Translating Research into Practice (TRIP)

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Statistical Analysis Plan *pages 53-55*

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1 List of Abbreviations

Abbreviations	Definitions
AB	Aunt Bertha
BMC	Boston Medical Center
BU	Boston University
BIDMC	Beth Israel Deaconess Medical Center
BWH	Brigham and Women's Hospital
BWFH	Brigham and Women's Faulkner Hospital
COC	Commission on Cancer
CTSI	Clinical and Translational Science Institutes
DFCI	Dana Farber Cancer Institute
DSMP	Data Safety Monitoring Plan
EHR	Electronic Health Record
HRSN	Health Related Social Need
MADPH	Massachusetts Department of Public Health
PN	Patient Navigator
SDOH	Social Determinants of Health
TRIP	Translating Research into Practice

2 Protocol Summary

Title:	Translating Research into Practice: TRIP
Population:	Newly diagnosed breast cancer patients 18 years or older who live within a 35 mile radius of Boston, MA and have any of the following risk factors for delays in care: are Black and/or Hispanic race/ethnicity, do not speak English as their primary language, and/or have only public insurance or are uninsured at the time of diagnosis.
Intervention:	Implementation of three evidence-based tools that facilitate timely treatment: (a) shared patient registry to identify and track patients from diagnosis through treatment; (b) systematic screening for SDOH with a web-based platform to support a personalized referral plan to regional resources; and (c) one-on-one patient navigation services. The integration of these tools into one integrated model of care will become the standard of care at each participating site, with the aim to improve the quality and timeliness of care delivery, for minority and/or low-income women with breast cancer.

Objectives:	The main study objective is to implement an evidence-based integrated care delivery model (patient registry, screening for social determinants of health (SDOH) and patient navigation) across six health systems in Boston and evaluate the impact on clinical care outcomes among minority, low-income women with breast cancer. The primary objective is to test the clinical effectiveness of the intervention, as measured by the time to first cancer treatment and receipt of guideline concordant care. The secondary objective is to evaluate the implementation of the intervention (fidelity to intervention protocol, local adoption/sustainability, and acceptability).
Design/Methodology:	We will conduct a stepped wedge hybrid effectiveness-implementation trial. The intervention proposed is a systems intervention. All subjects will be newly diagnosed breast oncology patients at one of the six participating clinical sites. In a stepped wedge design, sites are randomized to the time the site begins to implement the intervention and stratified by size. This will occur over an 18 month period, with a new site initiating the intervention every three months over this period. Historical data from each site serves as the comparison. Thus, 24 months prior to the time when the intervention begins at each site, women who meet the eligibility criteria will be given usual care (control) arm. Newly diagnosed cancer patients at the site after the time allocated to begin the intervention will be in the intervention arm. There will be no crossover.
Total Study Duration:	August 2018- July 2022
Subject Participation Duration:	Varies depending upon each patient's recommended cancer care as directed by their care team. Study participation will not influence the care recommended by the treatment team. Clinical outcomes will be collected from 0 to 24 months from the time of cancer diagnosis.

3 Background/Rationale & Purpose

3.1 Background Information

In Boston (Massachusetts) inequities in breast cancer mortality have persisted and increased among Black, non-Hispanic women compared to women of other racial/ethnic groups. These inequities were reported in a national study of breast cancer mortality disparities in the 50 largest U.S. cities and confirmed in local, more current data from the City of Boston and Commonwealth of Massachusetts public health departments. From 1990-1994 to 2005-2009, the Black-White breast cancer mortality rate ratio in Boston increased from 0.94 to 1.49. Local data for the period 2007-2012 show a continuing Black-White mortality rate ratio of 1.36, as well as a Black-Hispanic mortality rate ratio of 4.60 and a Black-Asian mortality rate ratio of 5.28. From 2001-2012, this health inequity resulted in 74 excess Black deaths among women less than 65 years. The inequity is especially striking given that Black women in Boston receive mammography screening at the same rates, have approximately equal likelihood of presenting with advanced disease (4-5%), and had a lower incidence of breast cancer than White women

during this time period. Eliminating disparities requires evidence-based interventions that address barriers to care in communities at risk.

The transfer and application of scientific evidence into everyday practice is necessary to mitigate health disparities, yet roadblocks persist in broad implementation of evidence-based interventions among vulnerable communities experiencing disparities. The *Boston Breast Cancer Equity Coalition* was formed in 2014 in response to persistent city-wide disparities in breast cancer mortality among minority, low-income women. The *Coalition* identified three evidence-based strategies known to reduce delays in care that have yet to be deployed into clinical practice, due to a lack of implementation strategies.

Translating Research into Practice (TRIP) draws upon the principles of community-engaged dissemination and implementation science to systematically facilitate deployment and utilization of: (a) regional patient registries; (b) systematic screening for SDOH with a personalized referral plan; and (c) patient navigation services into one integrated model of care to improve the quality and effectiveness of care delivery, in this case for minority and/or low-income women with breast cancer. The four Massachusetts CTSA hubs (Boston University, Harvard University, Tufts University, and University of Massachusetts) partnered with the *Boston Breast Cancer Equity Coalition* to overcome barriers to widespread implementation and dissemination of evidence-based practices that will improve the delivery of guideline-concordant care to vulnerable women.

Research Question

The goal of this study is to overcome barriers to widespread implementation and dissemination of evidence-based practices that will improve the delivery of guideline-concordant care to vulnerable women.

We plan to develop the three individual TRIP components (patient registry, systematic screening for SDOH using Aunt Bertha platform, patient navigation), and refine and integrate the intervention components into a cohesive package that can be implemented within the context of the clinical work flow of the partnering sites.

Hypothesis

Our main hypothesis is that widespread implementation of these tools will eliminate care delivery disparities by reducing delays in time to first treatment. CTSA hubs have the translational expertise to overcome barriers to such implementation.

All participating sites currently provide patient navigation services, but none have evidence-based protocols, functional registries or social determinants of health platforms to support their patient navigation programs. As an integrated care delivery model, TRIP will benefit patients with breast cancer through individualized support and guidance. The only potential risk is a breach of confidentiality of data shared among the navigation network and the research team. This study will be conducted in compliance with the protocol, applicable regulatory requirements, and BMC/BU Medical Campus Human Research Protection policies and procedures.

3.2 Rationale and Purpose

The TRIP intervention addresses a critical gap in the research enterprise, namely the transfer and application of scientific evidence that is necessary to mitigate health disparities into everyday practice. TRIP includes an integrated, multi-component intervention that builds from preliminary work of the investigative team and their community partner, the Coalition. Using a community engaged approach, this study is designed to overcome barriers to widespread implementation and dissemination of evidence-based practices that will improve the delivery of guideline-concordant care to vulnerable populations. Innovations include: a collaborative community-driven approach, the regional patient registry, the Aunt Bertha Social Determinants of Health (SDOH) platform and the study design.

4 Objectives

4.1 Study Objectives

The main study objective is to conduct a stepped wedge hybrid effectiveness-implementation trial at six health systems (Beth Israel Deaconess Medical Center, Boston Medical Center, Brigham & Women's Faulkner Hospital, Dana-Farber Cancer Institute, Massachusetts General Hospital and Tufts Medical Center) in Boston caring for minority, non-English speaking and/or low-income women with breast cancer to assess clinical effectiveness and implementation of the integrated intervention (patient registry, Aunt Bertha SDOH platform, and patient navigation).

The primary objective is to test the clinical effectiveness of the intervention, as measured by the time to first cancer treatment and receipt of guideline concordant care. The secondary objective is to evaluate the implementation of the intervention (fidelity to intervention protocol).

4.2 Study Outcome Measures

4.2.1 Primary Outcome Measures

Our primary study outcome is ***Time to initiation of cancer treatment****,* a continuous outcome defined as the number of days from diagnosis (Time 0) to treatment initiation (Time 1). Treatment initiation is defined as the time from biopsy until first treatment for cancer, either surgical, radiation, or systemic therapy. **Table 2** displays the specific data elements that will be used to define treatment initiation. As some patients have had pre-operative chemotherapy or hormone therapy, the time period will vary for each patient. This outcome has been widely used in existing navigation studies, as it has been linked to mortality and survival outcomes. Our study is powered on this clinical effectiveness outcome.

4.2.1.1 *Table 1. Data Elements for "Time to Initiation of Primary Breast Cancer Treatment" Calculations*

Time period	Date of
Time 0	**First definitive tissue diagnosis (i.e. biopsy)**
Time 1a	**First definitive surgical procedure (lumpectomy or mastectomy)**
Time 1b	**First external radiation therapy session**
Time 1c	**First chemotherapy infusion**
Time 1d	**First prescription for hormone therapy given**

4.2.2 Secondary Outcome Measures

Secondary clinical outcomes include select measures of ***Guideline Concordant or Quality cancer care***, as defined jointly by the Commission on Cancer and the National Comprehensive Cancer Network. Specific measures of guideline concordant/quality care (yes/no) are defined in ***Table 3.*** These measures of quality will allow us to monitor initiation and completion of specific types of cancer therapy (radiation, chemotherapy and hormonal therapy) for different subsets of women.

4.2.2.1 *Table 2. Secondary clinical outcomes: Guideline Concordant Care Quality Measures*

Treatment Domain	CoC* Criteria for Quality Cancer Care
Radiation	**Radiation therapy administered within 365 days of diagnosis for women < 70 years receiving breast conserving surgery.**
	Radiation therapy is recommended or administered following any mastectomy within 1 year (365 days) of diagnosis of breast cancer for women with ≥ 4 positive regional lymph nodes.
Chemotherapy	**Combination chemotherapy administered within 120 days of diagnosis for women <70 with AJCC T1c N0 M0, or Stage II or III ERA and PRA negative breast cancer.** **Completion of all planned chemotherapy cycles**
Hormonal	**Tamoxifen or third generation aromatase inhibitor administered within 365 days of diagnosis for women with AJCC T1c N0 M0, or Stage II or III ERA and/or PRA + breast cancer.**
***CoC=Commission on Cancer;** [**https://www.facs.org/quality%20programs/cancer/ncdb/qualitymeasures**](https://www.facs.org/quality%20programs/cancer/ncdb/qualitymeasures)	

Outcomes that pertain to the implementation of the intervention in routine practice will be assessed through fidelity to the intervention protocol.

Fidelity to Intervention Protocol

The assessment of intervention fidelity will utilize existing databases developed for the intervention components, protocol adherence monitoring reports, which will be reviewed at monthly in-person PI meetings (See Table 3). As part of their routine functions, navigators utilize these systems to track and monitor their activities and keep track of individual patients. Monthly aggregate reports using these databases will be generated for each navigator and reviewed by the study team. If a navigator does not achieve high levels of performance as determined by their adherence to navigation guidelines for the program, they will receive training buffer sessions as needed. If performance deficiencies are identified across navigators in specific areas, group meetings will be held to determine if protocol modifications are needed.

4.2.2.2 *Table 3. Implementation outcomes*

	Target	Data source	Time Period	Example Metrics

Fidelity to intervention protocol	Navigators	REDCap Registry	Monthly reports during intervention period	- adherence to the intervention protocol: (% elements on navigator protocol achieved, noted areas of deficiency)
	Navigators	Aunt Bertha Social Needs Screening platform	Monthly reports during intervention period	-adherence to the social determinants of health screening protocol: (% elements on navigator protocol achieved, noted areas of deficiency)

5 Study Design

5.1.1 Study design

We will conduct a randomized stepped wedge design. This pragmatic design involves a sequential, randomized roll-out of the intervention across 6 participating clinical sites over 3-month intervals or "steps". Thus, each site receives the intervention. **Table 4** details this approach: 21-month full historical control period followed, sequential roll out of the intervention every 3 months over an 18-month period, then an additional 24 months of full study intervention. A 3-month wash-out period between the end of the historical control collection period and the beginning of the intervention roll-out period is designed to minimize subject crossover contamination. Subjects diagnosed with breast cancer during the washout periods will be excluded from analyses.

5.1.1.1 Table 4. Stepped-wedge design of site rollout 2018-2019

		21 Month Full Historical Control Period			Rollout Period				24-Month Full Intervention Period								
	Pre-TRIP	Year 1			Year 2				Year 3				Year 4				Year 5
Sites	HISTORICAL CONTROLS	Sept-Nov 2017	Dec 2017- Feb 2018	March-May 2018	June-Aug 2018	Sept-Nov 2018	Dec 2018- Feb 2019	March – May 2019	June – Aug 2019	Sept – Nov 2019	Dec 2019 –Feb 2020	March – May 2020	June – Aug 2020	Sept –Nov 2020	Dec 2020- Feb 2021	March – May 2021	June – Sep 2021
1	Aug 2016→ May 2018			Wash-out (3M)	BW-Faulkner Hospital												
2	Aug 2016 → Jun 2018				Wash-out (3M)	Beth Israel Deaconess Medical Center											
3	Aug 2016 → Sep 2018					Wash-out (3M)	Tufts Medical Center										
4	Aug 2016 → Dec 2018						Wash-out (3M)	Boston Medical Center									
5	Aug 2016 → Mar 2019							Wash-out (3M)	Mass. General Hospital								
6	Aug 2016 → Jun 2019								Wash-out (3M)	Dana-Farber Cancer Institute							

5.1.2 Randomization scheme

Consistent with a stepped wedge design with one site implementing the intervention per step, prior to the collection of data in the pre-intervention period, a set of uniform random numbers has been generated for each of the six clusters to assign a starting period for the study intervention. There will be no crossover of patients from usual care to the intervention. That is, patients at each site during the pre-intervention period will experience only usual care and those enrolled after the initiation of intervention will experience the intervention.

5.1.3 Study sites

The city of Boston and surrounding area is home to 4 Clinical & Translational Science Institutes that will be working together to develop and lead the TRIP project. MA Cancer Registry data identified the following characteristics of Greater Boston residents with greatest delays in breast cancer treatment: Black, Hispanic, non-English speaking, public health insurance. Over 90% of these women are provided care by 6 health systems in Boston. Therefore, the study team has partnered with these 6 health systems for this study. Thus, this study is a collaborative effort comprised of **4 CTSI hubs** and **6 distinct Boston-based clinical sites** as outlined in table 5 below.

5.1.3.1 *Table 5. Overview of clinical and lead sites*

CTSI hubs	Clinical Site
Boston University CTSI	Beth Israel Deaconess Medical Center
Harvard Catalyst CTSI	Boston Medical Center
Tufts CTSI	Brigham and Women's Faulkner Hospital
University of Massachusetts Worcester CTSI	Dana Farber Cancer Institute
	Massachusetts General Hospital
	Tufts Medical Center

5.1.4 Study subjects

All adult females (18 years or older) with a new breast cancer diagnosis receiving or planning to receive care at a participating site during the study period will be eligible for inclusion if they have a residential ZIP code within a 35 mile radius of Boston and have any of the following risk factors for delays in care: are Black and/or Hispanic ethnicity, speak Non-English as their primary language, and/or have only public or no form of health insurance. Based on MA Cancer Registry statistics, **1,300** study subjects are expected over the study period (633 controls, 667 intervention) as outlined below in table 6.

5.1.4.1 *Table 6. Expected Recruitment Projections*

Sites	Control	Intervention	Total
Boston Medical Center (BMC)	224	224	448
Beth Israel Deaconess (BIDMC)	85	128	213
Brigham and Women's/ DFCI	156	104	260
Faulkner Hospital (BWFH)	58	108	166
Tufts Medical Center (TMC)	32	39	71
Massachusetts General Hospital (MGH)	78	64	142
Total	633	667	1300

5.1.5 Accrual and Enrollment

As the intervention is a health systems intervention targeting specific vulnerable patients seeking care across each of the participating health systems, TRIP's partner sites have agreed to roll out the intervention as a new navigation standard of care. As such, all patients meeting study enrollment criteria also meet these new navigation standards. Thus, it is expected that all eligible subjects will be enrolled into the study for the purposes of our effectiveness testing. All women will receive usual clinical care as directed by their treatment team. Navigators are employees of the clinical site and typically are part of the care team for these patients. Given this, and the fact that the intervention is low risk and likely to only improve care delivery, the study team will obtain a waiver of informed consent for study subjects, as it is not practical to obtain their consent and their rights and welfare are protected by rigorous confidentiality measures for the Electronic Health Record (EHR) data.

5.1.6 Data Sources/Collection

(1) The Electronic Health Records (EHR) will serve as the data source for all socio-demographic and clinical covariates, as well as the primary and secondary clinical effectiveness outcomes for historical controls and intervention subjects. At Boston Medical Center the EHR will also be used to source social needs screening data from a parallel instance of Aunt Bertha called THRIVE. The THRIVE SDOH for TRIP patients will be retrieved from BUMC's Clinical Data Warehouse (CDW) and merged with the social needs screening data from the TRIP instance of Aunt Bertha by the TRIP analyst. The clinical and demographic EHR data from the 6 sites will be used in two ways: 1) to create a *potential patient list* to aid Patient Navigators in identifying potentially eligible patients with new breast cancer diagnoses (these data will be kept at the clinical site) and 2) treatment data needed for TRIP analysis (i.e., Chemotherapy regimens)

Treatment variables will be *manually abstracted* for both historical controls and enrolled intervention subjects. Abstraction into a HIPAA compliant REDCap form will be completed by trained study personnel 16-18 months after diagnosis to ensure complete treatment information is documented through the 12 months following diagnosis. The electronic health records will also be used to obtain patient contact information (mailing address and phone number) for patient interviews assessing patient acceptability of the intervention.

(2) The REDCap registry and SDOH screening platforms (Aunt Bertha, THRIVE, QuickBase) are the main sources of implementation (Fidelity) data. Each will provide measures of fidelity to the intervention protocol. Navigators utilize these systems to track and monitor their activities related to individual patients. Monthly aggregate reports will be generated for each navigator, reviewed by the study team and used for performance improvement throughout the study. Fidelity metrics include categorical assessments of navigator use of these tools, and will be linked to outcomes. The REDCap registry and SDOH screening platforms will also be used to identify navigated patients for patient acceptability interviews. Only patients who have been contacted by a TRIP patient navigator and screened for social determinants of health will be contacted for participation in interviews.

(3) Cost Surveys will be completed by both study personnel and site administrators to systematically track all costs associated with the development and delivery of the multi-component intervention to estimate the costs that would be required to implement in practice. Patient Navigators and their Supervisors will fill out cost surveys daily for two weeks (10 consecutive working days), listing their time spent on a variety of navigation activities.

(4) Qualitative Implementation Data Collection via the following activities will be the source of our fidelity, acceptability, and penetration implementation data.

a. **Observations:** The study team will observe patient navigators in 4-hour sessions to 1) gain a more complete understanding of adherence to the core patient navigation intervention guidelines, and 2) determine barriers and facilitators to implementation of the patient navigation protocol. Observers will be observing the navigation process and the workflow of the navigators, but will not collect any patient information or PHI.

b. **Key Informant Interviews:** The study team will interview the patient navigators delivering the intervention as well as other members of the care team who are not directly involved with TRIP, but who play a role in the navigation process, in order to assess the acceptability and penetration of the intervention. An interview guide (See **Appendix I, II, III**) for each group was created with sections for demographic questions, general knowledge and opinions of TRIP overall, intervention acceptability and penetration, and component specific questions about the navigation guidelines, the Aunt Bertha platform, and the shared REDCap registry.

c. **Patient Interviews:** The study team will interview patients who received TRIP navigation services to assess the acceptability of the intervention from a patient perspective (see **Appendix XIX** for interview guide).

6 Potential Risks and Benefits

6.1 Risks

Risks to participants of the intervention itself are minimal and no different than those in usual care. Currently providers and patient navigators often engage patients in discussions of the

barriers to care and their social needs. These discussions may cause some emotional distress; providers are available to speak with patients, and the intent of the discussions is to help with findings solutions and supports to alleviate the distress. The Aunt Bertha SDOH platform will allow navigators to provide specific, geographically convenient referrals to free or low cost services to address patient-identified social needs.

The only potential risk identified for this study is loss of confidentiality, should any of the information in the registry, Aunt Bertha or the secure central data repository where data will be stored to be compiled and coded for analyses become stolen or inadvertently become public. Our Data Safety Monitoring Plan incorporates comprehensive plans for secure data collection, management and storage to minimize this risk.

6.2 Potential Benefits

As the intervention will be implemented as "standard of care" at each of these sites, there are no direct tangible benefits to the participants in this study. The benefit of this evaluation of the implementation of a new standard of care will be generalizable knowledge for quality of care improvements at the 6 participating hospitals, and potentially dissemination to other institutions.

6.3 Analysis of Risks in Relation to Benefits

The major risk of this study is loss of confidentiality which is reasonable in relation to anticipated benefits to generalizable knowledge to improve quality of care.

7 Study Subject Selection

7.1 Subject Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

Eligibility criteria: All women with breast cancer diagnosed during the study period will be eligible for inclusion if they meet three study criteria:

1. are an adult female 18 years of age or older;
2. reside within a 35 mile radius of Boston;
3. have any of the following risk factors for delays in care:
    a. Black and/or Hispanic race/ethnicity
    b. do not speak English as their primary language and/or
    c. have only public insurance or are uninsured at the time of diagnosis.

Women who do not meet all three criteria will be excluded from the study. In some cases it is possible, due to the scope of the patient navigator's responsibilities that patients who are ineligible will be entered into the Registry. As the registry is HIPAA compliant and these individuals will be excluded from compiled data sets, the study team does not perceive this to be a major risk.

7.2 Subject Exclusion Criteria

None

8 Study Intervention

The TRIP intervention consists of an **Integrated Patient Navigation Network** that aims to reduce delays from diagnosis → treatment initiation → treatment completion among Greater Boston residents with newly diagnosed breast cancer.

The **Integrated Patient Navigation Network** intervention has 3 components that are shared across 6 hospitals in Boston:

1. Patient Navigation Services that are implemented according to evidence-based best practices. Patient Navigation services following standard operating procedures that are guided by the Principles of Care Management in collaboration with a network of navigators across the six health systems. This includes: a) identifying women eligible for navigation services; b) identifying barriers to engaging in timely cancer care services, with a particular emphasis on social barriers; c) providing assistance to address these barriers through local and regional resources; and, finally, d) tracking women over time across the participating clinical sites to ensure they complete their entire course of cancer care. The innovation here is the integrated network of navigation across regional health systems, where navigators attend quarterly trainings together and communicated directly about patients who transfer services across clinical sites. Navigators will be employees of the clinical site and will comply with site-specific practices and standards.

2. REDCap Patient Registry will be used to track and monitor patients' navigation activities and will be shared across the six health systems. The registry will be built using the HIPAA compliant REDCap platform and function as a "tickler file" embedded into the navigator workflow. This navigator tool provides navigators with the ability to determine prioritization of caseload, track their patient's progress, and communicate across sites if patients transfer care. Sharing navigation process data across the health systems will address known fragmentation in care that leads to delays in treatment.

3. Social Determinant of Health (SDOH) Platform systematically identifies barriers to care and links the patient to available resources in the community to address them. The screening/referral system has been built using the Aunt Bertha platform. At time of diagnosis, the navigator will ask patients a series of 17 questions to identify needs categorized into 10 social domains (e.g., transportation, housing, food, paying for utilities). Women will then be referred to local resources aimed at addressing SDOH. These data will be available and stored in the Aunt Bertha platform for use by the patient navigators. At each contact, the navigator will check on the status of referrals and assess whether a woman would like to receive additional referrals for previously identified or new barriers to care. Sites that have a pre-existing platform for identifying and addressing social needs can continue to use their existing systems, and will document assessment and referral details in the shared REDCap registry to make it accessible to navigators at other sites.

As stated in the TRIP study design, there is no control intervention. All controls are historical, thus they represent usual care, prior to implementation of the intervention at each site.

9 Study Procedures

For this pragmatic clinical trial, Patient Navigators at each of the six participating clinical sites will continue to meet and follow-up with their patients as they do currently. As each site's navigators may have a different process for how many visits and follow-ups they will have with a patient and this may further vary depending on the treatment plan and navigation needs of an individual patient, this study does not have a set schedule of events. To understand the expected navigator coverage over the treatment spectrum please see **Appendix IV** in place of the schedule of events.

Because the TRIP intervention is being implemented as a new standard of care, patients will receive care according to a schedule determined by their health care providers. Thus, number of visits for each patient will be specific to their specific treatment regimens. Within these patient visits, the TRIP intervention will be implemented in a standardized way. The schedule of events for the TRIP intervention within a patient visit will include all Patient Navigation services as detailed below. These events include all visits/contacts between the navigator and the patient (or other care provider) from the time of diagnosis to completion of treatment. At a minimum these events will include: time of diagnosis and at each transition in cancer care (i.e.: from surgery to radiation, from radiation to chemotherapy). Additional visits/contacts will occur based on identified barriers or patient needs.

9.1 Patient Navigation services

Patient Navigation services at each site will follow standard operating procedures that are guided by the Principles of Care Management in collaboration with a network of navigators across the six health systems. In order to have the desired effect on treatment delays, we aim to disseminate the following 'best practices' of patient navigation across each hospital setting:

- Patient navigation is a process not a person: no one person can navigate alone, there is potential role for lay, nurse and SW in the process of navigating a patient through their treatment; multiple 'navigators' may participate across the treatment trajectory; the optimal structure will be specific to the needs and resources at each hospital

- The patient navigation process should begin within 7 days of diagnosis and continue until treatment recommendations have been completed

- Patient navigation services include the following 4 procedures:

    1. **Identify those in need of navigation:** TRIP eligibility criteria have been chosen to identify those most at risk for delays in care (as defined by MA Cancer Registry Data). Navigators will identify eligible patients in partnership with the oncology care team by any of the following existing processes: reviewing automated potential patient lists generated from upcoming oncology schedules, reviewing pathology reports, attending tumor board meetings, manually reviewing physician schedules, or direct referrals from providers. Once identified as eligible for navigation services, they will obtain permission to contact the patient from the care team and create a Patient Profile in the REDCap Registry based on available information from the EHR.

2. **Identify individual barriers to treatment:** Patient navigators participating in the TRIP program will provide one-on-one guidance and assistance to individuals upon diagnosis. The principal function of the navigator is to identify and eliminate barriers to timely treatment and provide support for each individual. The navigator will initiate contact with the patient either by phone or in person during a scheduled visit to begin the navigation program. During this initial assessment, the navigator will conduct a social needs assessment (see intervention component #3 below) that systematically identifies patient reported barriers to care. This systematic assessment will be repeated at each treatment transition (ie from surgery to radiation, from radiation to chemotherapy and from chemotherapy to hormonal therapy), in recognition of the fact that barriers may arise that are specific to the type of treatment.
3. **Link patient to available resources to overcome those barriers:** Women will be asked a series of questions to identify the precise services needed for each domain. These data will be available and stored in the TRIP instance of the Aunt Bertha platform (See intervention component #3 below) for use by the patient navigators. At each contact, the navigator will check on the status of referrals and assess whether a woman would like to receive additional referrals from similar or different domains. During these interactions, the navigator will provide assistance in accessing relevant services when appropriate.
4. **Track them over time to their treatment appointments:** The navigator protocol includes tracking each upcoming treatment visit, to ensure compliance with recommended care. The REDCap Registry will be used to document the status of these visits, providing a tool for the navigators to prioritize their caseload. Navigators are expected to initiate contact with patients either via phone or in person whenever they miss an appointment, or are at risk to miss an appointment. During these interactions, they will coordinate services in order to address barriers to patient care and assist in the alignment of services and treatment goals and promote treatment preparation through patient education. They will track them and offer navigation services until their treatment is complete.

- Navigators across hospitals work together to care for this population of women with breast cancer. First, they will be invited to quarterly Patient Navigation Network meetings where they will share resources and lessons learned. Second, when patients transfer care or are lost to follow up, navigators will utilize the registry to communicate patient needs.

9.1.1 Patient Navigator Training Methodology

All patient navigators will be asked to attend their respective site kick-off meeting, during which they will complete a workflow assessment and a navigator experience questionnaire. Navigators will complete the following training plan:

Workflow assessment	Review of Navigation Protocol	Platform demonstration webinar	On-site Case-based training	Adherence Monitoring
•PN is made aware of the purpose of the project •PN participates in an on-site in-person meeting with the TRIP team for the purpose of answering questions regarding their current workflow	•PN participates in an on-site in-person meeting with the TRIP team for the purpose of: •Reviewing the 11 Navigation Guidelines •Identifying site-specific modifications to the navigation protocol	•PN participates in a webinar hosted by the TRIP team via WebEx to review an introductory demonstration of both the REDCap Registry and Aunt Bertha SDOH platform	•PN participates in an on-site in-person meeting with the TRIP team for the purpose of: •Re-visiting the navigation protocol and any modifications needed •Practicing use of REDCap and Aunt Bertha through a case study	•Navigators who do not follow the expected navigation protocol will receive 2 e-mail follow-ups •If email follow-ups do not provide resolution, navigators will participate in an on-site refresher training session

The TRIP research team will provide oversight to each site in all areas pertaining to data management, regulatory compliance, and patient identification. The research team will also provide navigator support and training throughout the course of the study. On-site or virtual visits via BMC Zoom with the navigator and their supervisors will be scheduled at 1-3, 3-6, and 6-9 months post site initiation.

9.1.2 Human Subjects Protection Training

All study staff will be certified on HIPAA and Human Subjects. The format of the HIPAA authorization is established by the local IRB. Investigators should review information provided in Impact of the HIPAA Privacy Rule (https://www.citiprogram.org/) and contact their appropriate institutional officials to learn how the Privacy Rule applies to them, their organization, and their specific research project. Another helpful resource is Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule, NIH Publication 03-5388 at (http://www.bumc.bu.edu/hipaa/).

9.2 Patient Navigator Oversight

9.2.1 Patient Navigator Supervisor

Patient Navigator supervisors, who are employed at the 6 hospital sites and already serving as supervisors, will receive the same initial training as the Patient Navigators as well as some additional elements to be provided as part of an in-person curriculum provided by the study team:

- Navigation Protocol discussion
- Platform (REDCap and Aunt Bertha) explanation and demonstration
- Adherence monitoring reports and refresher training overview

Adherence to protocol data will be provided to each site in the form of a monthly report. Sites that are non-compliant with the study protocol will be provided additional training and support. Site PIs will also be expected to maintain monthly contact with their patient navigator team to ensure adequate study communication.

9.2.2 Refresher Training

If, upon assessment review at 1-3, 3-6, and 6-9 months post site initiation a Patient Navigator is identified as inadequately adhering to the intervention protocol, the patient navigator supervisor and study team will meet to determine whether additional one on one study training and monitoring is required. This refresher training will be customized on an individual basis as needed.

9.2.3 Observations of Patient Navigators

Trained TRIP study personnel will visit each site to unobtrusively observe the TRIP patient navigators in their practice for two purposes: 1) gain a more complete understanding of adherence to the core patient navigation intervention guidelines, and 2) to determine barriers and facilitators to implementation of the patient navigation protocol. The necessary authorization for observations will be obtained on a site by site basis. See **Appendix V** for the observation tool that will be used to collect data by TRIP study personnel. The data collected in the observation tool is considered research data and may be included in manuscripts and publications.

9.3 Use of Shared Registry

9.3.1 REDCap

A shared TRIP registry was developed using REDCap (Research Electronic Data Capture), a HIPAA compliant, secure web-based application for building and managing online surveys and databases. The purpose of the registry is to improve the workflow processes of the patient navigators as part of their routine clinical duties and as part of new standard of care. The registry will also permit close coordination of clinical care across hospitals for the estimated 20% of patients who receive their cancer care at more than one institution, or switch from one institution to another during their care.

The REDCap registry developed for TRIP resides on BMC HIPAA compliant server. Access to the TRIP shared registry will be based on permissions granted by username and password

which will be managed by the Boston Medical Center Office of Information Technology. Only authorized study members will be able to enter or view data.

9.3.2 User Permissions

Prior to initial site rollout, all sites will provide a list of authorized users designated by 'view only' or 'view and edit'. Patient navigators will be given highest level permissions in order to ensure that they can input patients, and run reports as needed. Navigator supervisors and any staff who provide coverage for navigators will also have full view and edit permission. Because the goal of the registry is to quickly allow navigators to coordinate care when patients move between hospitals, all navigators and supervisors will have access to all records in the registry. Other clinical providers (e.g., nurses, physicians, social workers) at the hospitals may request access to view the registry. After training, these clinicians will be granted view only status only of patients receiving care at their hospital site, to ensure that only individuals with active clinical roles in patient care will have access to the registry.

Any changes to the site permissions list should be sent to the TRIP project team and will be updated in the system by BMC IT personnel responsible for assigning REDCap access.

9.3.3 Data elements

The data elements included in the registry are the minimum information needed by navigators to actively manage and support their patients, assist them in keeping clinical appointments, and address the social determinants that often result in patients delaying or falling out of clinical care. Therefore the registry will not have extensive clinical information about the type of cancer, specific types of treatment, medications, comorbidities or complications of care. Additionally, only MRN, patient first and last name, date of birth, phone number, and study eligibility criteria are required, all other fields are optional, and navigators will be the only individuals entering data in these fields. The registry will include the following categories of data elements:

1. Patient demographics – Sufficient demographic information to uniquely identify women in the data base, including first and last name, date of birth and medical record number from each hospital system where a patient receives care. Preferred language, race/ ethnicity and gender identification fields will be available to assist navigators identify patients and their needs. A free text field will allow navigators to input specific biographical data which will help in the care of the patient (such as background, family structure, hobbies).
2. Minimal clinical information necessary for navigators to conduct their work. This will include stage of diagnosis and date of diagnosis, as this information will help navigators focus on meeting clinical benchmarks including first surgery within 45 days and first treatment within 60 days. It will also include insurance and a free text field to document any insurance restrictions/ need for prior authorizations, etc.
3. Patient contact information – detailed information to assist navigators in communicating with patients, including address, phone numbers, email, and social media as appropriate

4. Family/ secondary contact information – detailed information on 2 – 3 individuals the navigator can contact in event of emergency or patient not keeping appointments, including phone, email.
5. Patient navigator information– who is the navigator for the patient, and contact information for navigator and his/her supervisor
6. Referral source – how patient was referred to navigator and specific concerns that prompted referral
7. Provider information – for each medical provider involved in care, their name, hospital, and best methods to reach them or their clinical team. This may include a best contact of a nurse or patient coordinator who works with the provider.
8. Appointments – a listing of all medical appointments, including office visits, infusions, surgeries, radiation oncology visits, imaging studies will be listed by type of appointment, location, provider, and date and time. The outcome of each appointment (attended, rescheduled, cancelled) can be documented.
9. Navigator contacts with patients – the registry will include fields to document the date and time, type of contact (e.g., in person, phone, SMS message, email), duration and outcome of contacts with patients. Free text fields will allow navigators to note additional information as necessary.
10. Social Needs information—the registry includes fields for the navigator to indicate when a systematic assessment for social needs was conducted, the reason for doing the assessment, the type of assessment used (TRIP instance of Aunt Bertha or other validated tool, such as the THRIVE instance of Aunt Bertha at BMC), whether any needs were identified as a result of the assessment, and whether any referrals were made for the patient to address identified needs.

All entries into the registry will be time and date stamped, and will indicate which user entered the data.

Navigators can add information into the registry as frequently as is required depending upon the number of follow-up visits necessary, and the amount of contact the navigator has to support the patient through their care. This will be determined on a per patient basis, as it will likely vary from patient to patient.

9.3.4 Patient Identification

Navigators will identify patients in 2 ways: 1) using their standard methods as part of their clinical workflow. The majority of patients will be identified via physician or social worker referral at the clinical site of origin, or through discussion of the case in the Breast Cancer tumor board or case conference. 2) using a potential patient list provided by their site's IT/Research Administration to review patients that match eligibility criteria prior to an upcoming scheduled oncology appointment.

As part of the TRIP intervention, patient navigators at each of the 6 clinical sites are responsible for identifying eligible patients based on the aforementioned eligibility criteria. In order to facilitate effective identification of eligible patients as part of each navigator's workflow, the TRIP

team is collaborating with Information Technology personnel at each clinical site to produce a potential patient report. At each individual site, these reports will be generated weekly from electronic medical records and produce a list of patients who meet the following criteria:

1. A scheduled visit for a diagnosis of breast cancer in the next one to two weeks
2. A ZIP code within a 35 mile radius of Boston
3. Other key eligibility criteria (non-white, non-English speaking, and/or uninsured/public insurance)

The PHI data included in these reports are patient name, MRN, appointment type, provider, race/ethnicity, primary language, ZIP code, and insurance (if available). These reports are unique to each site and are accessible locally via secure folder or encrypted email by a patient navigator and in some cases, study team personnel at their site.

9.3.5 Reporting

To support the workflow, the registry will have custom reporting that will be available to both users with 'edit/view' permissions (navigators, supervisors, back-up) as well as 'view only' permissions (research staff, other clinicians). The study team plans to send weekly reports to each navigator, which will summarize patients who have been entered into REDCap and Aunt Bertha, and records that need to be reconciled. For navigators and clinicians, these may be at the patient level, navigator level or provider level. In addition, research staff can request reports at the hospital site and at the entire study level. The system will log all report requests by user and time.

9.3.6 Notifying a Patient Navigator a patient has transferred care

The registry will have a messenger function allowing navigators across hospitals to communicate with each other about patients. This feature will be used when a patient:
a) seeks a second opinion at another hospital
b) decides to receive different treatment modalities at different institutions (e.g. Radiation at one institution, but medical oncology visits at another)
c) decides to transfer all care to another hospital. The purpose of this feature, which we estimate will be used for 20% of cases, is to facilitate timely transitions and avoid delays in care.

9.3.7 Interfacing with Aunt Bertha

In order to standardize workflow and allow for direct accessibility to the Aunt Bertha Social Needs Assessment, an 'in frame' link to Aunt Bertha will be hosted within the REDCap forms. Navigators will log into REDCap using their assigned credentials and 2-factor authentication method (confirmation via Google Authenticator app or email), complete the intake and follow-up form as necessary, and click the link to Aunt Bertha to complete the assessment for each patient.

A referring URL within REDCap will be utilized to transfer the Subject ID number, First Name, and ZIP Code into the Aunt Bertha Assessment to ensure that patients are easily identifiable for referral retrieval and data matching purposes.

9.3.8 Registry Training

The TRIP Project team will provide comprehensive hands-on training to navigators and their supervisors via two required training sessions (see Patient Navigation section above for details). The initial one-on-one training on site with the navigator includes but is not limited to the following topics:

1. How to log in
2. What information is captured
    a. Data elements and definitions
3. How to use the forms
4. Log in and demonstration of usability
5. Reporting
    a. Sorting
    b. Filtering

Should any major changes be made to the Registry that impact usability or navigator workflow, the TRIP team will provide follow-up training for the navigator, either via Web-ex or in-person.

9.3.9 Technical support and troubleshooting

The REDCap registry will be housed locally on BMC virtual servers, thus any technical issues or user questions should be directed to the TRIP Research team at TRIPAdmin@bmc.org who will help to facilitate communication with local IT and ensure resolution of any issues identified.

9.3.10 Communication on Registry revisions

Development and alteration of the TRIP REDCap Registry is expected to be an iterative process as new needs are identified and each site is activated. Any maintenance shutdowns of the registry will be scheduled outside peak work hours to avoid impacting the workflow of the navigators. Patient navigators, site clinicians and navigator supervisors will be informed of any maintenance shutdowns, content changes or process alterations made to the REDCap registry at least 2 days prior to the expected date of occurrence.

9.4 Screening for Social Determinants of Health (SDOH)

9.4.1 Aunt Bertha

Aunt Bertha (https://www.auntbertha.com) is a public benefit corporation that works to connect people in need with social service agencies. The TRIP instance of Aunt Bertha provides a search, referral and application platform that will be used to screen and refer women to community resources. The TRIP instance of Aunt Bertha will be used for patient-specific tracking of SDOH domains and resources across sites. One site, Boston Medical Center, has a

separate contract with Aunt Bertha called the THRIVE program, which is a parallel system that screens for the same health-related social needs as the TRIP instance of Aunt Bertha, and is HIPAA-compliant and previously authorized by BMC. The THRIVE instance of Aunt Bertha is integrated with the site's Epic EMR and has been used by BMC breast oncology navigators prior to TRIP rollout. As BMC already has a comparable systematic social needs assessment and referral platform as part of their standard of care, social needs data collected via THRIVE for TRIP patients will be made available to the study team to merge with the TRIP instance of Aunt Bertha for analysis.

9.4.2 Security and Compliance

All Aunt Bertha employees are required to take annual HIPAA training. Aunt Bertha is hosted on a Google Cloud platform using AES-256 encryption. Data in transit on the Google Cloud platform is sent using AES-256 encryption, and on the internet the connection to the site is encrypted and authenticated using TLS 1.2, ECDHE_RSA with X25519, and AES_128_GCM.

9.4.3 User Permissions

Prior to initial site rollout all sites will provide a list of authorized users and their intended role in the TRIP project. The TRIP project team and Aunt Bertha team will predetermine the configuration of groups for the purposes of sharing notes and reporting. Patient navigators will be given highest level permissions in order to ensure that they can input patients, perform the social needs assessment and run reports as needed. Unless otherwise stipulated by the TRIP project team, accessory users such as clinicians will be granted permissions as 'view only' as requested. Any changes to the site permissions list should be sent to the TRIP project team and will be updated in the system by the Aunt Bertha Customer Success Manager.

The TRIP team will let Aunt Bertha staff know if a user should no longer have access, and these accounts will be deactivated within 24 hours. In addition, Aunt Bertha will generate a quarterly list of individuals with account permissions. This will be reviewed by the TRIP team and permissions of any users who are no longer at the clinical sites or part of the research team will be removed.

9.4.4 Screening for SDOH

The TRIP team has developed a custom social needs assessment with input from the partnering hospital sites. The assessment will be used to determine care related needs of the patient in the following categories

1. Transit
2. Food Security
3. Housing
4. Utility bills
5. Paying for Treatment
6. Employment
7. Education
8. Child or family care
9. Legal

10. Phone access

9.4.5 Aunt Bertha Needs Assessment

The TRIP Team has partnered with Aunt Bertha to host a needs assessment on the TRIP instance of their web-based screening and referral platform (See **Appendix VI**). The assessment will screen patients for SDOH falling into the following 10 domains: Transit, food security, housing, utilities, paying for treatment, employment, education, child or family care, legal, and phone access. The THRIVE instance of Aunt Bertha screens for the same domains, except for legal needs (see **Appendix VII** for a copy of the THRIVE needs assessment). At DFCI, the 17-question needs assessment has been built into their pre-existing QuickBase navigator database and directly mirrors the assessment in the TRIP instance of Aunt Bertha. This will allow for ease of clinical uptake at DFCI by integrating the assessment with an existing navigator database, while still allowing the navigator at DFCI to share assessment data with other sites through the REDCap registry.

The following types of questions will assess a patient's needs for each relevant domain, and the patient's answers will be used to refer them to community resources that are appropriate, convenient and affordable. The needs assessments has been translated to Spanish (see **Appendix VI** Spanish translation of Aunt Bertha Needs Assessment on page 49).

1. Transit
    a. In the past 12 months, has lack of reliable transportation kept you from medical appointments, work or from getting things needed for daily living?
2. Food security
    a. In the last 12 months have you worried that your food would run out before you had the money to buy more?
    b. In the last 12 months, did the food you bought just not last and you didn't have the money to get more?
    c. Do you currently have trouble going out to shop for food or preparing food?
3. Housing
    a. What is your housing situation today?
    b. How many times have you moved in the past 12 months?
    c. Think about the place you live. Do you have problems with any of the following?

4. Paying utility bills
    a. In the past 12 months, has the electric, gas, oil or Water Company threatened to shut off or shut off services to your home?

5. Paying for treatment
    a. Do you have trouble paying for your treatment, including medicines, visits or tests?
    b. Do you have trouble paying for other things related to your treatment, like wigs or prostheses?
6. Your job or finding work
    a. Are you worried about taking time off from your job because of your health/ treatment?
    b. Do you plan to work during your treatment?

    c. Are you currently unemployed and looking for a job, or working but looking for a better job?
7. Education or training
    a. Are you interested in going to school or getting job training?
8. Child or family care
    a. In the last 12 months, have you missed a health care visit or work because you needed to care for a child, family member or friend?
9. Legal
    a. Do you currently have any legal concerns or needs (like to prevent eviction, being fired, or discrimination)?
10. Phone Access
    a. In the past 12 months, has your phone service been shut off or disconnected?

9.4.6 Frequency of Screening for SDOH

The social needs assessment will be accessible during both the intake and follow-up visits with the patient navigators. At a minimum, the REDCap registry will remind navigators to perform SDOH screening on intake. Navigators are also expected to complete a second SDOH assessment at either 3 months into treatment or upon transition between treatment modality (e.g., surgery, chemotherapy, radiation).

9.4.7 Using Aunt Bertha

There will be two ways for the PNs to use the TRIP instance of Aunt Bertha: (1) using the SDOH-specific screening tool noted above to systematically identify needs of patients and then link to relevant resources in Aunt Bertha; (2) targeted search for specific resources in response to a request from a patient. In a targeted search, a patient would request a specific type of service (i.e., transportation), and the navigator would use Aunt Bertha to search for resources that provide services in the patient's zip code.

Upon patient referral to a navigator, the navigator will log in to REDCap and complete the initial intake form. At the end of the intake form, the navigator will click a link into Aunt Bertha to complete the SDOH assessment and provide referrals to the patient either via email, or printed list. This activity will then be documented in the patient's REDCap record. Upon follow-up the navigator will ask patients if they successfully used the referrals and if they need additional help. The needs assessment will be re-visited as needed.

For Boston Medical Center navigators using the THRIVE instance of Aunt Bertha (staff.bmcthrive.org), three methods of using the platform exist: 1) using the embedded social needs assessment in Epic to systematically identify needs of patients and then link to relevant resources in Aunt Bertha; 2) targeted ZIP-code search for specific resources in response to a request from a patient; 3) using the smartphrase ".THRIVEREFER" in the Epic EHR, which will generate a prompt to document both a list of the referral programs/agencies used as well as the needs the navigator aims to address with that referral. Referrals can be provided to the patient via email or printed list.

For Boston Medical Center patients, referrals can be sent directly to the referral program or agency. For any referrals related to HIV/AIDS status, substance use disorder diagnosis, mental health, domestic violence counseling, rape victim counseling, or sexually transmitted disease (including, gonorrhea, syphilis, chlamydia), patient navigators will obtain verbal or written consent from the patient prior to sending the referral to a referral program or agency (**Appendix XVI**). Navigators will not document patients' experiences with domestic violence or rape directly in the EHR.

THRIVE data will be retrieved from all BMC TRIP patients through the BUMC Clinical Data Warehouse and the THRIVE instance of a SQL feed from Aunt Bertha on a monthly basis and merged with the Aunt Bertha study data.

For Dana-Farber Cancer Institute navigators using QuickBase, navigators will complete the 17-question TRIP social needs assessment and select referrals from an internal list of resources. If additional resources are needed, the navigator will perform a targeted search in the Aunt Bertha platform. QuickBase data on assessment and referral details will be securely transmitted to the study team and merged with the other social needs data sources into the BMC central data repository.

9.4.8 Training

The TRIP team will provide Aunt Bertha training to site personnel in person during the technical training session. This training will cover use of Aunt Bertha to do systematic and targeted screening. We will also use a "train the trainer" model where the TRIP team, who have already been trained, will train additional PNs one-on-one prior to the initiation of the intervention at their site. Staff will also have access to weekly office hours and webinar trainings hosted by the TRIP project team, as well as access to a Help Desk and Training Library

The TRIP Project team will provide comprehensive hands-on training to navigators and their supervisors via two required training sessions (see Patient Navigation section above for details). The initial one-on-one training on site with the navigator includes the following topics:

1. Discussion of barriers to care
2. How to log in
3. What information is captured
4. How to use the social needs assessment
5. How to log and track referrals
6. Log in and demonstration of usability

Should any major changes be made to the Aunt Bertha Platform that impact usability or navigator workflow, the TRIP team will provide follow-up training for the navigator, either via Web-ex or in-person.

9.4.9 Identifying resources

Aunt Bertha already contains listings for > 2000 social service agencies in the greater Boston area. These will be supplemented by resources currently used by navigators. In order to ensure

that the preferred resources of all currently active patient navigators who are participating in the TRIP project are present in Aunt Bertha, the TRIP team compiled lists of resources from each site to provide to the Aunt Bertha team. The Aunt Bertha team will be adding any additional resources to the platform at a global level (available to any Aunt Bertha user). This process is expected to be iterative as sites rollout and begin to use the platform and identify missing resources.

9.4.10 Reporting

The TRIP team is developing custom reporting in REDCap and Aunt Bertha that will be available to both users with 'edit/view' permissions (navigators and their supervisors), as well as 'view only' permissions (research staff and clinicians) that will assist navigators in SDOH follow-up and prioritization two different reporting structures will be available monthly.

All report requests will be tracked by the TRIP Project team. In addition, Aunt Bertha reporting will enable tracking functionality such that a navigator can log in to see a live report of patients who have been screened. This report will allow the navigators to "screen" based on patient characteristics to generate a report to see who is in need of follow-up. For example, a navigator will be able to generate a report that will show patients who requested referrals in the prior week. This will enable the navigator to follow-up with the patient to follow-up with a patient to see if a referral was successful (and if not address if additional referrals are needed).

9.4.11 Interfacing with Shared Registry

For details regarding connectivity between the REDCap registry and Aunt Bertha, please refer to the Registry section 'interfacing with Aunt Bertha'.

9.4.12 Technical support and troubleshooting

Upon initial identification of an issue, the TRIP team recommends review of the Aunt Bertha frequently asked questions page (https://auntbertha.zendesk.com/hc/en-us/categories/200221080-Frequently-Asked-Questions)

The TRIP team has also developed a Technical Support Plan, in which at least one member of the study team is available by phone and email to troubleshoot technical issues during business hours (8:30-5:00pm EST, M-F).

Aunt Bertha will provide technical support and troubleshooting during business hours (8:00 PM – 6:00 PM EST) via phone or online help desk. However, should an issue arise, site personnel should also contact the TRIP team at TRIPAdmin@bmc.org to ensure the study team is aware of any issues, and can facilitate any necessary follow-up.

9.4.13 Communication about modifications to Aunt Bertha

We will be assigned a customer success manager at Aunt Bertha. This person will keep us apprised of any platform changes and expected work flow modifications. Patient navigators, site

clinicians and navigator supervisors will be informed of any maintenance shutdowns, content changes or process alterations made to the Aunt Bertha platform at least 2 days prior to the expected date of occurrence. Navigators will be informed of content changes by email or in person contact depending on the nature of the change (e.g., will be informed by email of important updates in the referrals that are available/ no longer available, will be informed by phone or in person for changes in platform functionality.

10 Data Management

10.1 Study Data

10.1.1 Data Source: REDCap

The Patient Navigators will collect participants' intake and follow-up forms in a **REDCap** project housed on a BMC HIPAA compliant server. REDCap will assign an individual patient registry ID number to each participant. Data elements include personal identifying data, including contact information, and data on patient follow-up needs.

10.1.2 Data Source: Aunt Bertha

The study collects a social needs assessment and data on patient social determinants of health in the HIPAA compliant platform, **Aunt Bertha**. This program will also track patient referrals to community resources for social support services.

While most data collection will be entered in real time and directly into the electronic platform, in some cases Patient Navigators may need to print out blank **paper copies** of the REDCap Registry forms and Aunt Bertha Social Needs Assessment to complete during their patient visits. The data from these forms will then be entered into the electronic registry and the paper forms shredded immediately afterwards.

10.1.3 Data Source: Quickbase

Dana-Farber Cancer Institute has their own instance of Quick Base, a cloud-based, low-code development platform, to manage all of their navigation-related data. This platform hosts the 17-question TRIP social needs assessment for DFCI, and the results of baseline and follow-up assessments for each TRIP patient, as well as data on which social services programs patients have been referred to for addressing positively identified needs. Quick Base exports custom reports as .csv files, and the TRIP team will receive a .csv download of social needs assessment and referral data for TRIP patients on a monthly basis via upload to a secure Box.com folder or SFTP to be merged with the TRIP central data repository.

10.1.4 THRIVE

At BMC, THRIVE data for TRIP patients will be retrieved from the Clinical Data Warehouse (CDW) and from a SQL feed directly from Aunt Bertha on a monthly basis and merged with

the social needs data for other TRIP patients in the Aunt Bertha SQL database. The THRIVE instance of Aunt Bertha is parallel to the TRIP instance, and screens for the same domains of social needs. The THRIVE SQL feed and CDW will provide the study team with a download of the social needs identified and referrals made, for all BMC TRIP patients screened using THRIVE who have documentation in the EHR.

This data will be merged with social needs data from the TRIP instance of Aunt Bertha in the Central Data Repository at BMC for analysis.

10.1.5 Data Source: Electronic Health Records

Treatment data elements will be manually abstracted for both historical control and intervention subjects from **Electronic Health Records (EHR**) at each site. Abstraction from the EHR will be conducted by a trained Research Assistant employed by that site and overseen by the site PI. Data elements from EHR abstraction will be uploaded or entered directly into the TRIP REDCap abstraction project. For more information, see *Figure 1 Table 1*.

Intervention patients: Potential Patient Lists will be generated locally at each participating institution to aid Patient Navigators in identifying potentially eligible patients with new breast cancer diagnoses. Every week, Patient Navigators will receive a list of patients who meet TRIP eligibility criteria and have an upcoming appointment for the following week. These lists will be generated by the EHR via a script developed by each site's IT department or research administration group and uploaded to a secure folder on the Patient Navigator's local drive or sent locally through secure email.

Historical Controls: Historical controls will be identified by working with each site's tumor registrar to generate a list of all breast cancer patients during the historical time period. These data will be securely stored locally at each site, and transmitted to the TRIP study team at BMC via secure Box.com folder, SFTP, or secure email. The data will then be saved to the secure tripdata$ folder. These data will be reviewed by the TRIP data analyst to ensure completeness and correct formatting of files, and to exclude all ineligible patients according to TRIP eligibility requirements. Then the TRIP data analyst will upload the eligible patients' data to a secure REDCap project for chart abstraction. This REDCap project will be used to store clinical data manually abstracted from each EHR, and entered by the site's Research Assistant.

Historical control datasets will include the following variables requested from each site:

a. First Name
b. Last Name
c. MRN
d. Sex
e. Race/ethnicity
f. Date of diagnosis
g. Date of birth

h. ZIP code at diagnosis
i. Primary institution
j. Primary payer at diagnosis
k. Date of last contact or death

In order to identify which historical control patients transferred their care to multiple institutions, the TRIP team will cross-reference historical control cases with the Massachusetts Cancer Registry (MCR) at the Massachusetts Department of Public Health (MADPH). The TRIP team will transmit the following data via SFTP to MCR, which will perform a matching query to report which patients have received care at more than one institution:

a. First Name
b. Last Name
c. MRN
d. Date of diagnosis
e. Date of birth
f. Reporting institution

The electronic health records will also serve as a data source for patient interviews. The site's RA will query the electronic health records directly through Epic or other electronic medical record system at a site for the following data:

a. First name
b. Last name
c. Mailing address
d. Phone number

These data will be securely stored locally at each site, and transmitted to the TRIP study team at BMC via secure Box.com folder, SFTP, or secure email.

10.1.6 Data Source: Central Data Repository

A **Central Data Repository** located on Boston Medical Center's (BMC) HIPAA compliant server (\tripdata$) will house datasets containing PHI from REDCap, Aunt Bertha and the EHRs to be compiled, de-identified and coded for analyses.

Using the instance of SAS on BMC's I2B2 restricted use server, the EHR data will be merged with the REDCap and Aunt Bertha data using medical record number (MRN) and date of birth, and incorporating the unique study ID assigned in REDCap. Once the EHR data is merged with project data, personal identifiers, such as patient name, medical record number, full address (excluding zip code) and phone number, will be removed from the dataset and stored as a separate encrypted dataset in a dedicated secure folder on the F drive within the restricted I2B2 BMC server. An individual's study ID will be the 'crosswalk' linking this master file containing PHI to the coded analytic dataset. Access to the master file will be limited to the BEDAC and BMC staff listed on this application who will be trained in handling confidential data and will be destroyed upon study completion.

Once treatment outcomes are verified by BMC staff, date of birth and treatment dates will be transformed into analytic variables (e.g. age at diagnosis, days to first treatment, # of days on chemotherapy, days to hormone therapy, etc.), removed from the dataset and stored as a separate encrypted dataset, linked only by the crosswalk file, as described above. For additional information regarding the data sources, process for codification and patient identifying variables see Figure 1, and Table 1.

The master file containing an individual's name and medical record number will be used to identify navigated patients to contact for interviews. The data analyst will generate a list of patient names, MRNs, and study IDs for navigated patients, stored on the tripdata$ server. This list will only be accessed by TRIP RAs when identifying navigated patients to contact for interviews.

10.1.7 Data Source: Cost Surveys

Using an annual survey of clinical site administrators and patient navigators, we will systematically assess all costs associated with the delivery of the multi-component intervention to estimate the costs that would be required to implement in other practice settings or continue the intervention in these settings at the conclusion of the study. This data collection will inform sustainability and dissemination efforts by assessing fixed and variable costs, including costs in developing the registry and Aunt Bertha platform; costs associated with training patient navigators; and costs associated with implementing the program. The surveys will collect aggregate data on the amount of time spent on discrete navigation activities and will not contain any patient-level information.

Navigators and their supervisors will be sent a blank template of the survey via a secure electronic data capture system or secure email, or delivered a printed copy during a regularly scheduled site visit. They will be instructed to complete the survey once per day over a two-week period (10 consecutive working days). At the end of each week, a research assistant will contact the navigator by secure email or phone to aid in completing the surveys and collect the paper forms, if there are any. If during the 2 week period the navigators do not interact with any TRIP participants or spend time on any TRIP activities, the process will occur again and they will be asked to fill out a cost survey for another 2 week period. The research team will send the completed surveys to the TRIP cost analyst, based at the Boston University Medical Campus, via secure email for analysis. Paper surveys will be scanned and stored in the secure Box.com folder, and paper copies shredded immediately afterward.

10.1.8 Data Source: Observations

To understand patient navigators' adherence to navigation guidelines, we will conduct observations of all TRIP Patient Navigators across participating sites at 12 months of the intervention period. We expect to observe approximately 8-12 navigators, knowing that staffing changes may alter the number of TRIP navigators over time. Observers will be IRB-approved study personnel. They will use implementation science frameworks and methods to examine the barriers and facilitators to implementation, as well as the Patient Navigators' degree of fidelity,

to the TRIP intervention protocol. Trained research staff will complete a minimum of two 4-hour observations per navigator and data will be recorded on an observation tool (**Appendix V**) to take field notes, and check off when activities from the 11 Step Navigation Guidelines are completed. The observer will begin a new written observation sheet every 15 minutes.

Pilot Observation Period: Observers will conduct a 2-hour pilot observation prior to formal observation activities. The pilot will ensure observers are recording observations and writing observation summaries in alignment with study protocol. No research data will be collected.

Formal Observation Period: Prior to the observation, the Study Coordinator will facilitate a warm hand-off between the observer and the patient navigator via email. The Study Coordinator will send an introductory email with additional details about the observation and confirm a time for the 4-hour observation periods. Observers will meet all site-specific criteria for visitor privileges ahead of the visit date. Before the start of the observation period, the observer will review an exempt information sheet (see **Appendix XI)** with the Patient Navigator, who will have the opportunity to provide verbal consent or opt out of the observation. The observer will also provide the business card of the PI, Dr. Tracy Battaglia.

During the observation period, the observer may ask probing questions to clarify patient navigator activities. Should the observer witness an in-person patient interaction or a phone call, between the navigator and the patient, the navigator will ask for the patient's permission for the observer to remain in the room using a provided script (**Appendix XII)**. If the patient does not agree, the observer will leave the room until the navigator is done interacting with a patient. If the patient is comfortable with the observer's presence, the observer will remain in the room and record notes**.** To remain as unobtrusive as possible this portion of the observation will be an "eyes-only" experience; the observer will not ask any questions while the patient is in the room or on the phone. Research team members will make all attempts to minimize their exposure to PHI throughout the observation period. Clinical staff can ask the research team members to leave the room at any time.

Immediately after the observation, the observer will complete an observation summary **(Appendix XIII)** independently to reflect on activities witnessed during observations and document emergent themes and questions. The observation team will review the observation summary the following day. The observer will update the summary with any remaining answers or clarifying information. No patient information will be recorded.

All observation data will be stored at BMC. Paper copies of observation notes will be scanned and stored in a secure, restricted access Box.com folder. Observers will type up hand-written field notes and store electronic copies, along with observation summaries, on a secure BMC Box.com folder. Hand-written notes will then be immediately destroyed. Observation data will be uploaded into Dedoose software for analysis by the subject's unique study ID. We will use content analysis (where we conduct counts for specific activities, e.g. entering data into the EHR, and the amount of time spent on those activities) and thematic analysis to analyze the tasks and work flow observed by the research team.

10.1.9 Data Source: Key Informant Interviews

12-Month Interviews: Interviews will be conducted with Key Informants approximately 12 months after each site goes live with the TRIP intervention to assess two implementation outcomes: acceptability and penetration of the TRIP protocol. These Key Informants will be the TRIP Navigators across the 6 participating sites, as well as select members of the Non-TRIP

Navigation Team identified by the TRIP Navigator or during navigator observations, such as resource specialists, nurses, social workers, and other staff involved in the navigation process (**see Appendix I for interview guide**). There are separate, tailored interview guides for the non-TRIP Navigation Team and TRIP Clinical Champions (**Appendix II and III).**

After the study information sheet (**Appendix XVII**) has been reviewed and the interview scheduled, study team personnel will arrange a time and location for the interview. The interview will be conducted preferably in person, but phone interviews will be permitted if scheduling constraints arise. Interviews will be arranged at a mutually agreeable time and private location (clinical space, research office). Prior to beginning the interview, the research team member will confirm that the participant agrees to have the conversation audio recorded. Navigator interviews will be focused on gathering their perspectives on the TRIP navigation protocol, experiences using the REDCap Registry and Aunt Bertha SDOH platform, and perceptions of TRIP in general. Non-TRIP Navigation Team interviews will focus on perceptions of the intervention, experiences with patients receiving the new standard of care, challenges encountered, and intention to continue implementing principles of TRIP after the study period. The interview will be conducted using a flexible interview guide, and participants will be provided with an opportunity at the end of the interview to ask questions or provide other information not solicited by the interviewer. Interviewees, both TRIP Navigators and non-TRIP navigation personnel, will each receive an honorarium of $50 for their time at the time of the interview. At the conclusion of the interview, the interviewer will make field notes, reflecting on the interview context, using an interview summary (**Appendix XII**). These notes will be marked with the participant's study ID (no names or other identifying information). If the interview is cut short or interrupted for any reason, the interviewer and interviewee will identify a mutually agreeable time, by phone or in person, to complete the rest of the interview.

Audio files will be transcribed by a verified transcription service and will be managed, coded and analyzed using qualitative data management software (either Dedoose or NVivo). All interview data – audio and written transcripts – will be stored securely in a restricted-access Box.com folder.

For analysis, at least two members of the study team will independently review transcripts from each of the first 3 Navigator and Non-TRIP Navigation Team interviews to identify important concepts that emerge and create a codebook used for subsequent interviews. Then, two coders will independently code three randomly chosen cases for agreement analysis in Dedoose or NVivo. Coders will meet twice monthly to review code interpretation and to discuss new codes. Disagreements about code meanings will be resolved by consensus.

The thematic analysis will focus on the perceptions of acceptability and penetration related to implementing the TRIP standard of care. After coding is finalized and consensus has been reached, codes will be reviewed to generate cross-cutting themes within each group. Similarities and differences in the themes will be compared across groups. This will allow us to identify the extent to which TRIP is seen as acceptable or having substantial reach within the health system among different sites.

<u>27-Month Interviews:</u> Interviews will be conducted with Key Informants approximately 27 months after each site goes live with the TRIP intervention to assess four implementation outcomes: fidelity, acceptability, adoption, and penetration of the TRIP protocol. These Key Informants will

be the TRIP Navigators across the 6 participating sites, as well as their direct supervisor or program clinical champion (**see Appendix XVI for interview guide**). Key informants will be recruited by email or at a regularly scheduled TRIP meeting (e.g. clinical advisory panel, navigator network meeting, or site visit).

After the study research information sheet (**Appendix XVII**) has been reviewed and the interview scheduled, study team personnel will arrange a time and location for the interview. The interview will be conducted preferably in person, but phone interviews will be permitted if scheduling constraints arise. Interviews will be arranged at a mutually agreeable time and private location (clinical space, research office). Prior to beginning the interview, the research team member will confirm that the participant agrees to have the conversation audio recorded. Navigator interviews will be focused on gathering their perspectives on the TRIP navigation protocol, experiences using the REDCap Registry and Aunt Bertha SDOH platform, and perceptions of TRIP in general. Supervisor and clinical champion interviews will focus on perceptions of the intervention, experiences with patients receiving the new standard of care, challenges encountered, and intention to continue implementing principles of TRIP after the study period. The interview will be conducted using a semi-structured interview guide, and participants will be provided with an opportunity at the end of the interview to ask questions or provide other information not solicited by the interviewer. The interviewee will complete a demographic survey, which is included at the end of the interview. Phone interviewees will receive the demographic survey as a REDCap survey link. Interviewees will each receive an honorarium of $50 for their time at the time of the interview. At the conclusion of the interview, the interviewer will make field notes, reflecting on the interview context, using an interview summary (**Appendix XII**). These notes will be marked with the participant's study ID (no names or other identifying information). If the interview is cut short or interrupted for any reason, the interviewer and interviewee will identify a mutually agreeable time, by phone or in person, to complete the rest of the interview.

Audio files will be transcribed by a verified transcription service and will be managed, coded and analyzed using qualitative data management software (either Dedoose or NVivo). All interview data – audio and written transcripts – will be stored securely in a restricted-access Box.com folder.

For analysis, at least two members of the study team will independently review transcripts from each of the first 3 Navigator and Supervisor/Clinical Champion interviews to identify important concepts that emerge and create a codebook used for subsequent interviews. Then, two coders will independently code three randomly chosen cases for agreement analysis in Dedoose or NVivo. Coders will meet two to four times monthly to review code interpretation and to discuss new codes. Disagreements about code meanings will be resolved by consensus.

The thematic analysis will focus on the perceptions of fidelity, adoption, acceptability, and penetration related to implementing the TRIP standard of care. After coding is finalized and consensus has been reached, codes will be reviewed to generate cross-cutting themes within each group. Similarities and differences in the themes will be compared across groups. This will allow us to identify the extent to which TRIP has been incorporated into an existing site according to the protocol, is seen as acceptable, or having substantial reach within the health system among different sites.

10.1.10 Data Source: Patient Interviews

Interviews will be conducted with 30 patients enrolled in the study across all 6 TRIP clinical sites to assess acceptability of the TRIP protocol, a key implementation outcome. Patients will be identified through the central data repository, which contains a record of patients who were navigated by a TRIP navigator and screened for social determinants of health. Patients will be sent an opt-out letter and research information sheet (**Appendix XVIII and Appendix XX**) to their mailing address listed in the clinical site's electronic medical record. Approximately 1 week after the opt-out letter has been mailed, a researcher will call the patient at their phone number listed in the clinical site's electronic medical record or the REDCap Patient Registry to schedule an interview time. All interviews will be conducted by phone. Patients who opt out will be removed from the calling list. This calling list will be stored in a secure Box.com folder.

Prior to beginning the interview, the research team member will review the research information sheet **(Appendix XX)** with the participant and confirm that the participant agrees to have the conversation audio recorded. The interview will be conducted using a flexible interview guide **(Appendix XIX)**, and participants will be provided with an opportunity at the end of the interview to ask questions or provide other information not solicited by the interviewer. Interviewees will each receive an honorarium of $25 for their time at the time of the interview. Participants' responses will not be linked to identifiable information. Participants and interviewers will be asked to use pseudonyms during the interview.

Audio files will be transcribed by a verified transcription service and will be managed, coded and analyzed using qualitative data management software (either Dedoose or NVivo). All interview data – audio and written transcripts – will be stored securely in a restricted-access Box.com folder.

For analysis, at least two members of the study team will independently review transcripts from the first 3 interviews to identify important concepts that emerge and create a codebook used for subsequent interviews. Then, two coders will independently code three randomly chosen cases for agreement analysis in Dedoose or NVivo. Coders will meet twice monthly to review code interpretation and to discuss new codes. Disagreements about code meanings will be resolved by consensus.

The thematic analysis will focus on the perceptions of acceptability related to implementing the TRIP standard of care. After coding is finalized and consensus has been reached, codes will be reviewed to generate cross-cutting themes within each group. Similarities and differences in the themes will be compared across groups. This will allow us to identify the extent to which TRIP is seen as acceptable by patients.

Figure 1 Data Sources and Codification Procedure

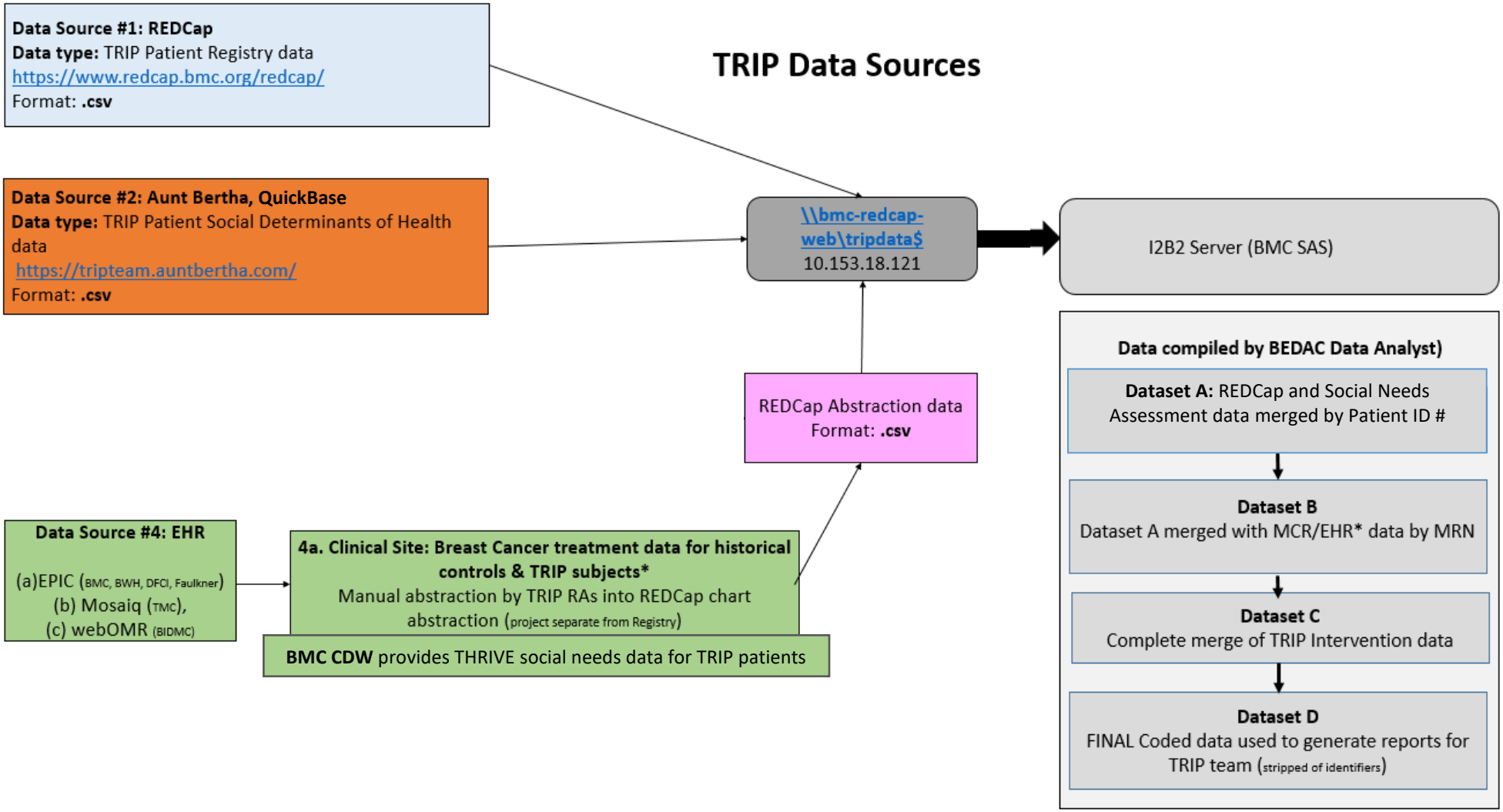

Table 1. Overview of Patient Identifying Elements

Data Source	Description	Access	Purpose of data	PHI data elements
HIPAA Compliant REDCap Registry	A tool to support the daily work of Patient Navigators to manage their active caseload and share information with Navigators when they transfer their care to another institution in the TRIP program. Use of the registry is considered a standard part of the Navigator's workflow.	Patient Navigators across all 6 sites, Select members of the TRIP program team (all IRB approved and compliant)	Implementation data: will determine if the standard of care navigation protocol was administered	• Intake date • MRN • Patient Name • DOB • Address • Phone number • Email • Appointment dates
HIPAA Compliant Aunt Bertha Platform	A tool to support the daily work of Patient Navigators to systematically screen patients for barriers to care and identify local resources to help them overcome those barriers. Use of the platform is considered a standard part of the Navigator's workflow.	Patient Navigators across all 6 sites, Select members of the TRIP program team (all IRB approved and compliant)	Implementation data: will determine if the standard of care navigation protocol was administered	• Patient Name • Email • Phone Number • Zip Code • Date Social Needs Assessment Completed
Electronic Health Record-Potential Patient List	Automated list of patients scheduled for breast cancer care in the coming week is generated by the Site. Another tool for Navigators to identify who needs their services. Use of the list is considered a standard part of the Navigator's workflow.	Site Specific Navigators, Select members of the TRIP program team (all IRB approved and compliant)	Implementation data: will determine if the standard of care navigation protocol was administered	• MRN • Zip code • Patient Name • Race • Date of visit
Electronic Health Records- Identification of historical controls	Site tumor registrars will compile lists of patients who meet the TRIP eligibility criteria within the historical control period, in the form of a .csv file and securely transmit to the TRIP team via restricted-access Box.com folders or via SFTP. These lists will be used to identify historical control cases for abstraction.	Select members of the TRIP program team (all IRB approved and compliant)	Identification of historical control cases	• Patient name • MRN • DOB • Date of diagnosis • ZIP code • Race/ethnicity • Institution of care • Insurance type • Preferred language • Date of last contact/death
Electronic Health Record- Manually abstracted chart data	Clinical data from patient charts will be abstracted and entered into a REDCap database. The abstraction will be performed on site by a Research Assistant	Site Specific Navigators, Select members of the TRIP program team (all IRB approved and compliant)	Outcomes data: will provide clinical data to determine care received and if any delays in care persist after the new	• MRN • Patient Name • DOB • ZIP Code • Insurance

Data Source	Description	Access	Purpose of data	PHI data elements
	employed by that site and overseen by the site PI.		Patient navigation standard is put in place.	• Institution of Care • Language • Date of diagnosis • Date of last contact or death • Breast cancer treatment dates • Hospital admission & ER visit dates
BMC Electronic Health Record- THRIVE social needs data	Social needs data collected via THRIVE for TRIP patients will be made available to the study team to merge with the TRIP instance of Aunt Bertha for analysis.	Select members of the TRIP program team (all IRB approved and compliant)	Implementation data: will determine if the standard of care navigation protocol was administered	• Patient name • DOB • MRN • Date social needs assessment completed
Electronic Health Record – Identification of navigated patients for interviews	A list of patient contact information at each clinical site will be compiled by a site RA from the electronic health record and saved in a secure Box.com folder. These lists will be used to contact patients for acceptability interviews.	Select members of the TRIP program team (all IRB approved and compliant)	Contacting patients for interviews	• Patient name • Mailing address • Phone number

10.2 Data Safety Monitoring Plan (DSMP)

10.2.1 Data Safety Monitoring Plan Overview

The Tufts CTSI provides a service for managing the Data Safety Monitoring Plan (DSMP) within their regulatory services that will be utilized for the proposed project. The DSMP for the trial will be managed by the study lead PIs and the site co-investigators, a biostatistician and additional clinical experts in breast cancer and health disparities.

In collaboration with the multiple lead study PIs, Dr. Tracy Battaglia has created the Data Safety and Monitoring Plan below which includes sections on monitoring objectives, platform data security details, the data to be considered, roles and responsibilities, and meeting plans and reports. The meeting section will lay out the frequency of meetings, pre-meeting materials, structure of the meetings, how voting and quorum will be conducted, and how adverse events (AEs) or emergent data safety concerns will be addressed.

10.2.2 Oversight Responsibilities

The DSMP for the TRIP study aims to protect participant safety and confidentiality from adverse events associated with participation in the study. In addition, the DSMP assures regular oversight and maintenance of data quality.

Oversight for the data and safety of the trial will be the responsibility of the study lead PIs (Dr. Battaglia, Dr. Freund, Dr. Haas, and Dr. Lemon). The DSMP has been created by Dr. Tracy Battaglia in collaboration with the Tufts CTSI Regulatory Knowledge Core and the study lead PIs.

10.2.3 Monitoring Procedures

While this project is intended to be ‘standard of care’ and will be reliant on a waiver of consent, principal investigators will ensure that all subjects meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan.

The study team will specifically monitor the performance of the trial and data quality of the study by reviewing:

a. Enrollment – the team will monitor enrollment quarterly for adequacy of meeting enrollment goals and ensuring eligibility criteria are met.
b. Follow-up – the team will monitor the study for completeness of registry and social needs assessment follow-up data on a quarterly basis.
c. Other metrics of clinical trial performance including data integrity (verification of quality, complete data received in a timely manner), protocol adherence, subject privacy, data confidentiality (secure data storage and transfer) and study management will be monitored on a quarterly basis

The lead PIs will review study conduct inclusive of site enrollment, eligibility, and protocol adherence and deviations during the quarterly review. The lead PIs will review any issues identified in real-time and in aggregate during the quarterly review. The lead PIs will ensure all protocol deviations, adverse events, and unanticipated problems are reported to the NIH and BMC IRB according to the applicable regulatory requirements. The biostatistician and statistical analyst will prepare detailed reports on enrollment, data capture from the registry and from Aunt Bertha, each quarter to facilitate these sessions.

10.2.3.1 Auditing and Risk Management

The TRIP program manager and data analyst, along with the BMC Privacy Officer and BMC Associate Director of Network Security and Data Engineering, will be granted access to the REDCap audit trail logs in order to monitor patterns of patient registry records access and ensure that patient records are only being accessed by team personnel that are actively involved in the individual patient's care.

The TRIP team will use the FairWarning® Software to monitor the activity of the REDCap and Aunt Bertha project platforms to ensure that patient records are only being accessed by relevant personnel. FairWarning® Software incorporates data delivered from electronic medical records (EMR) or other data sources into its interface and runs analytical programs using artificial intelligence to identify patterns of misuse.

Audit logs will be downloaded from REDCap and uploaded to the FairWarning® environment using a Secure File Transfer Protocol (SFTP). Audit logs from Aunt Bertha will be automatically uploaded via a SQL data feed. The FairWarning® environment will be used to generate reports to identify suspicious behavior. Should any aberrant patterns of misuse be detected the TRIP team will review these incidences with BMC Privacy and BMC Network.

The audit trail log will be reviewed by the TRIP study team on a quarterly basis and by Privacy and Network Security as necessary. Should any aberrant patterns of patient navigators regularly accessing patient registry records for patients outside of their caseload be detected, the TRIP team will review these outliers with BMC Privacy and Security to determine the best course of action.

10.2.4 General Electronic Data Procedures

The study project manager will work with the navigators, IT at each site and the lead PIs to oversee uniform data management procedures.

The REDCap database server will be backed up three times a day internally by BMC Information Technology (IT). The Aunt Bertha database server is backed up in real time at the secure Google analytics server facility.

All computers that will be used to collect and send data during implementation of the study or to receive or store data at all sites will be password protected. A password will be required to log on to the computer and a second, different username and password will be required to log in to both the REDCap Registry and the Aunt Bertha platform. REDCap requires two-factor authentication to complete log in. Both Aunt Bertha and REDCap require password changes every 60 days for all users. To train navigators on study activities, study personnel may use BMC's version of Zoom to show the navigators patient data in the Aunt Bertha or REDCap Registry platforms.

Electronic copies of forms will be stored on a secure dedicated server with appropriate firewalls. The system will use 128-bit encryption (SSL certificate) to transfer data between the machines. To add another level of security, the data stored within each database will be encrypted so that no one can read the actual contents, including the database administrators.

Servers are scanned for viruses and systems are in-place to detect attempts at unauthorized entry. Any database transactions are stored in archive logs and are accessible to enable quick recovery of all data should the need arise. Backup files are written nightly to back up servers. The daily copies are kept onsite for a month. A monthly backup copy is stored off-site in perpetuity.

Electronic files will consist of the following:

1) REDCap registry records
    a. Individual patient registry record
    b. Compiled records reports including information on patient follow-up needs
2) Aunt Bertha
    a. Individual patient social needs record
    b. Compiled records reports including information on patient social needs and referral resources
3) Quick Base
    a. Individual patient social needs assessment and referral data
4) Electronic Health Records (EHR)
    a. Lists of identified historical control patients for abstraction (.csv files)
    b. Historical control and TRIP subject demographic and cancer treatment data pertaining to breast cancer diagnosis & treatment
    c. Potential Patient List (site-specific)
    d. THRIVE Social needs data for TRIP patients (BMC-specific)
5) Central Data Repository
   The central data repository will house all datasets listed above (1-4) for the project before the data is cleaned and coded in preparation of analysis.
6) Interview transcripts and observation notes
   To minimize the chances that any personal information will be exposed, the following procedures are in place for **interviews and observations:**

    1. All study participants will be assigned to a unique study ID and identified by this number in all study documents. Interviews and observation notes will only be labeled with a Study ID, and not by any individually identifiable information. A separate, password-protected master code will document the participant's study ID, role and institution. Access to this password–protected file will be limited only to

study staff who have been trained in human subjects protection and are listed on the IRB application. The master code will be destroyed after data collection is complete.

2. **Interviews** will include open-ended questions and a 1-page demographic survey. Neither the open-ended questions nor survey questions will collect identifiable information. Responses from paper-based demographic surveys will be transferred to a secure REDCap form, and scanned copies of the paper-based forms will be uploaded to a secure, restricted access Box.com folder. Paper copies will be immediately shredded after upload to Box.com. It is possible that participants will disclose personal information during the interview that was not solicited by the interviewer. To ensure confidentiality, all interview audio files will stored on a secure server or Box.com folder. Transcripts will be de-identified of participant information, including site name, before being professionally transcribed verbatim with a BMC-approved transcription vendor. De-identified transcripts and audio files will be reviewed by members of the research team for accuracy and confirmation that all identifiable information is removed from transcripts, after which audio files will be destroyed. De-identified transcripts and audio files will be stored on a secure server.

3. **Observations** will include hand-written notes by observers. Observers will not record any patient navigator identifiable information in observation notes, including site name, and will only refer to patient navigators by study IDs in notes. Observers will scan paper-based notes into electronic copies, which will be stored in a secure folder. All paper-based notes will be immediately shredded after being uploaded to the secure, restricted access Box.com folder.

10.2.5 General Security Procedures for Paper Data

All study data will be collected electronically, however in some cases patient navigators may need to print out hard copies of the REDCap Registry forms or needs assessments to complete during their patient visits and will transcribe these responses into the electronic registry.

Paper files will consist of the following:

1) REDCap registry records
    a. Individual patient intake or follow-up forms
2) Aunt Bertha Needs Assessment
3) Observational notes
4) Demographic surveys

While most data collection will be entered in real time and directly into the electronic platform, in some cases patient navigators may need to print out blank paper copies of the REDCap Registry forms and Aunt Bertha Social Needs Assessment to complete during their patient visits. The data from these forms will then be entered into the electronic registry and the paper forms shredded immediately afterwards.

Observational data will take the form of notes, which will remain in the possession of the research team during the observations and will be transported back to the study offices (801 Massachusetts Avenue), where paper copies will be stored in a locked filing cabinet, to which only the PI and data Manager will have the key. Once data is entered into Dedoose software, electronic copies will be kept on BMC equipment, following all standard procedures for maintaining data security, and the paper copies immediately shredded.

10.3 Third Party Platforms

All data sources (REDCap Registry, Aunt Bertha platform, TRIP-patient THRIVE data, and TRIP-patient Quick Base data) utilized in this study are HIPAA compliant and will be accessible only to authorized and trained study personnel and only for the purposes of facilitating quality navigation related to clinical care. Good data management procedures to protect the electronic files will be followed as described above.

10.3.1 REDCap Registry

To facilitate effective patient navigation and improve the quality of care for our target population, the TRIP team is creating two electronic platforms: the REDCap patient registry and the TRIP-specific Aunt Bertha Social Determinants of health platform. These platforms will be available to all participating navigators as well as some secondary site personnel on a case by case basis as determined by the TRIP team at the following sites:

- Brigham and Women's Faulkner Hospital
- Beth Israel Deaconess Medical Center
- Tufts Medical Center
- Dana Farber Cancer Institute
- Massachusetts General Hospital
- Boston Medical Center

As all participating sites are HIPAA-compliant entities and this intervention will be implemented as the standard of care across institutions. BMC general legal counsel determined inter-institutional agreements for the shared registry to be unnecessary.

The registry will be used to track and monitor patient progress across their treatment trajectory shared across the six health systems. The registry will be built using the HIPAA-compliant REDCap platform and function as a "tickler file" embedded into the navigator workflow. The REDCap registry will host a link to the Aunt Bertha platform within the patient intake form that will allow the Patient Navigators to login to Aunt Bertha to complete the social needs assessment. The only data element that will be automatically carried over via referring URL will the automatically generated REDCap subject ID to allow for data matching.

10.3.1.1 Security and Compliance

The REDCap registry developed for TRIP resides on BMC HIPAA compliant server. Access to the TRIP shared registry will be based on permissions granted by username and password which will be managed by the BU CTSI Informatics core (Bill Adams and Galina Lozinski – also TRIP team internal personnel). Only authorized study members will be able to enter or view data.

Study team members will log into REDCap using their assigned username and password. Usernames and passwords will never be shared among individuals. REDCap supports two-factor authentication using e-mail or the Google Authenticator application. Two-factor authentication requires entry of a personal password and a second factor, something only the user has in their possession such as a mobile phone, or email, to provide unique identity verification. REDCap users are required to change their passwords every 90 days. Once a user is logged into REDCap the system will be set to automatically time out their session due to inactivity after 20 minutes.

10.3.1.2 User Permissions

Prior to initial site rollout, all sites will provide a list of authorized users designated by *view only* or *view and edit*. Patient navigators will be given highest level permissions in order to ensure that they can input patients and run reports as needed. Navigator supervisors and any staff who provide coverage for navigators will also have full *view and edit* permissions. Because the goal of the registry is to quickly allow navigators to coordinate care when patients move among hospitals, all navigators and supervisors participating in the study will have access to all cases in the registry.

Other clinical providers (e.g., nurses, physicians, social workers) at the hospitals may request access to view the registry. After training, these clinicians will be granted *view only* status to see patients receiving care at their hospital site. This will ensure that only individuals with active clinical roles in patient care will have access to the registry.

10.3.1.3 Changes in site personnel

Any changes to the site permissions list should be sent to the TRIP project team and will be updated in the system by BMC IT personnel responsible for assigning REDCap access. The TRIP research team will send an inquiry to confirm site personnel on a quarterly basis. Site Principal Investigators will be asked to update the TRIP team within a week of on-site personnel changes (new team member additions or current team member leaving). Site personnel will be reviewed by the TRIP team and confirmed with clinical site Principal Investigators on a quarterly basis.

10.3.1.4 Auditing and Risk Management

The TRIP program manager and data analyst along with BMC Privacy Officer and BMC Associate Director of Network Security and Data Engineering, will be granted access to the REDCap audit trail logs in order to monitor patterns of patient registry records access and ensure that patient records are only being accessed by team personnel that are actively involved in the individual patient's care.

The TRIP team will use the FairWarning® Software to monitor the activity of the REDCap and Aunt Bertha project platforms to ensure that patient records are only being accessed by relevant personnel. FairWarning® Software incorporates data delivered from electronic medical records (EMR) or other data sources into its interface and runs analytical programs using artificial intelligence to identify patterns of misuse.

Audit logs will be downloaded from REDCap and Aunt Bertha and uploaded to the FairWarning® environment using a Secure File Transfer Protocol (SFTP). The FairWarning® environment will be used to generate reports to identify suspicious behavior. Should any aberrant patterns of misuse be detected the TRIP team will review these incidences with BMC Privacy and BMC Network.

The audit trail log will be reviewed by the TRIP study team on a quarterly basis and by Privacy and Network Security as necessary. Should any aberrant patterns of patient navigators regularly accessing patient registry records for patients outside of their caseload be detected, the TRIP team will review these outliers with BMC privacy and security to determine the best course of action.

10.3.2 Social Determinants of Health Platform (Aunt Bertha)

Aunt Bertha (https://www.auntbertha.com) is a public benefit corporation that works to connect people in need with social service agencies. Aunt Bertha provides a search, referral, and web application platform that will be used to assess SDOH and refer patients to community resources. The TRIP screening/referral system will be built using the Aunt Bertha platform.

To accommodate existing clinical workflows at two of the TRIP sites, alternative sources of SDOH data will be utilized as follows:

a) Boston Medical Center: THRIVE
    a. THRIVE is a BMC-operated parallel instance of the Aunt Bertha platform, and THRIVE assessment data is stored in the BMC EMR and will be sourced via the Clinical Data Warehouse in the form of a .csv file downloaded to the secure tripdata$ folder.
b) Dana-Farber Cancer Institute: Quick Base
    a. The Dana-Farber Cancer Institute instance of QuickBase is a password-protected application platform for managing navigation-related data, and is accessible only by authorized DFCI personnel. Authorized personnel at DFCI will securely send TRIP-patient QuickBase data to the study team via a secure, restricted-access Box.com folder or SFTP, which will be downloaded to the secure tripdata$ folder to be merged with other datasets for analyses.

10.3.2.1 Security and Compliance

1) Aunt Bertha
    a. All Aunt Bertha employees are required to take an annual HIPAA training course. Aunt Bertha is hosted on a Google Cloud platform using AES-256 encryption. Data in transit on the Google Cloud platform is sent using AES-256 encryption, and on the internet the connection to the site is encrypted and authenticated using TLS 1.2, ECDHE_RSA with X25519, and AES_128_GCM.

b. Study team members log into Aunt Bertha using their assigned username and password. Usernames and passwords are never shared between individuals. Once a user is logged into REDCap the system will be set to automatically time out their session due to inactivity after 30 minutes.

2) THRIVE
   a. THRIVE data is governed by the same security and compliance protocols as the BMC EMR. Only the Clinical Data Warehouse Research Manager will have direct access to this data source, and she will securely transfer the THRIVE assessment data for BMC's TRIP patients via the tripdata$ folder.

10.3.2.2 Patches

Aunt Bertha automated patch management solutions to update system and software patches as they are released. Updates to code elements are updated as part of the software development life cycle process.

For any code other than the site code developed by our internal team, the underlying operating system and associated applications are updated automatically. For our code we use a Software Development Life Cycle plan following an agile development process.

10.3.2.3 Auditing and risk management

Aunt Bertha is hosted on the Google App Engine platform, thus physical and environmental security is the responsibility of Google. The Google data center has made a SOC2 report available for certification and auditing reports. Real-time alerts are set up for logs based on defined issues, but otherwise logs are reviewed monthly. For details regarding user audit log monitoring see section 11.2.6.4 Auditing and Risk Management.

10.3.2.4 Breach of Data Security

In the event of a security breach, Aunt Bertha performs an initial analysis to close the breach and investigate the scope of the breach. Once the situation is determined to be stable the notification process to the TRIP team would be implemented.

The use of digital media such as USBs or external drives is disabled at endpoints within the Aunt Bertha internal network.

10.3.2.5 User Permissions

Prior to initial site rollout all sites will provide a list of authorized users and their intended role in the TRIP project. The TRIP project team and Aunt Bertha team will predetermine the configuration of groups for the purposes of sharing notes and reporting. Patient navigators will be given the highest level permissions in order to ensure that they can input patients, perform the social needs assessment and run reports as needed. Unless otherwise stipulated by the TRIP project team, accessory users such as clinicians will be granted permissions as 'view only' as requested. Any changes to the site permissions list should be sent to the TRIP project team and will be updated in the system by the Aunt Bertha Customer Success Manager.

Access to identifiable TRIP-patient THRIVE and QuickBase data will be restricted to only the TRIP data analysts and internal study team who have access to the tripdata$ folder and the restricted-access TRIP data Box.com folders.

10.3.2.6 Changes in site personnel

Site Co-Investigators will be asked to update the TRIP team within a week of on-site personnel changes (new team member additions or current team member leaving). The TRIP team will let Aunt Bertha staff know if a user should no longer have access, and these accounts will be deactivated within 24 hours.

In addition, Aunt Bertha will generate a quarterly list of individuals with account permissions. This will be reviewed by the TRIP team and permissions of any users who are no longer at the clinical sites or part of the research team will be removed.

10.3.3 Electronic Health Records

EHR data has the highest level of security because it contains individually identifiable health information. Data from the EHR will be handled as follows in collaboration with IT teams at all participating sites (**Figure 1, Data source #3**):

3A. Potential Patient List:The TRIP team will work with individual site Information Technology Services and Research Administration to create a report of patients that match eligibility criteria. These lists will be produced automatically on a weekly basis and provided to Patient Navigators via upload to a local secure folder or via secure email.

3B. Treatment data for historical control and intervention subjects: Data for historical control and intervention subjects will be manually abstracted into a secure REDCap abstraction project from patient Electronic Health Records by trained study personnel at each participating site. This abstracted data will be checked for quality by TRIP study personnel by accessing the Electronic Health Records on a hospital-issued device using BMC's VPN services, or viewing remotely through BMC's instance of Zoom while using BMC's VPN services.

EHR data will be merged with data collected in the REDCap registry and Aunt Bertha using a medical record number (MRN) and date of birth and incorporating the unique Patient Registry ID assigned in the REDCap registry.

All data will be kept for the duration of the 5-year study, as well as an additional 3 years until all data analysis and manuscript preparation is complete; at which time, all study related materials will be shredded and deleted off the server using a secure file deletion program by the BU Office of Information Security. All research staff will undergo HIPAA training as well as responsible conduct of research training.

10.3.4 Central Data Repository

Once the EMR data is merged with project data, personal identifiers, such as patient name, medical record number, full address (excluding zip code) and phone number, will be removed from the dataset and stored as a separate encrypted dataset. An individual's study ID will be the 'crosswalk' linking this master file containing PHI to the coded analytic dataset. Access to

the master file will be limited to the BEDAC and BMC staff listed on this application who will be trained in handling confidential data.

The master file will be destroyed upon study completion (June 2022). Once treatment outcomes are verified by BMC staff, date of birth and treatment dates will be transformed into analytic variables (e.g. age at diagnosis, days to first treatment, # of days on chemotherapy, days to hormone therapy, etc.), removed from the dataset and stored as a separate encrypted dataset, linked only by the crosswalk file, as described above.

The central data repository will be maintained on a BMC secure, HIPAA compliant server for the purposes of matching the REDCap and Aunt Bertha data prior to de-identification for analyses. Good data management procedures to protect the electronic files will be followed as described above.

All patient information for data analysis will be transferred to the TRIP Central Data Repository to be stored on BMC virtual servers via secure, HIPAA compliant data transfer methods, with all data encrypted. Uploads into the repository will be protected using secure socket layering encryption technology. Web-forms and accompanying database will be stored on secure servers professionally maintained by the Boston Medical Center IT group, stored behind the BMC 'firewalls.' Access to data systems will be controlled by usernames and passwords and restricted to study personnel.

Datasets in SAS software will be stored on a HIPAA compliant network maintained by the BU Office of Information Security. Systems will be backed up incrementally and backups maintained offsite. All data will be stored in a HIPAA compliant manner and data storage techniques will be reviewed biannually by BU IT staff. Specific procedures, which have been approved by our institution review board (IRB) and used successfully in prior research, include protecting participant confidentiality as follows:

- Data will be stored in a centralized data warehouse located within the BU/BMC data centers and security procedures will be consistent with those already followed for EHR data.

- All project staff will sign an oath of confidentiality to ensure their understanding of the terms of confidentiality required.

- Only project staff will have access to the system via a secure name and password.
- All reports and publications will preserve the subjects' anonymity.

10.3.5 Protecting Confidentiality

This requires that identifying information (name, address, date of birth, social security or Medicare numbers) not be used as the final sources of identification for participants. Compliance of regulatory documents and study data accuracy and completeness will be maintained through an internal study team quality assurance process. Confidentiality throughout the trial is maintained by utilizing only HIPAA compliant systems to collect and store Patient Health Information.

The major risk of the trial is loss of confidentiality. Because of the nature of the information, data collected on the patients requires the presence of patient identifiers, until the final analytic file is complete for analysis. When a patient record is started in REDCap, the platform automatically assigns an identifying number to the patient. This number will then become the identifier of records for each participants (for all relevant data) once the data is coded for analytic purposes at the end of the study.

10.4 Data Safety Meetings

10.4.1 Participants

The TRIP team members and site investigators will participate in the Data and Safety Meetings. The meetings will be chaired by one of the lead PIs. For any decisions or resolutions requiring a vote, the four lead PIs, six site clinical advisors, and the biostatistician will be considered voting members. A **quorum for voting** will consist of at least three PIs and two additional voting members.

10.4.2 Frequency

The initial data and safety meeting will occur prior to the roll out of the intervention to discuss the protocol and establish guidelines for data review, and monitoring the study. Once the intervention is underway, the team will convene as often as necessary, but at minimum once a year (months 21, 33, 45, 57) to examine the enrollment data, review study progress and safety data, and discuss factors that might impact continuation of the study as designed.

10.4.3 Data for Meetings

Responsibilities for data reporting are as follows:

- The data manager, in collaboration with the biostatistician will prepare detailed reports on enrollment, follow-up, data capture from the registry and from Aunt Bertha, monthly Quality Assurance reports and cancer care variables
- The project manager will report on protocol adherence and violations
- The data manager will report on data confidentiality and any reported adverse events from the database

10.4.4 Structure of Meetings

Meetings will be open to invited members of the study team. If needed, a closed session may follow to allow discussion among lead PIs, site clinical advisors, project manager(s), biostatistician, and the data manager. Voting members and the quorum are described above.

10.4.5 Addressing Data and Safety Concerns

If issues are identified with data management or with participant safety or confidentiality, changes in the study protocol, data management, or data collection and maintenance will be discussed at the meeting and reflected in the minutes.

10.5 Reporting

10.5.1 Responsibility

It is the responsibility of the lead PIs to ensure that safety and data quality reports are prepared in a timely manner and submitted to the relevant IRB and sponsor(s). The project manager will assist with this and maintain copies of all reports in the regulatory binder.

10.5.2 Data and Safety Meetings Minutes

The minutes of the Data and Safety Meetings will be prepared by an assigned committee member and reviewed by the lead PIs. If required by the BMC/BU Medical Campus IRB, the minutes will also be sent to the IRB either after each meeting or on an annual basis for re-certification. The summary reports will be sent to each site investigator and filed with the BMC IRB.

10.5.3 Safety Definitions

10.5.3.1 Serious Adverse Events (SAEs):

As this is a study monitoring the timeliness and quality of medical care in women with breast cancer, we do not anticipate any serious adverse events. Events that may occur during the course of the study of patients with cancer including treatment related events or death will not be considered SAEs for the purpose of reporting unless they are related or probably related to participation in the study.

10.5.3.2 Adverse Events (AEs):

The study has designed and instituted measures to preserve participant confidentiality. In particular, the study aims to prevent breach of data and loss of confidentiality, should any of the information in the registry, Aunt Bertha, or the secure central data repository become stolen or inadvertently become public. The study will also monitor for other possible AEs such as loss of contact with participants, misdirection or navigator error in participants' appointments or transfer of care, or unauthorized disclosure of personal information.

10.5.3.3 Unanticipated Problems (UPs):

An unanticipated problem is defined as an event, experience or outcome that meets all three of the following criteria:

- is unexpected; AND
- is related or possibly related to participation in the research; AND
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research. *Unexpected* means the nature, severity, or frequency of the event is not consistent with either:

- The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; OR

The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event.

10.5.4 Safety Event Reporting

The Principal Investigator at BMC/BU Medical Campus will report Unanticipated Problems, SAEs, safety monitors' reports, and Adverse Events to the BMC/BU Medical Center IRB in accordance with IRB policies:

- Unanticipated Problems occurring at any participating site involving a fatal or life-threatening event will be reported to the IRB within 2 days of the investigator learning of the event.
- Unanticipated Problems occurring at any participating site not involving a fatal or life-threatening event will be reported to the IRB within 7 days of the investigator learning of the event.
- Reports from the safety monitor with recommended changes after review by the lead PIs will be reported to the IRB within 7 days of the investigator receiving the report.
- Adverse Events (including Serious Adverse Events) will be reported in summary at the time of continuing review, along with a statement that the pattern of adverse events, in total, does not suggest that the research places subjects or others at a greater risk of harm than was previously known.
- Reports from the safety monitor with no recommended changes will be reported to the IRB at the time of continuing review.

10.5.5 Protocol Deviations

The lead PIs will ensure all protocol deviations are reported to the NIH and BUMC IRB according to the applicable regulatory requirements.

10.6 Quality Assurance of Data

To ensure reliability of data entry and collection, a 15% random sample of completed manually abstracted data elements will be reviewed by the TRIP study team to ensure outcomes and covariates were accurately abstracted and data entered. This data will be checked for quality by TRIP study personnel by accessing the Electronic Health Records on a hospital-issued device using BMC's VPN services, or viewing remotely through BMC's instance of Zoom using BMC's VPN services. Any differences identified will be documented and brought to the data manager for resolution. If the data manager cannot resolve the differences identified, they will be reviewed by the Clinical Adjudication Panel, which will meet as needed through BMC's instance of Zoom. The Clinical Adjudication Panel will be composed of a rotating membership selected

from the six site clinical advisors, the study personnel who conducted the initial abstraction and the cross-check, the project manager, and the data manager.

Quality assurance reports will be prepared by the data manager on a quarterly basis and reviewed by the Principal Investigators. The reports will inform the Principal Investigators about missing, invalid, inconsistent data on selected key variables. The statistician, in collaboration with the data manager on the project will oversee preparation of the reports. The reports will contain a summary of monthly accrual and cumulative accrual, a summary of key characteristics of the study participants, a summary of the completeness and quality of data.

Quality assurance will involve engaging in good data management activities. Procedures that include checking the integrity of data storage (facilitate in collaboration with BMC IT) and examining frequency distributions statistically (in collaboration with the BU School of Public Health) to look for data anomalies such as an excessive number of 'no response' or problems with any skip patterns included in the REDCap registry forms will be in place.

10.7 Stopping Rules

The study has no stopping rules.

11 Study Records Retention

This study will follow recommended Boston Medical Center retention guidelines requiring that study records be retained for at least seven years after completion of the study. As the study team is requesting a waiver of consent, retention of consent forms will not be required. Records will be preserved in their original form (hardcopy, electronic or other media) and saved as an electronic back-up copy whenever possible. All records will be made accessible for inspection and copying by authorized individuals.

12 Statistical Plan

12.1 Study Hypotheses

Our main hypothesis is that the TRIP intervention will result in timelier breast cancer treatment that is more concordant with guidelines, compared with historical control data.
We also hypothesize that the integrated TRIP intervention will be implemented across each of the six study sites.

12.2 Sample Size Determination

Sample size estimates assume 80% power and a two-sided alpha of 0.05 for cross-sectional stepped wedge studies comparing intervention to usual care in two-group statistical analyses. This method incorporates information on the number of steps used in the stepped wedge design, the number of subjects per time period, and the degree of clustering via the intra-class correlation coefficient (ICC) to compute the design effect. A sample size of 220 subjects per

group in a log rank test will provide 80% power at a two-sided alpha of 0.05 to detect a difference in the proportion of subjects with treatment at time, *t*, of 81% in the intervention group compared to 70% in the usual care group, a level estimated from recent data from the clinical sites for the planned study.

This difference yields a hazard ratio of 1.75, a clinically meaningful effect size for time-to-treatment post-diagnosis. Based on our planned number of steps, enrollment per study period, and a reasonable ICC of 0.1, the design effect is 2.29. Thus, we will need to enroll and follow at least 1,008 subjects to provide 80% power for analysis of intervention effectiveness. Our planned sample size of 1,300 women will therefore provide more than adequate power to test our primary outcome.

12.3 Statistical Methods

Given the randomized stepped wedge design, we will report our results according to CONSORT guidelines. Our comparative analyses between the intervention and usual care (control) groups will employ the intent-to-treat principle. We will generate descriptive statistics (means, standard deviations, quantiles for continuous variables; counts/percentages for categorical variables) and schematic plots.

We will compare the intervention and usual care groups on salient variables in order to assess balance in the distributions of these variables. Variables found to differ between the study groups will be further evaluated to assess their confounding effects of intervention vs. usual care differences on primary and secondary outcomes. Given the nature of the cluster randomization employed, we will employ statistical analytic methods that take the correlated nature of the data into account.

Our primary analysis will use multiple logistic regression models to compare the proportion of patients with *timely initiation of treatment* across study groups, adjusting for the influence of race, language barriers to care, insurance status (private vs public), and other covariates that may have a significant effect on the outcome and may be unbalanced across the two study groups.

- To examine heterogeneity in intervention effect, exploratory analyses using multiple logistic regression interaction models will examine whether the effect of the TRIP intervention vary by three covariates of interest:
  - patient race
  - patient preferred language
  - insurance status

- Study groups will also be compared on the secondary clinical outcome of *time to initiation of primary cancer treatment* (the number of days from diagnosis to start of treatment) through Kaplan-Meier survival curves (unadjusted analyses) and Cox proportional hazards regression models controlling for cancer site and other covariates (adjusted analysis).

- *Receipt of quality care* will be analyzed through logistic regression.

For the analysis of the rate of missed appointments, patients will differ on the number of scheduled appointments over the study period. The odds of missing an appointment will be analyzed through generalized estimating equation (GEE) logistic regression models for repeated measures (appointments within patient) dichotomous data.

13 Ethics/Protection of Human Subjects

This study is to be conducted according to applicable US federal regulations and institutional policies (which are based in federal regulations, guidance, and ICH Good Clinical Practice guidelines).

This protocol and any amendments will be submitted to the Boston Medical Center and Boston University Medical Campus IRB, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator.

As this study is a health services quality improvement intervention meant to replace the current patient navigation process as the ‘standard of care’, the study team is seeking a waiver of consent for all eligible patients. Waiver of Consent will be documented as required by the IRB.