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EPIDEMIOLOGY

The Athena Breast Health Network: developing a rapid learning system in breast cancer prevention, screening, treatment, and care

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Abstract The term breast cancer covers many different conditions, whose clinical course ranges from indolent to aggressive. However, current practice in breast cancer prevention and care, and in breast cancer epidemiology, does not take into account the heterogeneity of the disease. A comprehensive understanding of the etiology and progression of different breast cancer subtypes would enable a more patient-centered approach to breast health care: assessing an individual's risk of getting specific subtypes of the disease, providing risk-based screening and prevention recommendations, and, for those diagnosed with the disease, tailored treatment options based on risk and timing of progression and mortality. The Athena Breast Health Network is an initiative of the five University of California medical and cancer centers to prototype this approach and to enable the development of a rapid learning system—connecting risk and outcome information from a heterogeneous patient population in real time and using new knowledge from research to continuously improve the quality of care. The Network is based on integrating clinical and research processes to create a comprehensive approach to accelerating patient-centered breast health care. Since its inception in 2009, the Network has developed a multi-site, transdisciplinary collaboration that enables the learning system. The five-campus collaboration has implemented a shared informatics platform, standardized electronic patient intake questionnaires, and common biospecimen protocols, as well as new clinical programs and multi-center research projects. The Athena Breast

The members of The Athena Breast Health Network are listed in the Appendix.

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Health Network can serve as a model of a rapid learning system that integrates epidemiologic, behavioral, and clinical research with clinical care improvements.

Keywords Breast cancer · Learning healthcare system · Precision medicine · Transdisciplinary science

Introduction

Breast cancer is now understood to comprise a constellation of heterogeneous diseases, driven by different molecular pathways and host environments, and associated with divergent outcomes [1, 2]. Accordingly, approaches to breast cancer prevention and treatment have begun shifting from a uniform standard-of-care for all women to "precision" medicine, where care is tailored according to patient characteristics [3]. Following the discovery of BRCA1 and 2, women with strong family histories of breast cancer are now referred for genetic testing, and risk-reducing interventions are offered to mutation carriers. For patients diagnosed with breast cancer, hormone receptor and Her2neu status are routinely assessed to guide adjuvant therapy decisions, and molecular markers increasingly influence chemotherapy use [4, 5]. A model for delivery of patient-centered breast cancer care is evolving as a new standard and includes shared decision-making, coordination of treatment by multiple providers, and survivorship care plans [6].

Despite these advances, major challenges must be overcome in order to realize the promise of precision medicine for breast cancer. For example, breast cancer *screening* recommendations are uniform for most women. Primary prevention of breast cancer is not a routine part of care for the general population, and there are few validated markers to identify women at greatest risk of dying from breast cancer, who would benefit most from prevention efforts. Further, while there are a number of established and emerging molecular biomarkers to stratify early stage breast cancer and guide therapy decisions, these tools are inconsistently utilized. For survivors who have completed active treatment, there is a dearth of data on long-term outcomes associated with specific disease biology and patient characteristics, and, accordingly, how best to tailor long-term management.

A learning health care system has been proposed as a means to advance precision medicine for cancer and other diseases. The concept of a learning system refers to the continuous cycle of generating knowledge from clinically relevant research and routine care, rapidly translating new knowledge into practice, and iterative quality improvement—all enabled by integrated information technology [6, 7]. First, a learning system is a collection of information on an "all-comer" patient population, with diverse circumstances and heterogenous disease characteristics, enabling the study of health care interventions and outcomes in typical patient populations. In contrast, large randomized studies, long considered the gold standard of evidence, show benefit applicable to narrowly defined patient populations and may not apply to the full spectrum of real-life patients [8]. Next, comprehensive data on persons at risk of disease are collected at the point of care and aggregated: patient specimens linked to risk factors, disease characteristics, treatment, and outcomes. Today, acquiring these data requires enormous resources, and is done with variable quality [6, 9–11]. Finally, a learning system requires a high degree of cooperation among stakeholders in diverse disciplines for strategic data collection and analyses, and willingness to apply new knowledge to practice. To date, few health care institutions have developed effective systems to support large-scale, transdisciplinary collaboration, and cooperation around care delivery across institutions is not common [6, 12, 13].

This paper describes the inception and early development of the Athena Breast Health Network ("Athena"), a comprehensive demonstration project formed to advance precision medicine for breast cancer prevention and care. Athena was established in 2009 as a system-wide University of California (UC) initiative, and it is developing as a learning system that supports efficient data collection to drive continuous improvement in care, research, and outcomes—consistent with twenty-first century medicine [6]. Key components of Athena are a patient-focused culture, a robust technological infrastructure, and a collaborative environment.

Description

Vision of the Athena Breast Health Network

The Athena Breast Health Network is designed to integrate clinical care and research to drive innovation in patient-centered prevention, screening, treatment, and management of breast cancer. The vision is to reduce suffering from breast cancer and improve survival by accelerating discovery, and the time it takes to implement innovations in clinical practice. When fully implemented, all women who access breast health services at UC medical centers will be part of Athena. Services will span the spectrum of breast cancer prevention, screening, diagnosis, treatment and follow-up care, and the organization is structured to maximize learning from every patient.

Currently, women who enroll in Athena at the time of screening provide information electronically about their health history, lifestyle behaviors, and family history of cancer; routine risk assessment based on these data enables more personalized screening and prevention options. Comprehensive

risk stratification will also be conducted for newly diagnosed breast cancer patients as part of an individualized care plan, designed to provide patients with tailored options for treatment and disease management. Follow-up care for women who have finished active treatment will target individual risk factors and circumstances, including genetic factors, tumor biology, and physical and psychosocial health status.

The Athena network will implement and evaluate new models for care delivery, whereby care can serve as an engine for discovery. Enrollees are invited to share their data and provide a biospecimen for research. Specimen data are linked to patient data, obviating the need for a separate specimen annotation system. Two cohorts, a screening cohort comprised of healthy women and a survivorship cohort of women with new or recent breast cancer diagnoses, are projected to reflect the racial and ethnic diversity of the state of California, and to be of sufficient size to support meaningful analyses of subpopulations. The data set from the screening cohort will include comprehensive, structured risk data *pre-diagnosis*, as well as prospective incidence of new breast cancer diagnoses. For the survivorship cohort, the data set will include patient characteristics present at diagnosis, molecular characterization of host and tumor biology, treatment, and outcomes. Linking these data from individual patients and across cohorts will support the development of improved risk models that predict risk of getting specific subtypes of breast cancer. Athena is thus positioned to advance understanding of breast cancer risk, breast cancer trajectory by subtype and other patient-specific predictors of disease outcomes, and to apply these insights to practice.

An infrastructure to support a learning system

A critical initiative is to develop robust data collection tools and integrated biospecimen and data repositories that facilitate collecting patient-reported, clinical, treatment, and outcomes data in standardized, structured formats that are computable, interoperable, and accessible across clinical and research disciplines.

The Athena shared informatics platform and central registry enable the storage of multiple types of data across institutions. The platform has five major functions: (1) collection and secure storage of longitudinal data from patients and providers, (2) real-time analysis and decision support to enable personalized care, (3) data analytics for both phenotypic and genomic data, (4) integration with prevailing electronic health record (EHR) systems for both data acquisition and personalized reporting, and (5) development of quality improvement tools, including dashboards, which highlight variations in care and outcomes (Fig. 1).

The platform's health questionnaire system provides means for collecting information directly from patients and is currently used to obtain over 100 data elements during the intake process for screening mammography and over 600 for patients diagnosed with breast cancer; extensive skip logic ensures that patients are only asked relevant questions. The questionnaire system can be accessed securely by patients through the web prior to the visit, or on a web-enabled computer or Apple iPad® in the mammography clinic. As of February 2013, ~25,000 women in the screening cohort had taken the Athena questionnaire using a combination of these modalities; approximately 100 diagnosed patients had taken the survivorship questionnaire, which was launched in December 2012. The questionnaire system integrates with EHR systems using health level-7 (HL-7) interface messages for both scheduling information and delivery of resulting reports to the patient record. Real-time breast cancer risk calculations are performed using information from the questionnaire and are reported back to the patient and her primary care provider.

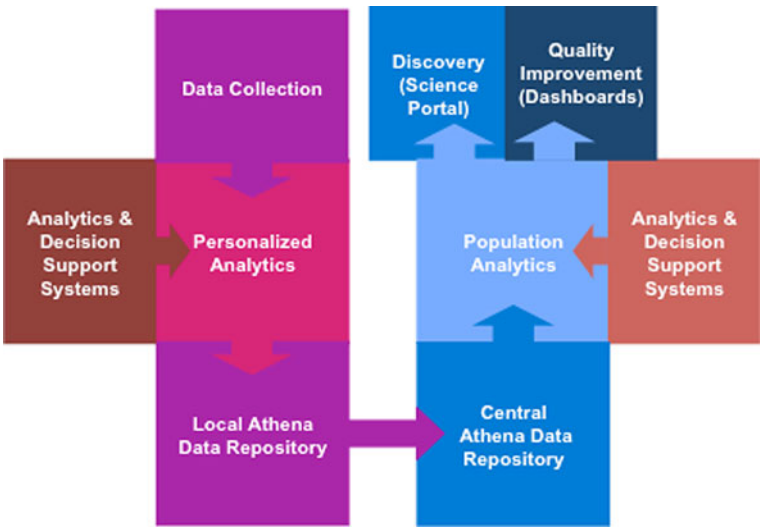

Fig. 1 Schematic of the Athena registry informatics platform

Risk scores are furnished through a web service that currently implements the Gail, Claus, and BRCAPro models, and is being adapted to incorporate others [14].

Presently, the Athena platform's functionality includes a patient-reported data system, personalized risk reporting, and integration with site-specific EHRs. In the near future, the remainder of the Athena platform will be completed and will include modules for diagnosis, treatment, and survivorship, a central registry, a scientist portal with advanced analytic capabilities, and further integration with site-specific biorepositories, radiology imaging systems, and a histopathology image archive.

Standard operating procedures (SOPs) for biospecimen acquisition and processing for future research have been developed. A banking protocol for host biospecimens includes standardized methods for processing plasma, serum, and genomic DNA from either blood or saliva. The SOP has been implemented in Athena statewide, and samples from over 7,800 women in the screening cohort had been collected as of February 2013. A tumor banking protocol prioritizes standard-of-care histological diagnostics and simultaneous retention of molecular data for discovery; key aspects include techniques for co-registration of tissue samples with mammography, workflows to minimize ischemic time, and a common scheme for partitioning tumor specimens for tissue preservation.

Organizational features of Athena

Athena is a statewide, public–private collaboration with primary initial funding from the UC Office of the President and the Safeway Foundation. Participating Network institutions are the five National Cancer Institute- (NCI-) designated cancer centers of the UC system and associated hospitals, which are described in Table 1. Additional participating institutions include the UC Berkeley School of Public Health, the Philip R. Lee Institute of Health Policy Studies at UC San Francisco, as well as private and nonprofit entities.

A matrix organizational structure, designed to maximize cross-site and cross-disciplinary collaboration, underlies the collaboration. A site principal investigator (PI) at each UC medical center coordinates center participation in individual projects, and represents campus-specific requirements and contributions to the network. An Executive Committee, which includes the Athena Founding Director, the site PIs, and individuals in key leadership positions at participating campuses, oversees Athena governance, clinical implementation, and research direction. Three statewide, multi-disciplinary "Clinical Care and Research Teams"—focused on screening and prevention, diagnosis and treatment, and survivorship—are responsible for development and oversight of Athena clinical and research programs. Core Support Groups provide expertise in specific areas, such as pathology, biospecimen management, and questionnaire design. A Central Data Coordinating Group oversees the creation and management of Athena data collection tools and registries. A Consumer and Community Advisory Committee informs clinical and research programs and assists with communication. Finally, a Program Management Office oversees finances, provides project management support, and manages statewide information technology infrastructure.

Early challenges to collaboration

Leaders at the five UC Cancer Centers have previously attempted to develop large, multi-site initiatives, with limited success. The potential advantages to such collaboration are numerous: a wealth of collective expertise; access to a large and diverse patient population, enabling novel clinical studies; an infrastructure to facilitate cross-campus comparative studies; and a clinical coalition to implement new, evidence-based improvements in the care process. Despite past efforts, Athena represents the first instance of a large-scale collaboration that successfully integrates all five UC medical and cancer centers under a broad, unified vision. The challenges faced by Athena during its development phase are instructive. Hurdles to collaboration have been significant. Like most academic institutions, the UC system's promotion policies currently lack incentives for participation in the kind of team approach central to Athena. Furthermore, the perception that Athena will compete with existing programs that enroll overlapping patient populations, rather than facilitate other research, still persists to some degree. Other challenges are operational. At the time of Athena's inception in 2009, there were no means to share patient data among UCs, nor common patient identifiers; pathology reporting systems and biospecimen management systems differed at each site. Despite these challenges, virtually all investigators initially involved in Athena in 2009 are still working actively on its success. Substantial shared infrastructure now exists, and the collaboration has enabled the launch of new clinical care programs and numerous multi-site research projects.

Interim progress: strategic initiatives that integrate clinical care and research

To provide initial focus for the collaboration, Athena leaders developed a set of strategic initiatives designed to address areas of unmet need in tailoring breast cancer prevention and care. Strategic initiatives are listed in Table 2 and described below.

Integrate risk assessment at the time of screening to identify high risk women and tailor prevention and

Table 1 Characteristics of the breast health services provided at the NCI-designated comprehensive cancer centers (CCCs) of the five UC medical centers

	UC Davis CCC	UC Irvine Chao Family CCC	UC Los Angeles Jonsson CCC	UC San Diego Moores CCC	UC San Francisco Helen Diller Family CCC
Is there a dedicated breast service?	Yes	Yes	Yes	Yes	Yes
Screening mammograms performed per year (rounded to nearest 1,000)[a]	18,000	3,000	21,000	7,000	13,000
Diagnostic mammograms performed per year (rounded to nearest 100)[a]	3,500	3,300	3,200	3,200	3,700
Number of new breast cancer patients per year[a]	200–300	100–200	400–500	500–600	600–700
Organization of breast oncology services[a]	Surgery, medical oncology, and radiation therapy are separate programs in the same building; coordinated care is provided.	Surgery, medical oncology, and radiation oncology separate departments with facilities in one cancer center building. Diagnostic mammography and biopsy services are in the cancer center building. Screening mammography is in a separate facility.	Surgery, medical oncology, and radiation therapy are separate entities, except in the case of the multidisciplinary clinic.	Breast surgery, radiation oncology, and breast medical oncology are in separate departments. Breast imaging, breast surgery, breast medical oncology, and part of radiation oncology are in one building. Radiation oncology is also located in two separate facilities.	Surgery, oncology, and radiation therapy programs are combined.
Numbers of dedicated breast imagers[a]	3	2	4	3	5
Numbers of dedicated breast pathologists[a]	2	0 (5 pathologists read breast cases)	4	3	3
Numbers of clinicians providing acute breast cancer care[a]					
Medical oncology	6	3	9	4	9
Radiation oncology	2	4	5	3	3
Surgery	4	3	2	2	3
% clinician effort in clinical care activities[b]					
>75 %	50 %	33 %	50 %	44 %	31 %
51–75 %	0 %	67 %	13 %	33 %	38 %
25–50 %	50 %	0 %	13 %	22 %	8 %
<25 %	0 %	0 %	25 %	0 %	23 %

Table 1 continued

	UC Davis CCC	UC Irvine Chao Family CCC	UC Los Angeles Jonsson CCC	UC San Diego Moores CCC	UC San Francisco Helen Diller Family CCC
Clinician participation in clinical trials for breast cancer[b]					
Investigator initiated	100 %	83 %	75 %	100 %	100 %
Industry sponsored	67 %	100 %	50 %	89 %	92 %
NCI cooperative group sponsored	83 %	100 %	63 %	100 %	85 %

[a] Data estimates from personal communication, 2011–2012

[b] Data estimates based on responses of clinicians participating in a statewide survey, 2011; response rates were: UC Davis—50 %; UC Irvine—75 %; UC Los Angeles—67 %; UC San Diego—100 %; UC San Francisco—81 %

screening strategies This initiative addresses two areas of unmet need: first, that screening programs are generally not tailored to individual risk, and second, that primary prevention is not an integral part of breast health care; conducting routine risk assessment is central to both. Current understanding of breast cancer risk factors, albeit imperfect, nonetheless enables identification of women at high risk who would benefit from counseling about risk and risk-reducing interventions. Athena has implemented automated risk assessment using validated risk models to systematically identify high-risk women when they receive screening mammograms. These women receive referrals for genetic counseling or a high-risk breast clinic, as appropriate, from an Athena Breast Health Specialist, who provides risk consultations and oversees referrals using standardized decision aid tools [15].

The next priority is to develop and test risk-based screening approaches based on emerging data indicating that individual risk factors—primarily breast density, family history, and genetic variants—can be used to personalize frequency and age of initiating screening mammography [16]. Accounting for life expectancy in the elderly and those with substantial comorbid conditions further offers to reduce screening and diagnostic work-up that unduly burden and do not benefit these patients [17]. Longer-term efforts will be directed to identifying and validating markers, including germ-line genetic variants and measures of breast density, that are associated with specific subtypes of disease. Subtype-specific risk prediction will allow improved surveillance and targeted primary prevention for women at high risk of poor-outcome disease, as well as a reduction in over-screening for women whose risk is only associated with indolent disease.

Provide lifestyle interventions to target poor physical health Accumulating evidence indicates that modifiable lifestyle factors, including physical activity, diet, body mass index (BMI), and alcohol consumption, contribute to breast cancer risk in populations at risk and to prognosis for breast cancer survivors [18, 19]. Exercise, maintenance of healthy weight, reduced alcohol intake, and a low-fat, plant-focused diet are generally recommended in the context of breast health and breast cancer risk reduction, as these behaviors contribute to overall health and are generally free of deleterious side effects. However, the evidence is inconsistent with respect to the real risk associated with specific factors, the degree to which lifestyle changes decrease risk, and the populations most likely to benefit. By collecting data on all women and following them over time, Athena provides an opportunity to implement lifestyle interventions in both the screening and survivor cohorts, and, concurrently, to collect evidence relevant to major outstanding questions about lifestyle factors and risk,

Table 2 Strategic initiatives of the Athena Breast Health Network

Strategic initiative	Target population
Integrate risk assessment at the time of screening to identify high risk women and tailor prevention and screening strategies	Breast cancer screening population
Provide lifestyle interventions to target poor physical health	Screening population and post-treatment survivorship population in poor physical health
Reduce false positive biopsies associated with breast cancer screening	Women with suspicious mammography findings
Implement comprehensive risk profiling at the time of diagnosis	Newly diagnosed breast cancer patients
Understand survivorship and the factors that affect breast cancer outcomes	Breast cancer survivors who have completed active treatment
Tailor survivorship care according to risk	Breast cancer survivors who have completed active treatment

including: the degree of lifestyle changes that modify risk, the effectiveness of specific interventions in specific populations, mechanisms of risk reduction, biomarkers of improved health status, and host and disease characteristics that predict benefit.

Reduce false positive biopsies associated with breast cancer screening There is substantial variability in interpretation of mammography images among radiology practices [20]. The Breast Imaging-Reporting and Data System (BI-RADS) was designed to standardize mammography reporting and recommendations. There are seven categories, ranging from incomplete (0) to known malignancy (6). Lesions suspicious for malignancy are assigned a BI-RADS score of 4 (suspicious abnormality) or 5 (highly suggestive of malignancy), and biopsy is recommended for both categories. However, BI-RADS 4 is associated with a wide range of risk of malignancy, 2–95 %, and no distinction is made between risk of invasive or in situ cancer. The primary objectives of this initiative are: (1) to establish BI-RADS reporting mechanisms that distinguish risk for invasive cancer from risk for ductal carcinoma in situ (DCIS), and (2) to set thresholds for biopsy that safely minimize unnecessary procedures for benign and very low risk lesions. As first steps, Athena has developed a library of de-identified diagnostic mammograms associated with known clinical and pathologic outcomes, and has conducted a study to assess variability in use of BI-RADS categories across the five UC medical centers.

Implement comprehensive risk profiling at the time of diagnosis This initiative focuses on improving the use of diagnostic tools to characterize tumors of women with new breast cancer diagnoses. One aspect is optimizing immunohistochemical (IHC) assessment of standard tumor markers, focusing on estrogen receptor (ER), progesterone receptor (PR), HER2neu, and Ki67 ("IHC4"). There is considerable inter-laboratory variation in evaluation of these markers, which can greatly affect disease prognosis and the treatments offered to patients [21, 22]. Anatomic pathologists in Athena are conducting a project to evaluate the variability in assessment of IHC4 across the UC medical centers, to optimize IHC methodology, and to harmonize evaluation. These efforts are intended to improve quality of care, to facilitate implementation of multi-site clinical protocols, and, ultimately, to enable routine generation of an IHC4 signature for Athena patients [23].

Further efforts are directed toward the use of genomic technologies. More comprehensive profiling of tumors of newly diagnosed breast cancer patients is a priority in Athena, intended: (1) to maximize capture of data on existing molecular signatures, and thus provide comprehensive information on prognosis and generate treatment options for patients; (2) to generate data on new and emerging signatures, and thereby support their rapid translation to clinical use; and (3) to produce a unique data set linking molecular tumor data to patient risk factors and outcomes, to support the development of subtype-specific risk models.

Understand survivorship and the factors that affect breast cancer outcomes As breast cancer treatments have become more effective, the number of breast cancer survivors has become large—over 2.7 million as of 2009—and is still growing [24]. These women face risk of disease recurrence and the potential for late effects of treatment and long-term physical and psychosocial effects. This initiative is directed to better understanding the predictors of these long-term outcomes, and how best to provide care to women after acute treatment for breast cancer. One objective is to optimize strategies for survivorship care. An ongoing study has generated information on structures for providing care at each UC medical center and identified

common problems [25]. Data from the study will serve as the basis for bolstering evidence-based practice for survivorship care, and developing interventions to improve quality of care, including use of care plans and care coordination.

A second component of this initiative addresses the biological, psychological, and social factors that affect breast cancer progression and post-treatment symptoms. To this end, data collection from the survivor cohort is designed to identify pre-treatment factors—comorbid conditions and their treatments, psychosocial functioning, and social and physical environment—that predict long-term outcomes including quality of life, cognitive functioning, and overall and disease-free survival.

Tailor survivorship care according to risk Accumulating evidence indicates that timing of recurrence risk differs according to breast cancer subtype. In particular, ER-negative breast cancers carry the highest risk of recurrence within 5 years post-diagnosis, after which risk drops significantly. In contrast, risk of recurrence for receptor-positive disease, although initially lower, persists over 15 years post-diagnosis [2, 26]. It is a priority to gather data on patterns of risk associated with specific molecular subtypes of disease, and to develop and test therapeutic programs—such as long term hormonal therapy—designed to mitigate long-term risk of recurrence. Better understanding prognostic factors will also help tailor follow-up schedules for women based on overall recurrence risk and timing of recurrence, thus minimizing the patient burden of survivorship.

Conclusion

The implementation of Athena's goals and infrastructure is timely, integrating well with innovations and policy developments emanating from the Affordable Care Act. Precision medicine and comparative effectiveness research are central themes in the health care dialogue, and a federal mandate now funds patient-centered outcomes research (pcori.org). At the same time, the science elucidating breast cancer biology, risk, and outcomes has been evolving quickly. This science, coupled with meaningful patient engagement, holds the promise of targeted, high-impact prevention and treatment interventions for women at greatest risk of dying from breast cancer, and a reduction in unnecessary and sometimes deleterious screening and treatment regimens for those unlikely to benefit.

We now have the technology to modernize our approach by merging the processes of care and research, harnessing tools from other industries. Coupled with a framework for effective collaboration and re-engineering of the care process, we can use digital tools to merge the expertise of multiple investigators and institutions, integrate and analyze complex data sets, and create a learning system to quickly advance the state of care. Through its documented planning and implementation process, Athena can serve as a model for the development of transdisciplinary collaboration in research and clinical care—the kind of collaboration that is critical to advance precision medicine.

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Conflict of interest The authors declare that they have no conflict of interest.

Appendix

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References

1. Ellsworth RE, Decewicz DJ, Shriver CD, Ellsworth DL (2010) Breast cancer in the personal genomics era. Curr Genomics 11(3):146–161
2. Esserman LJ, Moore DH, Tsing PJ, Chu PW, Yau C, Ozanne E, Chung RE, Tandon VJ, Park JW, Baehner FL, Kreps S, Tutt AN,

Gillett CE, Benz CC (2011) Biologic markers determine both the risk and the timing of recurrence in breast cancer. Breast Cancer Res Treat 129(2):607–616
3. National Research Council (US) Committee on A Framework for Developing a New Taxonomy of Disease (2011) Toward precision medicine building a knowledge network for biomedical research and a new taxonomy of disease. The National Academies Press, Washington, DC
4. Buyse M, Loi S, van't Veer L, Viale G, Delorenzi M, Glas AM, d'Assignies MS, Bergh J, Lidereau R, Ellis P, Harris A, Bogaerts J, Therasse P, Floore A, Amakrane M, Piette F, Rutgers E, Sotiriou C, Cardoso F, Piccart MJ (2006) Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer. J Natl Cancer Inst 98(17):1183–1192
5. Paik S, Tang G, Shak S, Kim C, Baker J, Kim W, Cronin M, Baehner FL, Watson D, Bryant J, Costantino JP, Geyer CE Jr, Wickerham DL, Wolmark N (2006) Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol 24(23):3726–3734
6. Abernethy AP, Etheredge LM, Ganz PA, Wallace P, German RR, Neti C, Bach PB, Murphy SB (2010) Rapid-learning system for cancer care. J Clin Oncol 28(27):4268–4274
7. Institute of Medicine (US) and National Academy of Engineering (US) Roundtable on Value & Science-Driven Health Care (2011) Engineering a learning healthcare system: A look at the future: workshop summary. The National Academies Press, Washington DC
8. Luce BR, Kramer JM, Goodman SN, Connor JT, Tunis S, Whicher D, Schwartz JS (2009) Rethinking randomized clinical trials for comparative effectiveness research: the need for transformational change. Ann Intern Med 151(3):206–209
9. Bast RC Jr, Lilja H, Urban N, Rimm DL, Fritsche H, Gray J, Veltri R, Klee G, Allen A, Kim N, Gutman S, Rubin MA, Hruszkewycz A (2005) Translational crossroads for biomarkers. Clin Cancer Res 11(17):6103–6108
10. Hood L, Friend SH (2011) Predictive, personalized, preventive, participatory (P4) cancer medicine. Nat Rev Clin Oncol 8(3): 184–187
11. Sung NS, Crowley WF Jr, Genel M, Salber P, Sandy L, Sherwood LM, Johnson SB, Catanese V, Tilson H, Getz K, Larson EL, Scheinberg D, Reece EA, Slavkin H, Dobs A, Grebb J, Martinez RA, Korn A, Rimoin D (2003) Central challenges facing the national clinical research enterprise. JAMA 289(10):1278–1287
12. Disis ML, Slattery JT (2010) The road we must take: multidisciplinary team science. Sci Transl Med 2(22):22–29
13. Hiatt RA, Breen N (2008) The social determinants of cancer: a challenge for transdisciplinary science. Am J Prev Med 35(2 Suppl):S141–S150
14. Evans DG, Howell A (2007) Breast cancer risk-assessment models. Breast cancer research 9(5):213
15. Ozanne EM, Annis C, Adduci K, Showstack J, Esserman L (2007) Pilot trial of a computerized decision aid for breast cancer prevention. Breast J 13(2):147–154
16. Nelson HD, Zakher B, Cantor A, Fu R, Griffin J, O'Meara ES, Buist DS, Kerlikowske K, van Ravesteyn NT, Trentham-Dietz A, Mandelblatt JS, Miglioretti DL (2012) Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. Ann Intern Med 156(9):635–648
17. Walter LC, Lewis CL, Barton MB (2005) Screening for colorectal, breast, and cervical cancer in the elderly: a review of the evidence. Am J Med 118(10):1078–1086
18. Cummings SR, Tice JA, Bauer S, Browner WS, Cuzick J, Ziv E, Vogel V, Shepherd J, Vachon C, Smith-Bindman R, Kerlikowske K (2009) Prevention of breast cancer in postmenopausal women: approaches to estimating and reducing risk. J Natl Cancer Inst 101(6):384–398
19. Patterson RE, Cadmus LA, Emond JA, Pierce JP (2010) Physical activity, diet, adiposity and female breast cancer prognosis: a review of the epidemiologic literature. Maturitas 66(1):5–15
20. Elmore JG, Jackson SL, Abraham L, Miglioretti DL, Carney PA, Geller BM, Yankaskas BC, Kerlikowske K, Onega T, Rosenberg RD, Sickles EA, Buist DS (2009) Variability in interpretive performance at screening mammography and radiologists' characteristics associated with accuracy. Radiology 253(3):641–651
21. Bueno-de-Mesquita JM, Nuyten DS, Wesseling J, van Tinteren H, Linn SC, van de Vijver MJ (2010) The impact of inter-observer variation in pathological assessment of node-negative breast cancer on clinical risk assessment and patient selection for adjuvant systemic treatment. Ann Oncol 21(1):40–47
22. Dowsett M, Nielsen TO, A'Hern R, Bartlett J, Coombes RC, Cuzick J, Ellis M, Henry NL, Hugh JC, Lively T, McShane L, Paik S, Penault-Llorca F, Prudkin L, Regan M, Salter J, Sotiriou C, Smith IE, Viale G, Zujewski JA, Hayes DF (2011) Assessment of Ki67 in breast cancer: recommendations from the International Ki67 in Breast Cancer working group. J Natl Cancer Inst 103(22):1656–1664
23. Cuzick J, Dowsett M, Pineda S, Wale C, Salter J, Quinn E, Zabaglo L, Mallon E, Green AR, Ellis IO, Howell A, Buzdar AU, Forbes JF (2011) Prognostic value of a combined estrogen receptor, progesterone receptor, Ki-67, and human epidermal growth factor receptor 2 immunohistochemical score and comparison with the Genomic Health recurrence score in early breast cancer. J Clin Oncol 29(32):4273–4278
24. http://seer.cancer.gov/csr/1975_2009/
25. Hahn EE, Ganz PA, Melisko ME, Pierce JP, von Friederichs-Fitzwater M, Lane KT, Hiatt RA (2013) Provider perceptions and expectations of breast cancer posttreatment care: a University of California Athena Breast Health Network project. J Cancer Surviv. doi:10.1007/s11764-013-0269-7
26. Natarajan L, Pu M, Parker BA, Thomson CA, Caan BJ, Flatt SW, Madlensky L, Hajek RA, Al-Delaimy WK, Saquib N, Gold EB, Pierce JP (2009) Time-varying effects of prognostic factors associated with disease-free survival in breast cancer. Am J Epidemiol 169(12):1463–1470