

SUMMARY MEMO

To: Marion ('Mhel') Kavanaugh-Lynch, Director
California Breast Cancer Research Program

From: Special Research Initiative Peer Review Committee

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Subject: SRI Peer Review Committee Conclusions and Recommendations

BACKGROUND

The California Breast Cancer Research Program (CBCRP) is the nation's largest state-funded breast cancer research fund with a mission to "...eliminate breast cancer by leading innovation in research communication and collaboration in the California scientific and lay community." To address this mission, CBCRP launched the Special Research Initiative (SRI) in 2004 and allocated 30 percent of its 2004-2009 research funds to support coordinated, directed, and collaborative breast cancer research to further understand the effects of the environment on the development of breast cancer and disparities in breast cancer. The SRI vision and goals as laid out at its inception are shown in Figure 1. Other key features of the SRI's design were that the research was California-based, directed, and collaborative.

SRI Vision	SRI Goals
To identify and support research strategies that increase understanding of, and create solutions to, environmental links to breast cancer and disparities in breast cancer, including solutions to reduce suffering and move us closer to eliminating the disease.	<ol style="list-style-type: none">1. Support a coordinated statewide effort to explore innovative ideas and new theories.2. Leverage California's unique and diverse geographic and population resources.3. Undertake critical studies that significantly move these fields forward.

Figure 1. SRI Vision and Goals

With the SRI, CBCRP embarked on a round of program-directed funding focused on the environmental causes of breast cancer and disparities in breast cancer. In order to plan strategically for the use of the research funding, CBCRP first convened a national advisory group and then asked the advisory group to develop ideas for research themes that would fall under this initiative. The SRI planning process (2004-2007) was a collaborative effort between CBCRP and more than 50 scientific and advocacy experts in breast cancer research in the areas of environmental impact and disparities. The process involved 5 phases of activities:

- The first phase involved recruiting and forming a SRI Steering Committee to provide guidance throughout the strategy development process.
- In the second phase, CBCRP staff, SC, and Science Advisors came together to generate a document with comprehensive information on current research and funding surrounding questions investigated under SRI.
- The third phase involved informing stakeholders and engaging them in developing strategy for SRI. And then recruiting and registering interested investigators.
- The fourth phase involved brainstorming, prioritizing, and developing strategies that coordinate and leverage California resources to conduct research that will have the greatest impact.
- In the fifth phase, the Advisory Council reviewed the recommendations from the Strategy Report and identified the strategies that CBCRP would begin implementing.

When the strategy development process was complete, CBCRP issued individual Requests for Proposals (RFPs) for each identified research project. Figure 2 shows the 9 initiatives for breast cancer research in disparities, the environment, or both disparities and the environment that resulted from the strategy development process. The figure also lists the 17 research projects across 26 grants funded from 2009-2011. These research projects (and the associated grants) were active until 2019.

Throughout the initiative, CBCRP collected evaluation data on the planning and early implementation phases (2010 process evaluation) and on the short-, medium- and long-term outcomes of the initiative (2016-2021 full evaluation). The 2010 process evaluation was designed to review the SRI planning process and early implementation of the first 8 SRI research projects with the goal of identifying initial outcomes from the projects. The methods included document review and interviews. For the full evaluation, the first goal focused on understanding how the 9 SRI initiatives and 17 funded research projects (26 grants) increased knowledge about the prevention of breast cancer by focusing on environmental exposures and health disparities. The second goal focused on collecting and analyzing the research outputs of SRI research projects including data on publications, citations, and follow-on funding after SRI. The methods included, document review, database extraction, surveys, interviews, and focus groups.

In the overall CBCRP timeline, two other initiatives followed the SRI: the California Breast Cancer Prevention Initiatives (2011-2021), and the Preventing Breast Cancer initiative (2017-present).

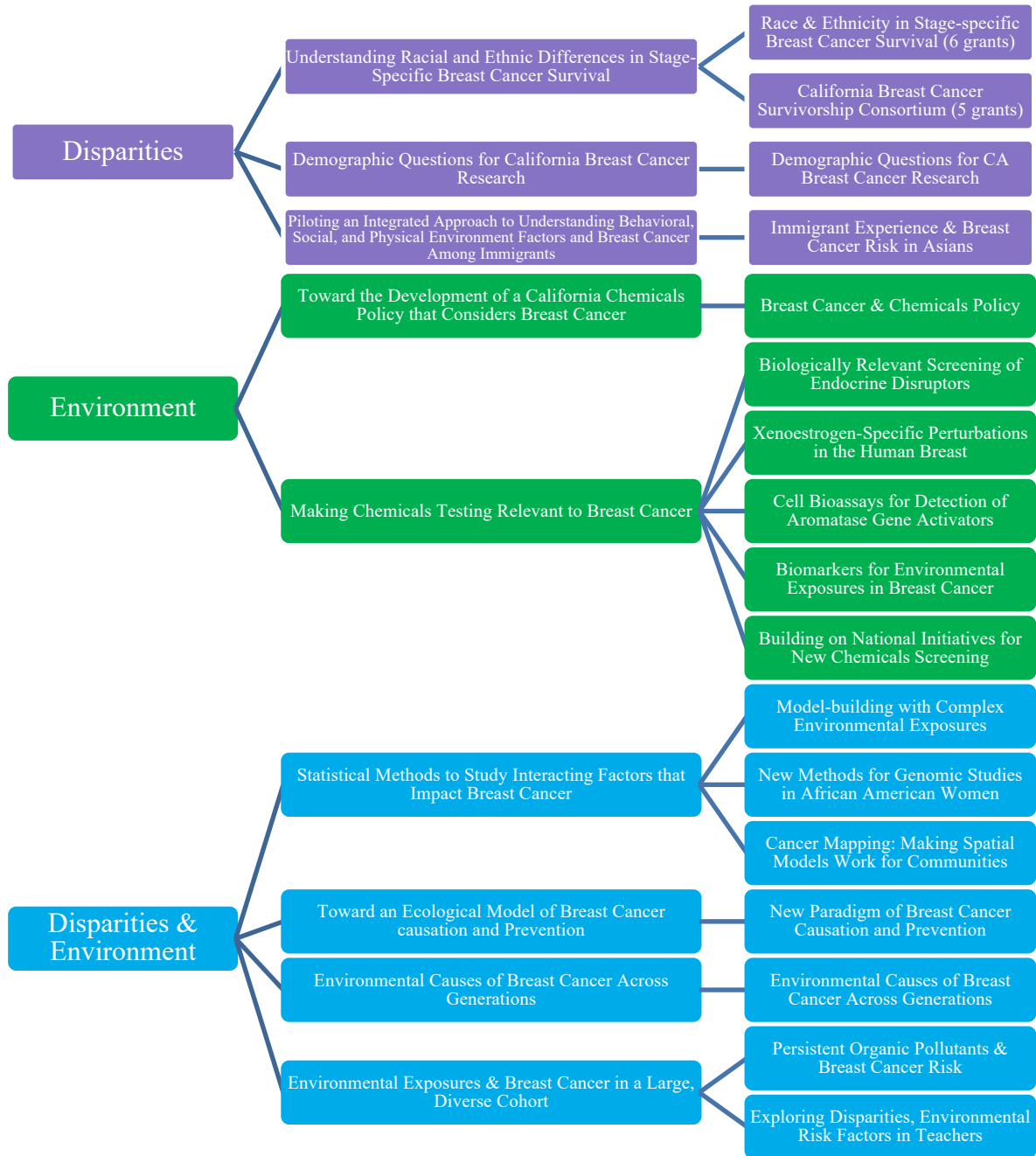


Figure 2. SRI Topic Areas, Initiatives, and Research Projects

The SRI evaluation framework that CBCRP developed specified 5 short-term/process, 5 medium-term, and 10 long-term evaluation questions (Figure 3). CBCRP compiled the evaluation data and findings into an extensive slide deck with detailed notes aligned to this framework.

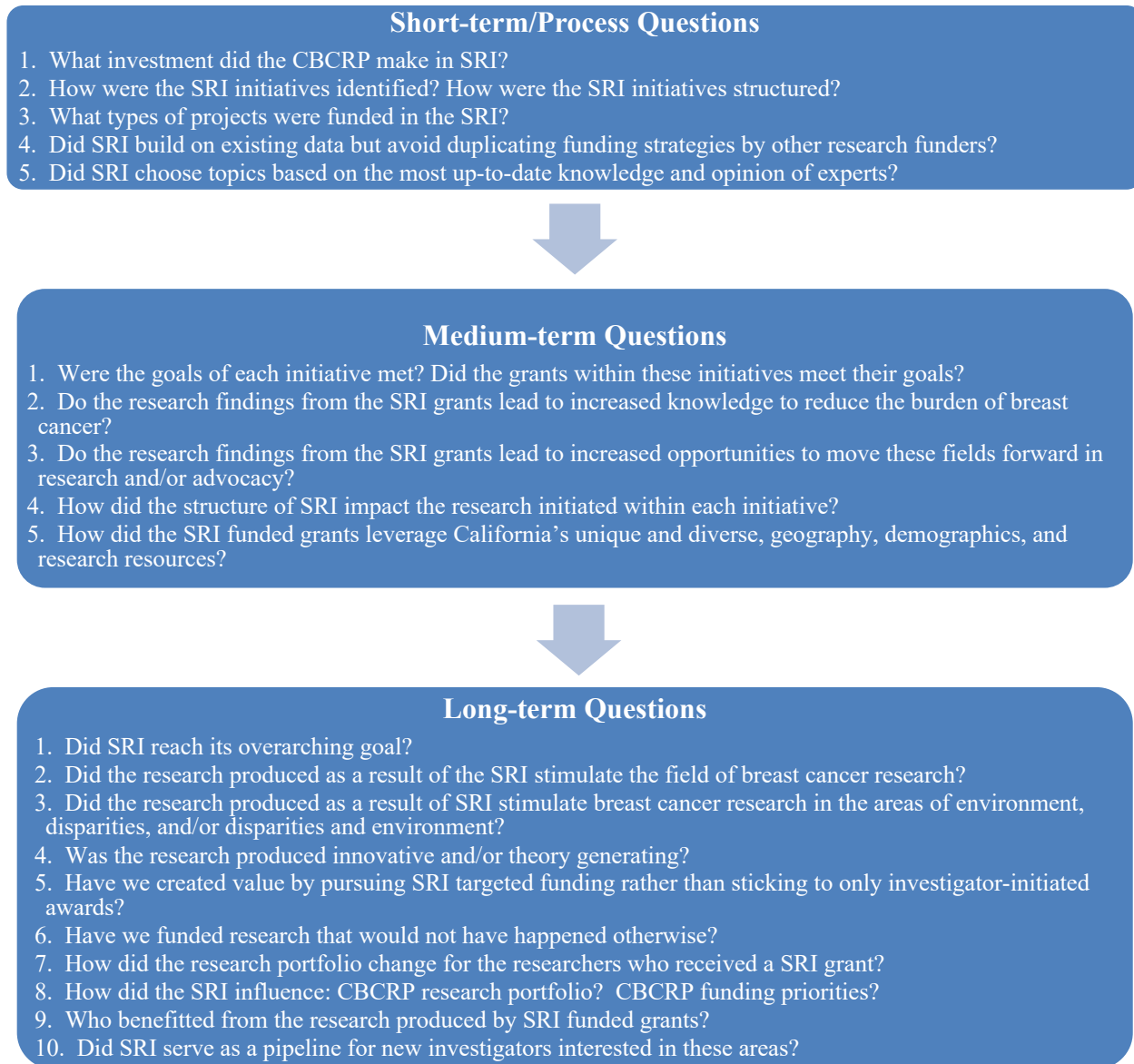


Figure 3. SRI Evaluation Questions

PEER REVIEW COMMITTEE CHARGE

To get a more comprehensive understanding of the outcomes and impact of the SRI, CBCRP embarked on a portfolio review process to convene a peer review committee of breast cancer experts and advocates to review the existing evaluation data and findings. The overall goals of this peer review process were to assess the impact of the SRI, determine whether the overall aims were met, and assess how information gained from SRI can be used to inform future initiatives.

Specifically, we (as the peer review committee) were charged with reviewing the existing evaluation data, assessing results against the SRI evaluation framework, and making recommendations to CBCRP that would be useful for its future funding efforts. The scope of our review was limited to the existing evaluation data and analysis – no new analyses were conducted. RAND’s role was to form the peer review committee, design and manage the peer review process, and support the committee in developing this summary memo.

With this memo, we are summarizing our conclusions and recommendations based on our review of materials, two peer review committee meetings (see Attachments A and B for the slide decks from the two meetings), and discussion and feedback from the peer reviewers (see Attachment C for a slide deck with the discussion notes and other committee feedback).

PEER REVIEW COMMITTEE CONCLUSIONS

PROCESS/SHORT-TERM EVALUATION QUESTIONS

The process/short-term goals focused on the set up process and resulting structure of the SRI, including work conducted during the strategy development process. To assess SRI’s impact on process outcomes, we examined the evaluation indicators listed in the left column of Figure 4.

Overall, we find that CBCRP made an impressive commitment to SRI with well-chosen topic areas and initiatives that were relevant and ambitious. With the SRI, CBCRP identified nine initiatives using a process that involved external scientific leadership, an extensive literature review, and stakeholder input through a formal five-phase strategy development approach. This systematic and comprehensive approach identified topics and gaps in the scientific literature on breast cancer research with a focus on disparities and the social and physical environment. Further, prior rounds of investigator initiated CBCRP funding had failed to elicit proposals to address the gaps that were identified through the strategy development process. Many of the identified gaps are still relevant today.

CBCRP set aside 30% of their funding (\$18M) between 2004 and 2009 to support research projects within the 9 initiatives that addressed several of the gaps identified through the strategy development process, which we believe meant that they were leading the way by providing directed funding during a time when there weren’t many targeted programs in this area. CBCRP used three different funding strategies for proposals that were ultimately funded: Requests for Proposals (RFPs), Requests for Qualifications (RFQs), and Program-directed awards. These funding mechanisms are in order from least CBCRP involvement (RFPs) to greater CBCRP involvement (program-directed) in specifying the research question and aims. In all, we see that

the SRI funded 17 research projects (with 26 research grants) within 9 initiatives distributed across the three topic areas (see Figure 2).

In our assessment, the research grant abstracts and summary final reports aligned closely with the SRI objectives. Within disparities, the overall percentages of applicants and funded grants were good, despite the fact that the initiative that included study participants from immigrant communities had challenges generating low fundable proposals with only one of seven applications awarded. Yet, there was a need to find a way to fund disparities research since not many institutions were funding these types of studies at the time. For environment, the topics were well-received and CBCRP worked with applicants to allow them time to revise proposals before final submissions, offering grantees an opportunity to address proposal limitations prior to funding decisions.

We find it difficult to assess whether SRI avoided duplicating funding strategies by other research funders. While the question is challenging to conceptualize since we do not know if these research projects would have been funded by other organizations, the SRI strategy process to identify underfunded areas of high need, and the survey and interview data from SRI researchers make a compelling case. We did see that SRI appeared to be successful in encouraging investigators to conduct breast cancer research on disparities and/or (chemical) environment. Some investigators continued this area of work after their funded project, even if they were not in these fields prior to their SRI grants. Overall, the increases in disparities and environment funded research projects were positive since these were understudied areas at the time of the SRI. We note that while some SRI investigators were able to find additional funding streams after their SRI research project, other SRI investigators indicated some challenges in receiving more funding.

MEDIUM-TERM EVALUATION QUESTIONS

The medium-term goals focused on outcomes during the research projects and the period surrounding the end of projects. To assess the impact of SRI on these medium-term outcomes, we examined the evaluation indicators listed in the middle column of Figure 4.

Overall, we find that the work resulting from the initiatives clearly contributed to increased knowledge on the specific topic areas, as well as breast cancer more generally. Further, we believe that the initiatives met their goals. Based on an evaluation of the publications that reported on the findings from the SRI, all nine initiatives are represented by publications, though two research projects did not result in any publications. While the Breast Cancer Survivorship Consortium publications seemed low given the amount of funding, we recognize that there is often a time lag between research and publications so we may have missed some information given the timeline of the data provided. Some projects focused on development of infrastructure of breast cancer research, cohorts, and other research tools. The generation of publishable research and contributions of these types of resources to research take long time frames. In all, 74 publications and 1495 citations were noted as of June 2021. Further, we note that these papers are published in high impact journals in general, and several would be considered seminal in the field.

Process/Short-term	Medium-term	Long-term
<ul style="list-style-type: none"> • Description of the strategy development process • Description of the initiatives and funded projects • Applications received by topic and initiative • Grants awarded by topic area and initiative • Grants awarded by funding mechanism • Funding by topic area and initiative • Pre- and post-SRI project counts for SRI investigators 	<ul style="list-style-type: none"> • Description of goals of the initiatives and grants • Publications by topic area, initiative, and grant • Citations over time by topic area • Example presentations and tools • Pre- and post-SRI project counts for SRI investigators • Qualitative information on PI perspectives on whether SRI led to increased knowledge and opportunities • Description of funding mechanisms • CBCRP disparities and environment funding over time • Funding and publications by institution • Degree to which SRI funded projects utilized research resources 	<ul style="list-style-type: none"> • Description of involvement of scientists, advocates, and research administrators in strategy development process • Pre- and post-SRI project counts for SRI investigators • CBCRP disparities and environment funding over time • SRI publications and citations over time by topic area and initiative • Example new methods and technologies • Total number of publications, citations, media mentions, news mentions, academic and non-academic presentations • SRI investigators receiving disparities and environment funding, funding sources • Qualitative information on breast cancer prevention pathway, SRI targeted funding, and impact on pipeline • Description of the gaps identified during the strategy development process • CBCRP projects and funding pre-SRI, during SRI, and post-SRI • Description of CBCRP initiatives after SRI

Figure 4. SRI Evaluation Indicators

For investigators, junior researchers, and post-doctoral students that worked on a SRI funded research project, we find that their experience appeared to have led to increased opportunities, particularly in research. Of those surveyed, three out of seven investigators were funded in environmental (chemical) exposures and breast cancer by National Cancer Institute (NCI), Avon Foundation, and National Institute of Environmental Health Sciences (NIEHS). Also, two out of four investigators were funded in health disparities and breast cancer research by NCI, American Cancer Society (ACS), Department of Defense (DoD), Avon Foundation, and the Komen Foundation. There was not sufficient evidence to address whether the SRI funded research projects led to increased opportunities to move these fields forward in advocacy; more data on the methods used for community engagement and dissemination would also have benefitted our assessment. We note that CBCRP did not yet have an advocacy requirement for all research projects at the time of the launch of the SRI, but they recognized that it was important for researchers to gain experience working with advocates. This is even more important today since other funders are now requesting or requiring research teams to include advocates.

As we noted above, the three funding mechanisms drove grant applications and types, and we find that the directed funding for disparities and the environment made an impact. By developing strong initiatives, CBCRP appears to have driven research to the environment and disparities topic areas. Further, we saw that at CBCRP, there was a clear increase in funding for disparities and environmental (chemical) exposure research in breast cancer over time starting with SRI.

Overall, we find that SRI funded grants clearly built on California-based research resources as well as demographics. California's diversity provided a broad range of resources and collaboration opportunities which we thought was evident in the distribution of grants to various institutions across the state and the high number of publications that resulted. In our assessment, SRI clearly took advantage of opportunities in California to enable robust research and collaborations. For the race/ethnicity categorizations, we noted that it is possible that one study is driving the low proportion of Latinos which might warrant further analysis.

LONG-TERM EVALUATION QUESTIONS

The long-term goals focused on outcomes in the categories of SRI research, SRI researchers, CBCRP, and broad impact of SRI during the period after the end of research grants. To assess the impact of SRI on these long-term outcomes, we examined the evaluation indicators listed in the last column of Figure 4.

SRI RESEARCH

Overall, we find that the goals and vision of the SRI program were met as demonstrated in three ways. First, SRI nurtured and moved research and researchers in the direction of the topic areas. Second, SRI-funded research projects continue to impact the scientific and other stakeholder communities. And third, the volume of publications as well as the depth and breadth of the contributions cited show that the research findings, publications, and other products are timeless and still relevant years later in the current research environment.

We also find that the research produced from SRI stimulated both the field of breast cancer research in general and the specific topic areas of areas of environment, disparities, and/or the combined area of disparities and environment. We think this can be attributed to the thoughtful and comprehensive review CBCRP undertook to initiate this program which identified research gaps in breast cancer research, specifically in the areas of disparities and the environment. At the time, the SRI funding was applied to areas previously overlooked or newly emerging.

In our assessment, SRI-funded research generated novel methods (e.g. the novel screening assays to identify chemicals that cause estrogen dependent breast cancer), fundamental knowledge on new topics (e.g. new statistical methods to analyze African American breast cancer data), and continued publication efforts that have resulted in multiple citations. We find that the research produced was innovative, hypothesis-generating, and relevant long after the SRI program as seen by continued citations, translation into policy, or uptake by new research groups. We believe a key element of this was the collaboration requirement that helped provide an environment conducive to producing innovative methods and novel ideas. Some RFPs required collaboration with other grantees, particularly for initiatives with multiple grants. CBCRP facilitated two meetings: one for epidemiologic studies and statistical methods and another for grantees working on chemical testing. Moreover, some funded investigators expressed that their research portfolio expanded because of their SRI research project. Funded investigators also reported growth in grants focused on environment and disparities from 44% pre-SRI to 59% post SRI, an increase of 15 percentage points, including support from new funders. In turn, we see that these research projects impacted policy through presentations and dissemination into the community and brought new awareness to the science that informs public health and policies relating to the

environment. Further, we acknowledge that CBCRP has invested in sustaining the momentum of the SRI by funding two additional program initiatives.

We note that to better understand the context and the stimulation of SRI funding for long-term assessment it would have been useful to have information on concurrent funding opportunities outside of CBCRP on disparities, environment and/or both disparities and environment. Further, we believe that it is also possible that the expanded portfolio of researchers may continue to generate valuable findings for these topics but the information to make this assessment is not currently tracked. As mentioned in the medium-term goals section, there were 74 publications and 1495 citations generated from the SRI research projects as of June 2021. In recent years, there was an exponential growth in the citation index, and we think that this demonstrates how the findings are still relevant. However, we recognize that the impact of the research by SRI funded research projects themselves may not yet be fully realized, and that the research findings may continue to have impact for several more years.

SRI RESEARCHERS

For researchers, we find that SRI funding increased the research areas of environment as well as the combined topics area of disparity and environment in the post-SRI portfolios of SRI-funded investigators. In general, in these topic areas, research project counts increased by 15 percentage points and funding increased by 16 percentage points for SRI-funded investigators after their SRI funded research project. We do note that post-SRI research projects did not include disparities only projects but did include projects in the combined topic area of disparities and environment. We believe that this change in the research portfolio of SRI-funded investigators was for some investigators driven in part by an increase in funding from a diverse array of breast cancer-specific funding sources. At the time of the survey, SRI investigators identified SRI funding as a key source for their funding in breast cancer prevention that wasn't being addressed by other sources. In our assessment, the contribution of SRI funding to fill funding gaps underscores the significance of the SRI.

We also find that SRI served as a pathway for new investigators to move into the areas of environmental research and health disparities. With three out of four graduate students and six out of seven post-doctoral fellows and junior faculty continuing work in the areas of their SRI-funded research (as of 2017), we see this as an impressively high proportion of SRI investigators progressing in the same line of research as their SRI research project.

CALIFORNIA BREAST CANCER RESEARCH PROGRAM

We find that SRI program-directed funding and structure allowed for leveraging targeted awards to fund research in the identified topic areas, and it is possible that this work wouldn't have happened without the support of the SRI. We see this as consistent with feedback from SRI investigators who agreed that a targeted approach for SRI added value with some investigators noting that they felt that their SRI research would not have happened without the SRI funding. In our assessment, the continuity of the work and funding mechanisms first introduced by SRI are unique and can be observed in the transitions to the next Program Initiatives at CBCRP.

The SRI and the two following program initiatives demonstrate increased funding in the CBCRP research portfolio in the areas of disparities and environment, as compared to funding prior to the SRI. When looking at the CBCRP portfolio using the International Cancer Research Partners (ICRP) categories before, during, and after the SRI, it does appear that post-SRI, the proportion of the funded research projects in “Cancer Control, Survivorship and Outcomes Research”, “Causes of Cancer/Etiology”, and “Prevention” increased although the number of projects overall decreased. In general, environment maps to “Causes of Cancer/Etiology”, disparities maps to “Cancer Control, Survivorship and Outcomes Research (CCSOR)”, and prevention usually maps to “Prevention” but can also go to CCSOR.

We also recognize that SRI’s early efforts to identify key gaps in the literature were important and guided the funding into understudied and underfunded areas. As mentioned above in the “Research” section, we note that it is challenging to answer whether other funders would have funded these research areas without having the funding context for the time period. We would also find it helpful to know other concurrent funding mechanisms to help to clarify the contribution of the SRI in the overall funding climate.

BROAD IMPACT

We find that the SRI and SRI-funded research benefited by working with many different stakeholders. We see that the SRI benefited researchers, both newer researchers brought into the topic areas and established researchers who pursued new directions. Junior investigators and those focused on environment and prevention, in particular, were advantaged by the SRI. We find that the SRI funded research impacted the greater breast cancer, environmental health, and health disparities scientific communities through the creation of new knowledge published in high impact scientific journals. In our assessment, there was some evidence that the SRI and SRI-funded research informed the larger scientific community, policy makers, and general public.

We believe that CBCRP was a leader in recognizing the value of the advocate role, both promoting it and training researchers to work with advocates in cancer research. We find that the move toward a stronger emphasis on advocate engagement and communication that evolved during the course of the SRI was important. We note that since advocates are usually tasked with disseminating the research information to the community it would have been helpful to see in more detail how or whether that was achieved.

OVERALL ASSESSMENT

We find that SRI’s targeted approach was clearly effective in addressing gaps identified during the comprehensive strategy development process and creating synergy among the cohort of SRI-funded research projects. Further, we believe that an investigator-initiated approach would not have produced such a diverse set of work in ways that targeted approach can encourage researchers to bring focus to a specific area and innovation and creativity to address the identified gap. However, the review panel collectively felt that there is always a need for a balance between targeted and investigator-initiated approaches in order to fund the best quality work.

We also find that the SRI nurtured research in the field in a way that was sustainable as demonstrated by researchers and post-docs continuing to work in this field post-SRI and by ongoing funding through CBCRP's follow-on initiatives that committed 50 percent of research funds to the California Breast Cancer Prevention Initiatives and Preventing Breast Cancer: Community, Population, and Environmental Approaches. We do note that this sustainability depends on continuing attention and cultivation of this kind of work since there continues to be needs in this area.

RECOMMENDATIONS

We recommend that CBCRP continue this funding approach to address environmental health and disparities in breast cancer and consider replicating it in other topic areas within breast cancer research. The strategy development process and program initiatives with the SRI were successful in terms of addressing gaps in the field of disparities and/or environmental (chemical) exposure in breast cancer. We make this recommendation based on the strong data, including the seminal papers and important studies that resulted from this set of initiatives. We note that a comprehensive gaps identification may not be needed in the future or necessary for all topics, or there may be less labor-intensive ways to identify research priorities

Further, we believe that replicating this kind of targeted approach can also address disparities among researchers and institutions. Too often, larger, research-intensive institutions and successful researchers receive continued support from a variety of funding agencies. A targeted approach such as the SRI can help support a diversity of researchers at all career levels and can target minority serving institutions that have not traditionally applied or been successful with other agencies and CBCRP research programs. Supporting diverse researchers and institutions is critical to studying breast cancer disparities and can identify important research gaps.

We also recommend that CBCRP consider additional longer-term or delayed impact measures for the SRI and future initiatives since the full impact of SRI research may not yet be observed. We suggest CBCRP:

- Continue to capture publication and citation counts over time to see the ongoing impact of the research that was generated from SRI.
- Collect additional data on co-investigators, junior faculty, post-doctoral students, and graduate students to better understand career trajectories and characterize success and drivers of success (e.g., total number trained, number of publications, subsequent employment, and funding).
- Develop a framework for analyzing qualitative data.
- Gather more actionable feedback from advocates on dissemination into the community and the community value of the initiatives.
- Collect data on concurrent national and state-level funding programs in areas targeted by future initiatives to enable assessment at policy and funding levels

Overall, we commend CBCRP for its success with the SRI and appreciate the opportunity to review the SRI and its progress and outcomes.