extremely dense breasts to those with almost entirely fatty breasts is 4.64 (95% CI 3.64–5.91) (1)

Both sensitivity and specificity of mammography for detecting breast cancer decreases with higher breast density (88.2% sensitive and 96.5% specific for women with fatty breasts compared to 62.2% sensitive and 89.9% specific for women with extremely dense breasts) (45)

High mammographic breast density is associated with higher likelihood of an interval breast cancer in mammography screening (14)

Evidence summary of studies reporting on the impact of enactment or potential introduction of breast density (BD) notification legislation

Table 1:

Study	Purpose of study	Methods	Population/ subjects or dataset	Main findings
<i>Studies assessing supplemental screening (and testing) utilisation and performance</i>				
Aripoli et al 2018 (18)	Examine effect of BD notification method on screening breast ultrasound utilisation	Retrospective review of radiology reports (2013–2014); 'dense breasts' notification by lay letter, using 3 different patient results letters based on radiologist preference	3,012 women who attended NCI-designated academic institution (University of Kansas) and were assigned dense tissue designation on mammography screening	<ul style="list-style-type: none"> Of 3,012 women with dense tissue, 450 (15%) underwent automated screening breast ultrasound after being informed (even distribution across three letter types) A greater proportion of women (86.9%) returned for supplemental ultrasound if they received a letter indicating dense breasts combined with a courtesy phone call Women who received a letter with an additional statement stating that they may benefit from supplemental screening were 9.91 times more likely to return for screening ultrasound
Chau et al 2017 (20)	Examine the impact of the California BD notification legislation on screening rates (for mammography, MRI)	Retrospective cohort study in an integrated healthcare system, comparing 2 years pre- with 2 years post-legislation	Women aged 40–74 enrolled in Kaiser Permanente Northern California (pre- 614,663; post- 631,748 women); overall 42% classified as having dense breasts.	<p>Significant changes in screening rates pre- to post-legislation:</p> <ul style="list-style-type: none"> Significant reduction in mammography rates (from 82.4% to 77.2%) evident in all age-groups except those aged 70–74 years Significant increase in MRI rates (from 12.1 to 13.8 per 1000) Increase in MRI rates was most evident in women aged 42–44 years Odds of having MRI (within 9 months of mammography) decreased with increasing age, increased with higher neighbourhood median income Higher BD associated with having supplemental MRI
Weigert 2017 (27) (updates earlier study (46))	Assess the performance of screening breast ultrasound in women with dense breasts at longer follow-up from enactment of BD legislation in Connecticut	Retrospective chart review from one institution in Connecticut, 2009–2013 (4 years post-legislation)	Performance of radiologists (no number given) across five sites affiliated with a single institution	<ul style="list-style-type: none"> Only 30% of women who qualify for supplemental screening under Connecticut legislation return for the additional test Supplemental screening ultrasound added 4 per 1000 additional cancers detected the first year and 3.2 per 1000 additional cancers the following three years PPV after abnormal screening ultrasound for the first year was <10% but significantly increased to 20% by year 4
Sanders et al 2016 (30)	Assess the impact of New Jersey's BD legislation on imaging and intervention utilization and modality of cancer diagnosis	Retrospective chart review of patients at outpatient breast centre November 2012–April, 2015; 18-month pre- and 18-month post-legislation.	Large non-profit teaching hospital in New Jersey; 1,213 biopsy-proven cancer patients included in analysis (592 pre- and 621 post-legislation)	<p>Changes pre- to post-legislation:</p> <ul style="list-style-type: none"> Mammography volume decreased by 6% (59,618 vs 56,057) Screening ultrasound volume increased by 651% (1,530 vs 11,486) Breast MRI use increased by 59.3% (2,595 vs 4,134) Overall core biopsy volume decreased by 3% (stereotactic biopsy decreased by 16.4% but ultrasound biopsy increased by 3.6%) Screen-detected cancers increased by 11% with no change in screening mammography-detected cancers but increased cancer detection by screening ultrasound (600% increase) and screening MRI (189% increase)
Mason et al 2015 (34)	Examine the impact of the introduction of BD notification legislation (Henda's law) in Texas on the use of screening MRI	Retrospective single institution study comparing 1 year pre- with 2 years post-legislation	MRI exams at Baylor University Medical Center (2011–13), all screens and subset for dense breasts (1 year pre- 32 MRIs; 2 years post- 143 MRIs)	<p>Increase in the number of screening MRIs pre- to post-legislation:</p> <ul style="list-style-type: none"> four-fold increase in the number of screening MRIs 23-fold increase in MRIs performed for screening dense breasts
Sobotka et al 2015 ^b (35)	Examine the impact of the introduction of BD notification legislation in New Jersey on	Retrospective single institution study conducted 2014 comparing 3 months pre- with up to 6 months post-legislation	Sample of patients attending a regional medical centre, and having mammography (pre-1245; post-2179)	<p>Significant increase in the proportion of women who have ultrasound (as follow-up after screening mammography) post-legislation:</p> <ul style="list-style-type: none"> more than two-fold increase in the number of ultrasounds

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	utilisation of supplemental ultrasound			<ul style="list-style-type: none"> ■ proportion having supplemental ultrasound increased from 17.6% to a range of 41.5% to 42.4%. ■ Extrapolated data on ultrasound utilisation to the entire state, to estimate increase in reimbursements of \$4.9–9.8 million <i>per month</i>
Hooley et al 2012 ⁵ (37)	Assess the performance and utilization of screening breast ultrasound in women with dense breasts in the first year post-enactment of BD legislation in Connecticut	Retrospective chart review of women with dense breasts who underwent screening US October 2009 – September 2010	935 women at one institution; 65.7% at low risk, 15.9% at intermediate risk, and 9.3% at high risk of cancer	<ul style="list-style-type: none"> ■ Overall, 75% of screening ultrasound exams were negative or benign ■ 20% were classified as BI-RADS 3 requiring short interval imaging follow-up and 5% were categorized as BI-RADS 4 requiring tissue biopsy ■ Of 63 biopsies, 3 yielded malignancy (one malignancy in each risk group) ■ Overall cancer detection rate was 3.2 per 1000 women screened with supplemental ultrasound (95% CI: 0.8 per 1000 to 10 per 1000) ■ Approximate cost of \$60,267 per detected cancer
Parris et al 2012 (38)	Assess the performance of screening breast ultrasound in women with dense breasts following enactment of BD legislation in Connecticut	Retrospective chart review of screening ultrasound performance one year pre- (2008/09) and one year post-legislation (2009/10) at a single institution	5,519 women post-legislation and 1,319 women pre-legislation having screening ultrasound after negative mammography	<ul style="list-style-type: none"> ■ Establishment of formal breast ultrasound screening program after legislation led to increased cancer detection: ■ Post-legislation, screening ultrasound cancer detection rate of 0.18%, biopsy rate of 3.3%, and PPV of 5.5% ■ Pre-legislation, screening ultrasound led to 20 biopsies that were all benign
<i>Studies exploring the effect on women, based on various domains such as knowledge, perceptions, emotions</i>				
Gunn et al 2018 (17)	Assess how 'dense breasts' notifications impact women's perceptions and participation in follow-up care	Qualitative study using semi-structured telephone interviews (30 from 202 invited participated in interviews)	English-speaking women aged 40 to 74 who had received 'dense breasts' notification (following negative screening mammography) from a Massachusetts hospital	<ul style="list-style-type: none"> ■ Most women (81%) recalled received notification; however, most did not recall specific content or key messages; expressed preferences for more specific and straightforward communication (content was perceived as vague or confusing) ■ Women were unfamiliar with or misinterpreted the concept of BD; >50% expressed initial concern and worry at receiving the information, although some considered the notification as a positive health message ■ Most indicated or intended engaging in some follow-up, such as interacting with the health care system (seeing physician, seeking supplemental screening), or making a lifestyle or attitudinal change, and/or seeking advice outside the medical system
Manning et al 2017 (22)	Assess between-race differences in women's responses to BD notification	Web-based survey of Michigan women post introduction of BD legislation, with 21% response rate (multiple behavioural and knowledge domains examined – details beyond scope of summary)	Women with dense breasts who had negative screening mammography and received BD notification (457 women)	<ul style="list-style-type: none"> ■ African American women generally reported more negative psychological responses to receiving BD notifications than Caucasian women, but had more favourable perceptions related to talking to their physicians about BD notifications ■ Race-related perceptions, socio-economic status, and knowledge partially accounted for the effect of race on psychological response to receiving BD notification; race-related perceptions and socio-economic status partially accounted for differences in behavioural intentions ■ Between-race differences in emotional responses to notifications did not explain differences in women's intentions to discuss BD notifications with their physicians
Moothathu et al 2017 (25)	Assess patients' BD awareness and attitudes regarding supplemental breast ultrasound screening post-implementation of the Connecticut BD density notification law	Self-administered paper survey (12 questions) distributed to women presenting to a Connecticut academic breast imaging centre 2013–2014	Women presenting for screening and had prior mammography reports describing dense breasts (950 women completed survey)	<ul style="list-style-type: none"> ■ Majority of surveyed women (92%) were aware of their BD, and 77% had undergone a prior screening ultrasound ■ Around half (43%) of participants who were aware of their BD expressed increased anxiety about developing BC due to having dense breast tissue ■ Caucasian race and higher education were significantly associated with knowledge of personal BD and having prior screening ultrasound

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				<ul style="list-style-type: none"> ■ Participants with less than a college degree were significantly more likely to rely on their provider's recommendation regarding obtaining screening ultrasound
<i>Studies exploring the effect on physicians, radiologists or radiological practices, based on domains such as knowledge, perceptions, practice or recommendations</i>				
Gunn et al 2018 (19)	Explore primary care provider attitudes, knowledge, and impact on clinical practice of the Massachusetts BD notification legislation	Web-based survey of Massachusetts primary care physicians and nurse practitioners (2015–2016), with a 55% response rate	80 respondents of 145 primary care providers invited from general internal medicine at two urban safety-net hospitals	<ul style="list-style-type: none"> ■ None of the respondents could identify all 8 required components of notification under Massachusetts legislation ■ 49% did not feel prepared to address patient questions about dense breasts ■ 85% desired further training for discussing dense breast risks and supplemental screening with patients ■ Female and less experienced providers were more in favour of notification (49% vs 11%, female vs male; 76% < 5 years vs 9% > 20 years of experience)
Lourenco et al 2017 (21)	Assess radiologists' knowledge about BD legislation, and perceived practice changes post-enactment of BD notification legislation	Email survey (29 questions) with a response rate of 18%	Radiologists who are members of New England Roentgen Ray Society (73% of 96 respondents practiced in states mandating BD notification)	<p>Perceived effects of BD legislation:</p> <ul style="list-style-type: none"> ■ increased patient anxiety about BC (69%) ■ increased patient (74%) and provider (66%) awareness about effect of density on mammography sensitivity <p>Knowledge and recommendations:</p> <ul style="list-style-type: none"> ■ variability on which imaging test to recommend in average risk women with dense breasts (DBT 53%, ultrasound 26%) ■ modest knowledge of relative risk associated with BD when comparing women with different BD categories ■ uncertainty about 'best approach' to counsel women on supplemental screening (44% advised risk assessment; 32% were unsure)
Maimone et al 2017 (23)	Assess primary care physicians' awareness and understanding of BD legislation and strategies for managing women with dense breasts, in the context of advocacy for BD notification	Email survey (15 questions) with a response rate of 44%	Mayo clinic staff physicians, residents, and fellows; 59% of respondents from internal medicine, 31% family medicine, 10% obstetrics-gynecology	<p>Most respondents (68%) aware of BD notification laws, but half of respondents were not comfortable answering questions regarding BD (32% 'slightly comfortable' and 18% 'not comfortable')</p> <p>Variable implementation of density laws:</p> <ul style="list-style-type: none"> ■ 26% offered supplemental screening ■ 47% offered it to certain patients based on risk factors ■ 15% did not offer supplemental screening
Maimone et al 2017 (24)	Assess current strategies and sentiments regarding BD notification laws and supplemental screening among radiologists	Web-based survey conducted in November 2014	Radiologists who are members of the Society of Breast Imaging (223 radiologists, 38% from states without laws, 62% from states with laws)	<ul style="list-style-type: none"> ■ Among respondents in states <i>without</i> reporting laws, 60% claimed that they lacked adequate resources to offer supplemental screening ■ Among respondents in states <i>with</i> reporting laws, 51% claimed that they lacked adequate resources to offer supplemental screening; 41% offered supplemental screening to all patients with dense breasts, while 59% offered supplemental screening based on a set of risk factors ■ Among respondents in states <i>with</i> reporting laws, 61% stated that discussing BD and supplemental screening rests with the primary care physician and 20% claimed radiology representatives should be responsible
Bahl et al 2016 (28)	Examine the impact of BD notification legislation on BD reporting by radiologists	Retrospective state-level study comparing 20 months pre-legislation with 10 months post-legislation	Mammographic reports from a national database of 1,333,541 exams	<ul style="list-style-type: none"> ■ A modest but significant decrease in the percentage of mammograms classified as dense in the month before (43.0%) versus month after (40.0%) enactment of BD notification, but no long-term effect ■ Percentage of mammograms reported as dense was slightly but significantly higher in states without (versus with) BD notification legislation (43.9% vs 42.4%)

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Nayak et al 2016 (29)	Assess the impact of BD legislation on radiology practices (implementation of risk assessment and supplemental screening)	Web-based survey (20 questions) conducted 2013–2014, response rate not reported	Radiologists who are members of the Society of Breast Imaging (121 respondents from 110 facilities; 50% from states with BD legislation)	Comparison of radiological facilities in states with (vs without) an enacted BD notification law: <ul style="list-style-type: none"> ■ No difference in the proportion performing formal BC risk assessment ■ A significantly higher proportion offered screening whole breast ultrasound (66% vs 29%)
Gur et al 2015 (31)	Examine the effect of BD notification act of Pennsylvania on radiologists' perceived and actual reporting of BD	E-mail survey (2 questions) of radiologists one month after legislation enacted at single institution (76% response rate); comparison with actual BD reporting pre- and post-legislation	16 MQSA-qualified academic breast imaging radiologists with 4–34 years of experience in mammography reporting	<ul style="list-style-type: none"> ■ 56% of respondents did not favor the law, 13% favoured it, 31% were neutral ■ 50% of respondents stated that they were more likely to downgrade heterogeneously dense breasts (BI-RADS density c) to scattered fibroglandular breasts (BI-RADS density b) due to the law ■ In practice, 25% (4/16) radiologists increased the frequency of BI-RADS density b category post-legislation versus pre-legislation, adjusting for patient age differences
Khong et al 2015 (32)	Assess primary physicians' awareness of the California BD law and assess its impact on primary care practice	Web survey (10 questions) conducted 10 months after legislation implementation, 45% response rate	Physicians within a single primary care network; 39% internal medicine, 47% family medicine, 9% obstetrics-gynaecology	<ul style="list-style-type: none"> ■ 49% were not aware of density reporting legislation before taking the survey ■ 32% reported a change in patient level of concern about BD since date of legislation enactment ■ 20% of physicians never answered patients' questions related to BD ■ Only 6% of physicians reported being "completely comfortable" ■ answering patients' questions related to BD ■ 26% of physicians reported performing BC risk assessment themselves, without significant differences between specialties
<i>Studies assessing population screening effectiveness and health outcomes</i>				
Richman et al 2017 (26)	Examine changes in BC stage after enactment of BD notification legislation in Connecticut, and assess stage-specific incidence of BC associated with BD legislation (across counties)	Population-based study using the SEER registry; difference-in-differences analysis of changes in BC stage at diagnosis among Connecticut women compared to changes in women in control states	Women aged 40–74 diagnosed with BC 2005–2013 (466,930 including 25,592 Connecticut residents).	In Connecticut (enacted BD legislation) versus control states (no BD legislation) and accounting for trends in non-legislation states, there was: <ul style="list-style-type: none"> ■ 1.38% (95% CI 0.12 to 2.63) increase in the proportion of women who had localized invasive BC at diagnosis ■ 1.12% (95% CI –2.21 to –0.08) decrease in the proportion of women with ductal carcinoma in situ at diagnosis ■ No significant change in the proportion of women with regional-stage (–0.09%, 95% CI –1.01 to 1.02) or metastatic disease (–0.24%, 95% CI –0.75 to 0.28)
Lee et al 2015 ^{\$} (33)	Estimate the comparative effectiveness of combined mammography and DBT for women with dense breasts in the context of advocacy for mandating BD notification	Simulation modelling using a validated CISNET micro-simulation model; incorporated evidence from observational studies to estimate the impact of screening scenarios on BC outcomes	Simulated model cohorts: women with dense breasts eligible for routine screening from age 50 through age 74 with different screening strategies: mammography alone; mammography plus tomosynthesis	For the base-case analysis of women aged 50–74 having biennial screens, adding tomosynthesis to digital mammography screening in women with heterogeneously or extremely dense breasts, estimated <i>per 1000 women</i> : <ul style="list-style-type: none"> ■ averted 0.5 additional BC deaths ■ averted 405 false-positive screens ■ had a cost-effectiveness ratio of \$53,893 per QALY gained ■ likely to be cost-effective if cost of combined screening is up to \$226 (vs \$139 for digital mammography alone)
Sprague et al 2015 ^{\$} (36)	Assess potential impact of mandating BD notification by estimating population benefits, harms, and cost-effectiveness of supplemental screening ultrasound for women with dense breasts	Comparative modelling using three validated CISNET micro-simulation models; incorporated evidence from clinical trials and observational studies to estimate the impact of various screening scenarios on BC outcomes	Simulated model cohorts: women eligible for routine screening from age 40 and having different screening strategies (various comparisons and screen intervals reported); mammography alone; with supplemental ultrasound in	For the base-case analysis of women aged 50–74 having biennial screens, adding ultrasound after negative mammography screening in women with heterogeneously or extremely dense breasts, estimated <i>per 1000 women</i> with dense breasts versus mammography alone [range across models]: <ul style="list-style-type: none"> ■ averted 0.36 additional BC deaths [0.14 to 0.75] ■ gained 1.7 QALYs [0.9 to 4.7] ■ caused 354 false-positive ultrasound biopsy recommendations [345 to 421]

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			heterogeneously or extremely dense breasts (base-case)	<ul style="list-style-type: none">■ cost-effectiveness ratio \$325,000 per QALY gained [\$112,000 to \$766,000] For annual screening of women aged 40–74, all estimates of benefits, harms and costs (<i>per 1000 women</i> with dense breasts) increased from adding ultrasound: <ul style="list-style-type: none">■ averted 0.43 additional BC deaths [0.08 to 1.28]■ gained 3.0 QALYs [0.7 to 9.4]■ caused 1,219 false-positive ultrasound biopsy recommendations [1,174 to 1,333]■ cost-effectiveness ratio \$728,000 per QALY gained [\$223,000 to \$3,583,000]

Footnote for Table 1 – \$ symbol indicates that the study included assessment of costs or cost-effectiveness

BC (breast cancer); BD (breast density); CISNET (Cancer Intervention and Surveillance Modelling Network); DBT (digital breast tomosynthesis); MRI (magnetic resonance imaging); MQSA (Mammography Quality Standards Act); NCI (National Cancer Institute); QALY (quality-adjusted life years); SEER (Surveillance, Epidemiology, and End Results Program).