

Appalachian MammoCare
A Rural Breast Care Prescription

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An important healthcare study, with implications for improving health outcomes for residents of our region, was reported in a 2016 issue of the **Journal of the American Medical Association (JAMA)** (1.) US county-level, cause and age-specific, standardized mortality rates between 1980-2014 were studied and reported. A total of 3110 geographic areas and 80,412,524 deaths were analyzed. Very significant disease specific mortality rate disparities were noted and residents of our region rated among the worst in the nation for multiple categories of disease. Neoplasms accounted for 24.3% of all deaths. Cancer was the second leading cause of death behind cardiovascular disease and the leading cause of life years lost (LYL). Very high mortality rates were noted in Eastern Kentucky and Western West Virginia. The utility of this study's focus on the county-specific mortality rate disparity, is that it highlights the importance of access to treatment and quality of care, and can be used by our community as evidence when advocating for change. It is very disturbing to find that our geographic area ranks among the nation's worst in terms of mortality for: Neoplasm; cardiovascular disease; diabetes, urogenital disease, blood and endocrine diseases; self-harm and interpersonal violence; chronic respiratory disease; mental and substance abuse disorders; and cirrhosis and other chronic diseases liver diseases. If there is a silver lining to this horrible "report card" it is that with appropriate focus of effort, successful improvement should be attainable.

With so much data, and so many competing interests, reporting apparently contradictory analyses, modern American healthcare can often feel complicated and confusing, even to experienced healthcare professionals. Screening for and treatment of breast cancer is a perfect case in point. The development of an independent, charitable, not-for-profit organization with a specific breast care focus is a prescription for improving breast cancer outcomes for a vulnerable population—residents of the rural Appalachia.

Rather than having to wait its turn for funding, based on anticipated financial return on investment (ROI) to a parent organization, an independent, not-for-profit breast care organization could prioritize breast cancer best practice initiatives such as: 3D mammography, contrast enhanced mammography, 3D breast biopsy, cryoablation, intraoperative radiotherapy (IORT), and an Appalachian MammoCare-dedicated nurse navigator, etc., on the basis of anticipated outcome improvements and obtainable funding. Such an initiative would also be more likely than the status quo to foster a shared, collaborative regional effort, for the benefit of all areas of residents. To better understand this idea, let us first explore the most important breast cancer intervention, it is early detection and then go on to discuss a few of the best practice treatment options which should be made available locally.

From the mid-1980s onward, Dr. Laszlo Tabar has been reporting results of the Swedish Two County Trial. That randomized controlled trial, studied the effect of inviting women to have four view screening mammograms at regular intervals. When compared with women who were not invited, the screened women had about a 40% reduction in breast cancer mortality. Importantly the survival advantage was present across all studied age groups of women 40-74.

In **Breast Cancer, the Art and Science of Early Detection with Mammography**, Tabar, et al. (2.) discussed in detail the lessons we should have learned from the Swedish to County Trial. It is a sad

testament to the poor quality of analysis, that this study is not cited by those who have concluded that there is little benefit for women 40 and older to have annual mammograms. This criticism applies most specifically to the 2009 recommendations of the United States Preventive Services Task Force (USPSTF), a publication that has done so much to confuse members of the lay and medical communities.

Analysis of the data of the Swedish Two County Trial, has been widely cited in the medical literature. It revealed that women whose breast cancers were smaller than 15 mm at the time of diagnosis had an 83.8% chance of 20-year disease free survival (cure). Those whose cancers were smaller than 9 mm at diagnosis fared even better. Women whose breast cancers were 20 to 30 mm at diagnosis did substantially worse. Their 20-year disease-free survival was only about 60%. Women with larger than 30 mm breast cancers did even worse. Unfortunately, the average size of breast cancers first identified by physical exam, is about 22 mm. Notably, it has been shown, that the value of detecting breast cancer and surgically removing it before the cancer grows beyond 15 mm surpasses any of the other treatment option(s). This is why an effective early detection program is so important.

The fact that breast cancer screening programs save lives is scientifically irrefutable. The only questions that remain are, "who benefits the most" and "at what cost."

The principal downside of breast cancer screening with mammography is the anxiety and expense that result from "false alarms.". False alarms are those situations where additional imaging or biopsy is recommended on the basis of the screening mammogram, and which are ultimately proven to be of no clinical relevance. Accurate interpretation of screening mammography is essential for minimizing these false alarms. The interpretive skill of individual interpreting physician can be ascertained by analyzing metrics of their mammography interpretations. In essence, looking at their "Report Cards". Cancer detection rates of greater than 4.5 cancers/ 1000 screens, suggests an adequate detection rate has been achieved. Recall rates for additional studies of between 7-10%, coupled with appropriate cancer detection rates, suggests interpreting physicians have sufficient confidence in their own interpretive skills. A positive predictive value of biopsy (# of cancers found/ # of biopsies performed) of 30% or more, with adequate cancer detection rates, serves as a benchmark of satisfactory interpretive skill. The work of interpreting physicians who do not measure up to the standards should be supervised by those who do. Were this kind of policy to be implemented, we would be moving a long way towards improving breast cancer screening outcomes in the US.

Unfortunately, rather than focusing concerns on how to improve the quality of American screening mammography, well-intentioned investigators have chosen to allow us all to ignore the metrics of high-quality mammographic screening. Instead, their efforts get us lost in the weeds, performing meta-analyses of seriously flawed studies, or looking for new methods of screening which are far likely to be practical and cost effective. The 2009 recommendations regarding screening mammography guidelines put forth by the USPSTF is just the most glaring example of a quasi-governmental-created healthcare problem. Because no breast imaging experts were on the task force, by using the meta analyses of numerous flawed breast cancer screening studies, the task force came to a conclusion that is unsupported by a body of sound scientific evidence. Understandably, many doctors rely on the Task Force's recommendations to decide what tests they should order for their patient. Hence the Task Force unwittingly created a situation that continues to adversely impact many Americans.

Despite being vigorously challenged by the very well respected breast imaging experts, such as Drs. Berg, Kopan's, and many others, the USPSTF's recommendations not to screen women in the 40-50 age

group and to offer mammography to women 50 and older only every other year, has gained some influential supporters. As recently as March 2013, the cover of **Consumer Reports** announced "Save Your Life, 3 Cancer Tests You Need, Plus 8 You Don't". (3.) Although there is some very good information in the **Consumer Reports** article, the article appears to suggest that the USPSTF's breast cancer screening guidelines are considered a consensus opinion of medical experts in the field. In point of fact their reported guidelines are not supported by: the American Cancer Society, the Society Breast Imaging, the American Society of Breast Surgeons, the American College of Radiology, or the American College of Surgeons.

The folly of the USPSTF change in breast cancer screening guidelines is strongly criticized by Dr. Daniel Kopan's and his article, "The Recent US Preventive Services Task Force Guidelines Are Not Supported by the Scientific Evidence and Should be Rescinded", **Journal of the American College of Radiology** 2010; 7: 262-264.(4.) This and a companion article, coauthored with Dr. Wendie Berg and others, entitled, "Frequently Asked Questions About Mammography and the USPSTF Recommendations: A Guide for Practitioners", (www.semanticscholar.org/paper/Frequently-Asked-Qu...) is a well-researched argument to continue recommendations for annual screening mammograms for all women of average breast cancer risk 40 and older. (5.)

The scientific basis for reaching this conclusion is thoroughly explained in understandable terms. She and others go even further in an article appearing in the **Journal of the American College of Radiology** 10; 7: 18-27, entitled "Breast Cancer Screening with Imaging: Recommendations from the Society of Breast Imaging and the ACR on the Use of Mammography, Breast MRI, Breast Ultrasound and Other Technologies for the Detection of Clinically Occult Breast Cancer."(6.)

The lifesaving benefits of early detection of breast cancer relies on high-quality screening mammography, performed frequently enough to minimize the interval development of breast cancers 15 mm or larger in between screenings. Tabar has made the point that if, for whatever reason(s), the breast cancer screening efforts fail to increase the detection rate of clinically occult disease and decrease the rate of advanced disease, they will subsequently fail to decrease overall breast cancer mortality.

A generally available innovation in mammography holds out tremendous promise of bringing mammography to a higher level of accuracy. Tomosynthesis, also referred to as 3D mammography, has been shown to substantially improve detection of small breast cancers while decreasing the rate of false alarms. Using 3D mammography, the need for firm compression of the breast, which can be painful for some women, can be mitigated. Firm compression is essential for making high-quality mammographic images. Just as a CT scan contains more clinically important information than plain x-rays of the same body part, so too does 3D mammography when compared with both standard 2D digital or analog mammograms. In fact, currently, the most significant impediment to the wholesale adoption of tomosynthesis for breast cancer screening is probably is cost. The machine capable of performing 3D mammograms cost almost twice as much as a 2D digital unit.

As a consequence of financial issues, in geographic areas where early adoption of this technology has not been viewed as a competitive advantage, tomosynthesis has become available more slowly. This kind of financial challenge can easily be overcome by efficient use of equipment, making sure the screening mammography schedule is full, or by using a shared technologies model, much as that which has been successfully implemented for lithotripsy, stereotactic biopsy, CT, MRI and PET scanning. West

Virginia University's Bonnie's bus, with its mobile 3D mammography unit, is such an example. It is well suited for service areas where fixed tomographic units may not currently be available.

It is quite natural that, as we look to advance best practices, we rely on the advice of experts who have earned our respect for their important contribution a field of shared interest. Tabar, Kopan's, Berg, and Lee have been referenced above as experts in the field of breast imaging. Tom Stavros, Steve Parker, and many others deserve our respect and gratitude as well. In the following review articles, "The Changing World of Breast Cancer – A Radiologists Perspective", Dr. Christine Kuhl, MD, helps us better understand a European radiologist's perspective. (Invest Radiol 2015 September; 50 (9) 615- 628. Published online <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4623842/> and Bonnie Jo and Edward Sickles', in "The Evolution of Breast Imaging: Past to Present": Radiology volume 273, No 25 published online Oct 23, 2014, <https://pubs.rsna.org/doi/full/10.1148/radiol.14141233> covers much the same territory from an American radiologist's perspective.

Moving now from the identification and diagnosis of breast cancer with breast imaging, to surgical breast cancer treatment, what follows is excerpted from Dr. Dennis Holmes' Curriculum Vitae. Dr. Holmes is a well-known and respected breast surgeon. Any of us who are surgeons who treat women with breast cancer should be interested in Dr. Holmes' perspective, (www.drholmesmd.com). Excerpted from his Personal Statement, are areas that deserve further development right here in rural Appalachia:

1. Oncoplastic Surgery, which combines breast conserving surgery and plastic surgical techniques to optimize cancer resection while preserving or enhancing breast appearance and patient quality of life.
2. Intraoperative radiotherapy (IORT). Stemming from an international IORT clinical trial in 2003, this technique for delivering the radiation component of breast cancer treatment in the operating room at the time of surgical resection, has been found helpful for improving the quality of care of early stage breast cancer by reducing treatment burden and radiation noncompliance.
3. Lymphedema surgery. Axillary Reverse Mapping (A.R.M.) is a technique that shows promise in reducing the risk of breast cancer related lymphedema by facilitating the identification and preservation of arm lymphatic drainage.
4. Cryoablation. First used for the destruction of benign breast tumors, " fibroadenomas", its use has been extended to part of the treatment plan of small breast cancers. The American College of Surgeons Oncology Group's Z1072 cryoablation–followed–by–excision feasibility trial showed cryoablation to be highly effective in ablating small breast cancers. Early results of an investigator-initiated multicenter cryoablation-without- excision trial called FROST (Freezing without Resection of Small Tumors) trial, shows excellent early results with cryoablation as an alternative to surgery for stage I breast cancer. Relying on more than merely physically destroying viable tissue, cryoablation is now understood to induce a beneficial systemic immune response similar to that stimulated by radiotherapy. As Dr. Holmes points out, "if cryoablation can be proven effective in killing breast cancer while also enhancing the anticancer immune response (with or without the assistance of pharmacological or other agents), cryoablation could one day provide each of the following: 1) an effective alternative to surgery for selected patients with early stage breast cancer; 2) a neoadjuvant treatment administered with or prior to systemic therapy for higher stage cancer, whether or not surgery is performed; 3) a primary therapy along with systemic therapy for stage IV disease; or 4) a palliative treatment for metastatic cancer."

5. Value-based breast cancer care. Long awaited, this initiative combines innovation, patient centered care, and cost-effective healthcare. More than a particular technique, value-based breast cancer really amounts to a philosophy of care, and must be appropriately adapted each individual patient's needs within the context of her community's resources.

In a personal communication with Dr. Holmes, available upon request, he puts into focus why bringing IORT back to our community is so important and why up to now American radiation oncologists have been slower than might have been expected to embrace this valuable technique.

In conclusion, with so much data and so many competing interests, optimal screening for and treatment of breast cancer in rural Appalachia was complicated and confusing even before COVID-19. For the foreseeable future, hospitals, particularly those in rural Appalachia, will be financially struggling and prioritizing initiatives in "survival mode". Now more than ever, residents of the rural Appalachia need a constructive, hopeful change in the status quo of breast cancer screening and treatment. This article offers a prescription for improving breast cancer outcomes for a vulnerable segment of society by the development of an independent, charitable, not-for-profit organization with a focused mission of improving breast cancer outcomes for residents of rural Appalachia. What remains to be seen, is whether the medical and lay communities of our region are willing to follow the prescription. If they do, might such an endeavor serve as a model for addressing other health care disparities of our region for the benefit of those we are here to serve?

References

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7. Personal Communication with Dr. Dennis Holmes www.drholmesmd.com.