

Density: Science, Sensitivity, Specificity, and Screening

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In response to Alena Allen, *Dense Women*, 76 OHIO ST. L.J. 847 (2015).

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I. INTRODUCTION

Professor Allen’s analysis in *Dense Women* is timely and insightful.¹ Briefly, her argument is this: dense breast tissue renders mammograms more difficult to read.² Hence, those mammograms are less likely to detect cancer.³ While women with this condition may be better able to make informed decisions if they are told their tissue is dense, the information should come not from legal mandates, but rather from public information campaigns and similar voluntary outreach.⁴ State-prescribed disclosures, as Allen proposes, do not just interfere with women’s autonomy; they also pose potential legal perils for physicians.⁵ The threat of malpractice litigation for failure to address density can not only distort physician-patient communication, but can inappropriately ramp up screening standards by legislative fiat rather than by sound medical judgment.⁶

This Response proposes that Allen’s analysis goes astray in one respect—namely, her argument that notification statutes undermine women’s autonomy.⁷ Elsewhere, however, she hits the mark squarely, particularly her conclusion that excessive concerns about density can promote increased levels

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¹ See generally Alena Allen, *Dense Women*, 76 OHIO ST. L.J. 847 (2015).

² *Id.* at 883.

³ *Id.* at 861.

⁴ *Id.* at 894–97.

⁵ *Id.* at 873–88.

⁶ *Id.* at 891–94.

⁷ Allen, *supra* note 1, at 873–78.

of screening that can, in turn, do more harm than good.⁸ Indeed, there are additional considerations supporting that conclusion, which this commentary will explore.

II. THE AUTONOMY ARGUMENT

Allen distinguishes among statutes according to their level of directiveness.⁹ After telling the woman that her breast tissue is dense, highly directive language would say, for example: “This information about the result of your mammogram is given to you to raise your awareness. Use this information to talk to your doctor about your own risks for breast cancer. At that time, ask your doctor if more screening tests might be useful, based on your risk.”¹⁰ Moderately directive language, by comparison, would say: “This information is being provided to raise your awareness and to encourage you to discuss with your health care providers your dense breast tissue and other breast cancer risk factors. Together, you and your physician can decide if additional screening options are right for you.”¹¹

Such instructions, Allen maintains, “dictate to women how they should use the information given” to them.¹² The instructions “command,”¹³ “unduly trample[e] upon,”¹⁴ and “direct[] women towards the preferred choice,”¹⁵ with the net effect being that “the ability of women to make an autonomous choice is now being thwarted by the state.”¹⁶ Moreover, this information is delivered right after the mammogram, the time in which the woman’s “ability to process the information is compromised by worry and anxiety.”¹⁷ In the end, says Allen, the directive statutes “usurp the power of women to make independent unbiased choices about their medical care.”¹⁸

Dictate. Command. Trample. Direct. Thwart. Usurp. Let us take another look. The most highly directive language simply tells women to have a conversation: “Use this information to talk to your doctor . . . [and] ask your doctor if more screening tests might be useful”¹⁹ This language does not tell women how the conversation should go or what the woman and doctor should conclude, nor does it direct women to get additional screening. It just

⁸ *Id.* at 879.

⁹ *Id.* at 873–78.

¹⁰ *Id.* at 874 (quoting ALA. CODE § 22-13-71(a) (Lexis Nexis Supp. 2014)).

¹¹ *Id.* at 875–76 (quoting ARIZ. REV. STAT. ANN. § 36-415(A) (Supp. 2014)).

¹² *Id.* at 875.

¹³ Allen, *supra* note 1, at 875.

¹⁴ *Id.* at 878.

¹⁵ *Id.* at 897–98.

¹⁶ *Id.* at 897.

¹⁷ *Id.* at 896.

¹⁸ *Id.* at 873.

¹⁹ Allen, *supra* note 1, at 874 (quoting ALA. CODE § 22-13-71(a) (Lexis Nexis Supp. 2014)).

says: “talk to your doctor.”²⁰ Nevertheless, Allen determines that this statement on a piece of paper will “usurp the power of women.”²¹

Allen’s leap is more than a *non sequitur* that could be deemed fairly insulting to women.²² More importantly, evidence indicates that Allen’s view here is empirically incorrect. First, there is the commonplace reality that many people often disregard health warnings, including prescriptions from their own doctors. Many of us continue to smoke, eat unhealthy foods, abjure exercise, consume alcohol beyond moderation, and fail to take our hypertension medications faithfully.

More to the point, a recent meta-analysis expressly focused on studies of women with dense breasts.²³ In one of the studies analyzed, women were randomly assigned either to a control group that did not receive notification about breast density along with their mammography results, or to an intervention group that did receive this information.²⁴ Contrary to Allen’s proposal that, at the conclusion of a mammography screening a woman’s “ability to process the information is compromised by worry and anxiety,”²⁵ this study found that:

At [four] weeks, more women in the intervention group had statistically significantly increased knowledge of breast density . . . and were more likely to perceive themselves as having elevated breast cancer risk. These differences did not persist at [six] months. Psychological distress, breast cancer worry, and preoccupation with breast cancer did not differ between groups.²⁶

Certainly anxiety is increased when the woman’s mammography result is positive.²⁷ Being told that one may actually have cancer is indeed cause for

²⁰ *Id.*

²¹ *Id.* at 873. Common definitions of “usurp” include “to seize,” take without lawful right, commandeer, appropriate, grab, arrogate, and take over. See *Usurp*, DICTIONARY.COM, <http://www.dictionary.com/browse/usurp> [<https://perma.cc/BPM3-N45Z>]; *Usurp*, MERRIAM-WEBSTER.COM, <http://www.merriam-webster.com/dictionary/usurp> [<https://perma.cc/95H2-YZPT>].

²² On what basis, one wonders, can one conclude that a directive to “talk to your doctor” supposedly renders an ordinarily competent woman too helpless to make her own decisions? See Allen, *supra* note 1, at 874 (quoting ALA. CODE § 22-13-71(a)).

²³ See generally Joy Melnikow et al., *Supplemental Screening for Breast Cancer in Women with Dense Breasts: A Systematic Review for the U.S. Preventive Services Task Force*, 164 ANNALS INTERNAL MED. 268 (2016).

²⁴ *Id.* at 274 (citing Joan L. Bottorff et al., *Women’s Responses to Information on Mammographic Breast Density*, 39 CAN. J. NURSING RES. 42–43 (2007)).

²⁵ Allen, *supra* note 1, at 896.

²⁶ Melnikow et al., *supra* note 23, at 274.

²⁷ Albert L. Siu, U.S. Preventive Servs. Task Force, *Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement*, 164 ANNALS INTERNAL MED. 279, 290 (2016).

concern. This, however, is not the same as being told one has dense breast tissue. As noted, there is no evidence that such information, by itself, causes psychological distress.²⁸ Conversely, evidence suggests that the information increases women's knowledge about breast cancer, although the enhanced understanding did not persist for even six months.²⁹

III. THE LIKELIHOOD AND PROBLEMS OF RAMPED-UP SCREENING

Allen suggests that the notification statutes are likely to lead to increased screening for women with dense breasts and that such a ramp-up is not necessarily a good thing.³⁰ While Allen does get this right, I would like to re-frame the discussion.

A. Likelihood of Ramped-up Screening

A legal requirement that a radiologist tell a woman that she has dense breast tissue does not inherently mean that the doctor must change the way he or she treats patients. Arguably, the only necessary change is that the doctor (or his or her office staff) must hand the requisite paperwork to the woman or include the required wording in an electronic message. If failure to provide this information is a potential source of liability, the fix is simple enough.³¹

Nevertheless, as a broad reality, it takes very little to prompt physicians to fear malpractice liability and to modify their practices far more than the actual liability risk might suggest. As a long-time medical school professor, I have often emphasized to my students and residents that doctors often learn about law the same way teenagers learn about sex: they ask each other, and the mythology they generate is comparable. More eloquently, Alex Capron has said, "If patients behaved as irrationally about treatments as physicians do about liability, the patients would be labeled incompetent."³² In other words, physicians generally need very little prompting to become concerned about a hypothetical malpractice risk and to modify their practices in ways more commensurate with the depth of their fears than with the magnitude of the risk.

That said, important complexities should be noted. First, in the case of mammography and follow-up conversations, two different physicians are usually involved, not just one. The physician with the legal obligation to notify the woman is ordinarily the radiologist, since he or she is often the one to make that diagnosis. However, a new duty to pass along information is not the

²⁸ See Bottorff et al., *supra* note 24, at 38.

²⁹ *Id.*

³⁰ Allen, *supra* note 1, at 879–80.

³¹ *Id.* at 884 (explaining that density notification statutes in most states broaden malpractice risk by creating a standard of care, which, if not followed, may lead to medical malpractice liability).

³² Alexander Morgan Capron, *Legal and Ethical Problems in Decisions for Death*, 14 L. MED. & HEALTH CARE 141, 142 (1986).

radiologist's greatest concern. Rather, potential liability for failing to diagnose density in the first place will cause the greater worry.³³ If that leads to diagnosing more women as dense, then concerns about excessive follow-up screenings are amplified.³⁴

Typically, the conversation that follows notification is between the woman with dense tissue and her primary care physician (PCP), not the radiologist. Here, the pressure to recommend additional screening could depend, in part, on precisely how the woman received her mammography results and notification. Where a result is positive, the radiologist has a strong duty to alert the PCP, so the PCP can then respond to the patient. Conversely, benign results of routine screenings do not necessarily prompt any alerts to PCPs. They may not become aware of mammography results or the density determination until they browse the report during the patient's next visit, whenever that may be, or if the woman makes an appointment after reading the message about density.

A PCP who had no duty to diagnose breast density and no statutory duty to alert the patient may not feel any special urgency to propose additional screening. If that PCP is keeping abreast of the relevant literature, then the conversation may not result in further screening. The most up-to-date studies suggest that although additional screening can indeed identify a few more cases of breast cancer, the price is not just increased anxiety and distress—it can include radiation-induced breast cancer.³⁵ On the other hand, many PCPs may indeed feel pressure to recommend additional screening where a patient shares the notification about her dense breasts and asks about follow-up testing. The course of least resistance (and which would take the least time out of a busy PCP's schedule) may well be to say, "Sure, let's schedule some tests."

Allen suggests that an aggressive public information campaign about breast density and its potential implications would be superior to notification

³³Diagnosing breast density is not a simple matter. As Allen notes, there are four categories of density: (a) almost entirely fatty, (b) scattered areas of figro-glandular density, (c) heterogeneous mixture of dense and fatty tissue, and (d) extremely dense tissue. Categories (c) and (d) generally qualify for deeming a woman to have dense breasts. Allen, *supra* note 1, at 862 (citing AM. COLL. OF RADIOLOGY, ACR BI-RADS ATLAS—MAMMOGRAPHY 124 (5th ed. 2013), <http://www.acr.org/~media/ACR/Documents/PDF/QualitySafety/Resources/BIRADS/01%20Mammography/02%20%20BIRADS%20Mammography%20Reporting.pdf> [<https://perma.cc/WN3N-GJTZ>]). Diagnoses of density can vary not only from one radiologist to another, but for the same radiologist from one time to the next, for the same patient. *See, e.g.*, Melnikow et al., *supra* note 23, at 271.

³⁴Indeed, "[t]he likelihood of a woman being told she has dense breasts varies substantially according to which radiologist interprets her mammogram." Brian L. Sprague et al., *Variation in Mammographic Breast Density Assessments Among Radiologists in Clinical Practice*, 165 ANNALS INTERNAL MED. 1, 1 (July 19, 2016), <http://annals.org/article.aspx?articleid=2534407> [<https://perma.cc/99EQ-V9GE>].

³⁵*See* Siu, *supra* note 27, at 290.

statutes.³⁶ Maybe so, maybe not. Widespread public discussion, public service announcements in the media, news stories, and the like can have their own effect on a physician's psyche and, in the end, could be just as likely to pressure physicians into excessive screening as notification statutes. Whatever the source of patients' questions and requests, whether a statutorily-required piece of paper or a heavy media campaign, physicians can be persuaded into ramping up screening practices. Hence, Allen's proposals for reducing pressures on physicians may not work as hoped.

B. *Problems of Ramped-up Screening*

Allen rightfully argues that there is a great need for diligence and circumspection when screening is ramped up solely on the ground that a woman's breast tissue is dense.³⁷ The U.S. Preventive Services Task Force (USPSTF) recently reasserted the guidelines initially issued in 2009, recommending biennial, not annual, mammography for average-risk women beginning at age fifty, with individualized discussions and decisions for women under that age.³⁸ While recognizing that more frequent screening can detect a few more cases of cancer, the USPSTF emphasizes that the harms of excessive screening are very real:

The most important harm is the diagnosis and treatment of noninvasive and invasive breast cancer that would otherwise not have become a threat to a woman's health, or even apparent, during her lifetime (that is, overdiagnosis and overtreatment). False-positive results are common and lead to unnecessary and sometimes invasive follow-up testing, with the potential for psychological harms (such as anxiety). False-negative results (that is, missed cancer) also occur and may provide false reassurance. Radiation-induced breast cancer and resulting death can also occur, although the number of both of these events is predicted to be low.³⁹

The USPSTF's observation regarding the likelihood of false-positive results merits amplification. We begin by explaining the concepts of sensitivity, specificity, and positive predictive value. The sensitivity of a screen or diagnostic test is the likelihood that, if the disease or condition is present in the patient, the test will detect it (i.e., if someone has the disease, how often will the test be positive). Specificity refers to the likelihood that a positive result actually reflects the presence of the condition/disease, rather than something else (i.e., if the person does not have the disease, how often

³⁶ Allen, *supra* note 1, at 896.

³⁷ *See id.* at 900.

³⁸ *See* Siu, *supra* note 27, at 279.

³⁹ *Id.* at 280.

will the test be negative).⁴⁰ Positive predictive value (PPV), in turn, “answers the question: ‘How likely is it that this patient has the disease given that the test result is positive?’”⁴¹

Consider the following example. For illustrative simplicity, let us consider 1,000 women and say, hypothetically, that eight of these 1,000 women actually have breast cancer. Suppose further that the sensitivity of mammography is 90%—that for every ten patients who actually have breast cancer, the test picks up nine of them. Suppose further that the test’s specificity is 93%—that is, for patients who do not have the disease, the test will incorrectly say that 7% of them do have it, even while properly yielding negative results for the other 93% who do not have the disease.

We can now trace out some implications. Per our earlier hypothetical numbers, of the 1,000 women, eight have the disease. Therefore, 992 do not. We have assumed, hypothetically, that the sensitivity for this test is 90% and the specificity is 93%. Therefore, with a sensitivity of 90%, the test will correctly pick up seven out of the eight women who actually have the disease, but will miss that last affected woman. In addition, the test will look at the 992 women who do not have the disease. With a specificity of 93%, the test will correctly say that 93% of those disease-free women do not have the disease and will incorrectly tell us that 7% of them do have it. Thus, seventy of those 992 disease-free women will be falsely diagnosed as positive.

Overall, the test will show seventy-seven positive results: seven will be true-positives and seventy will be false-positives. As a result, the PPV is only 10%. For every ten women who are said by this test to have the disease, only one will actually have the disease.

Let us now turn to actual figures for sensitivity, specificity, and PPV for women who receive supplemental screening because they have dense breast tissue. As Allen discussed, sensitivity and specificity of mammography for women with dense breast tissue is significantly lower than that for less dense women.⁴² Thus, we want to consider sensitivity, specificity, and PPV for various kinds of follow-up screening that might be undertaken for women who have been identified as having dense tissue.

Consider ultrasound results for these women with a negative mammogram but dense tissue. Here, sensitivity ranges from 80% to 83%, specificity from 86% to 94%, and PPV from 3% to 8%.⁴³ That is, for every 100 women whose ultrasound concludes “this woman has cancer,” only three to eight of those women will actually have cancer.⁴⁴

The numbers for magnetic resonance imaging (MRI) are analogous. Sensitivity ranges from 75% to 100%, specificity from 78% to 94%, and, at

⁴⁰ Abdul Ghaaliq Lalkhen & Anthony McCluskey, *Clinical Tests: Sensitivity and Specificity*, 8 CONTINUING EDUC. ANESTHESIA CRITICAL CARE & PAIN 221, 221 (2008).

⁴¹ *Id.* at 221–22.

⁴² See Allen, *supra* note 1, at 861; see also Siu, *supra* note 27, at 285.

⁴³ Melnikow et al., *supra* note 23, at 268.

⁴⁴ See *id.*

best, PPV ranges from 3% to 33% across three studies.⁴⁵ Thus, for every 100 women whose MRI says they do have breast cancer, maybe only three women actually have it—or maybe as many as thirty-three, or somewhere in between.⁴⁶

Perhaps it is for these reasons that there are no accepted clinical practice guidelines to direct adjunctive screening for a woman with dense breast tissue whose mammogram is negative.⁴⁷ The caution is warranted: early detection does not necessarily save lives. For some kinds of cancer it does, and for others, not really.

Screening has been shown to be helpful for some kinds of cancer, such as colon and cervical cancer.⁴⁸ For other kinds of cancer, screening has not been shown to reduce mortality rates.⁴⁹ A Cochrane review of several controlled clinical trials, with nearly 350,000 participants, found that prostate screening did not significantly reduce the death rate from prostate cancer.⁵⁰ Similarly, a twenty-five year longitudinal study in Canada, with nearly 90,000 women from 40–59 years of age, found that annual mammograms did not reduce breast cancer mortality.⁵¹

The unfortunate reality is that “some tumors will lead to death irrespective of when they are detected and treated. Meanwhile, aggressive early screening has a slew of negative health effects. Many cancers grow slowly and will do no harm if left alone, so people end up having unnecessary thyroidectomies, mastectomies and[,] prostatectomies.”⁵² Perhaps the greatest challenge in the

⁴⁵ *Id.*

⁴⁶ *See id.*

⁴⁷ *See* Siu, *supra* note 27, at 286.

⁴⁸ Megan Scudellari, *Myths that Will Not Die*, 528 NATURE 322, 323 (2015).

⁴⁹ *See generally* Nazmus Saquib et al., *Does Screening for Disease Save Lives in Asymptomatic Adults? Systematic Review of Meta-Analyses and Randomized Trials*, 44 INT’L J. EPIDEMIOLOGY 264 (2015) (finding that few screening tests for nineteen major disease conditions reduce mortality).

⁵⁰ Dragan Ilic et al., *Screening for Prostate Cancer (Review)*, COCHRANE DATABASE OF SYSTEMATIC REVIEWS 2–3 (2013), <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004720.pub3/epdf> [<https://perma.cc/EL8H-HJQD>]. More recently, a ten-year study of 1,643 men with prostate cancer concluded that the death rate did not differ significantly between men who were treated with surgery and radiation versus those who declined such treatment. *See generally* J.L. Donovan et al., *Patient-Reported Outcomes After Monitoring, Surgery, or Radiotherapy for Prostate Cancer*, NEW ENG. J. MED. (Sept. 14, 2016), <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1606221> [<https://perma.cc/8GS6-QV8U>].

⁵¹ *See generally* Anthony B. Miller et al., *Twenty Five Year Follow-up for Breast Cancer Incidence and Mortality of the Canadian National Breast Screening Study: Randomised Screening Trial*, 348 Brit. Med. J. g366 (2014), <http://www.bmj.com/content/bmj/348/bmj.g366.full.pdf> [<https://perma.cc/FX6E-VEV5>].

⁵² Scudellari, *supra* note 48, at 323. In southwest Korea, an aggressive program for early detection of thyroid cancer has led to a great increase in the numbers of thyroid cancers detected. *Id.* at 322. Many people diagnosed have had their thyroid glands removed and been placed on lifelong drug regimen, with notable risks for both. *Id.* Nevertheless, there has been no change whatever in the death rate from thyroid cancer in that region. *Id.*

realm of breast cancer science, diagnosis, and treatment may be to figure out how to distinguish better between fast- and slow-growing tumors.

In the end we can conclude that, on the whole, Allen is mostly right. The problem is not that a piece of paper telling women to talk to their doctors will somehow render women less competent to engage in a conversation or to make their own decisions. Rather, the problem is that the science does not support the politics. Mandatory disclosures regarding density of breast tissue appear to have a fairly high likelihood of prompting increased screening for this large group of women, in the absence of solid evidence that the information will actually make a significant, population-wide difference in morbidity or mortality from breast cancer.⁵³ Although some women will be diagnosed earlier through such extra screens, perhaps with benefit to them, the poor PPV of these tests suggests that far more women will undergo needless interventions, and in some cases harm-causing treatments, for no good reason. As the new USPSTF recommendations recognize:

Increased breast density is common in the general population; however, critical questions remain about how best to manage this condition and to support these women. Research to help improve the validity and reproducibility of serial BIRADS assessments would be useful if breast density is to be considered as a factor for personalized, risk-based approaches to breast cancer screening.⁵⁴

⁵³ See *supra* Part.III.B.

⁵⁴ Siu, *supra* note 27, at 287.