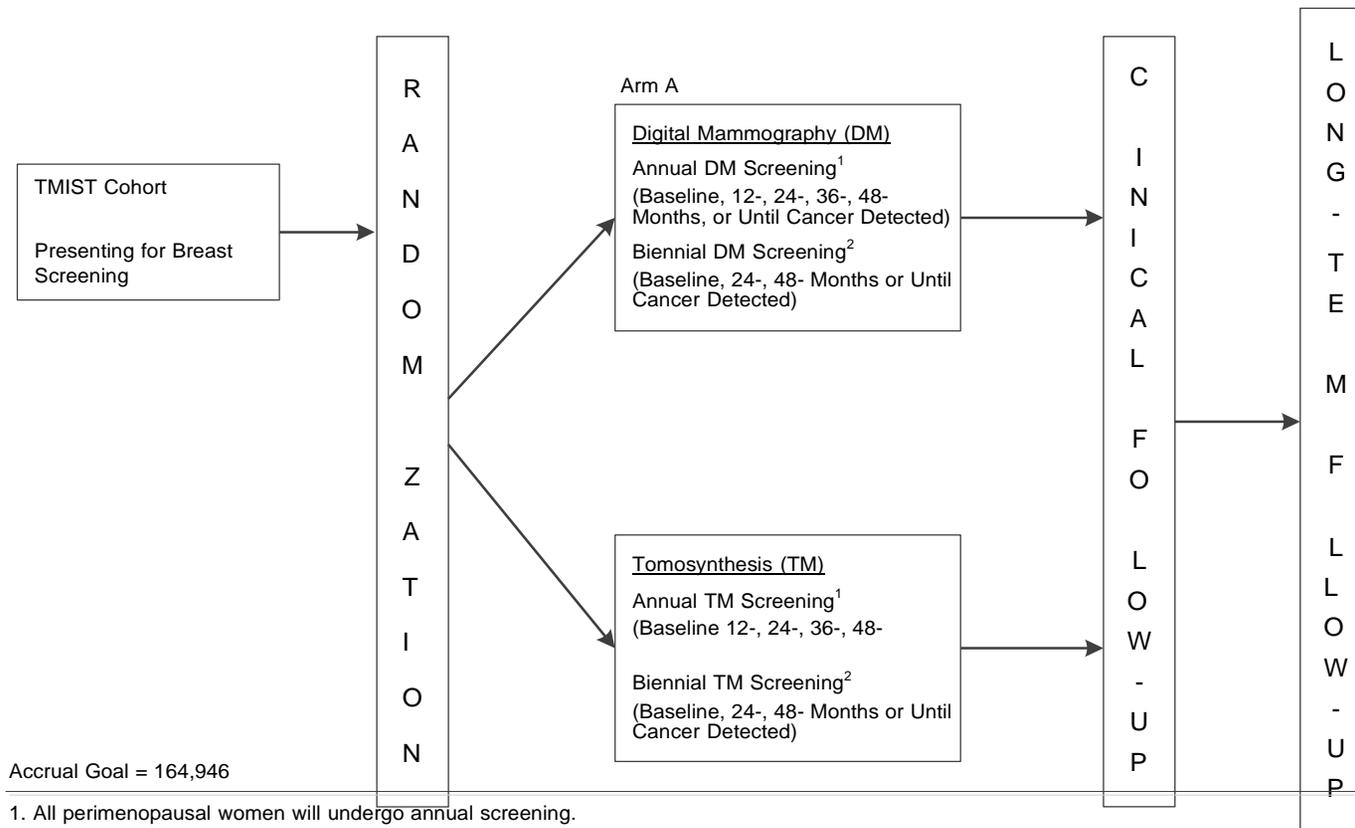


Schema



1. All perimenopausal women will undergo annual screening.
2. Postmenopausal women will undergo biennial screening unless they have any specific risk factors as listed in Section 3.1.10.
3. After their initial protocol screen, women will be followed for up to 4.5 years for assessment of clinical outcomes.
4. Suspicious lesions will undergo diagnostic imaging, biopsy, cancer diagnosis, and/or Tx decision making per local standard practice.
5. Tissue will be collected for analysis for all women who undergo breast biopsy during protocol screening and clinical follow-up periods.
6. On detection and confirmation of breast cancer, patients will cease protocol screening and begin annual Long-term follow-up.
7. Long-term follow-up will last for at least 4.5 – 8 years after study entry.

1. Selection of Patients

Each of the criteria in the checklist that follows must be met in order for a patient to be considered eligible for this study. Use the checklist to confirm a patient's eligibility. For each patient, this checklist must be photocopied, completed and maintained in the patient's chart.

ECOG-ACRIN Patient No. _____

Patient's Initials (L, F, M) _____

Physician Signature and Date _____

NOTE: CTEP Policy does not allow for the issuance of waivers to any protocol specified criteria (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm). Therefore, all eligibility criteria listed in Section 3 must be met, without exception. The registration of individuals who do not meet all criteria listed in Section 3 can result in the participant being censored from the analysis of the study, and the citation of a major protocol violation during an audit. All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (EA.ExecOfficer@jimmy.harvard.edu) or the Group's Regulatory Officer (EA.RegOfficer@jimmy.harvard.edu).

NOTE: Institutions may use the eligibility checklist as source documentation if it has been reviewed, signed, and dated prior to registration/randomization by the treating physician.

1.1 Eligibility Criteria

- ____ 3.1.1 Patients must be women age 45 or older and under age 75 at the time of study entry.
- ____ 3.1.2 Women of childbearing potential must not be known to be pregnant or lactating.
- ____ 3.1.3 Patients must be scheduled for, or have intent to schedule, a screening mammogram.
- ____ 3.1.4 Patients must be able to tolerate digital breast tomosynthesis and full-field digital mammographic imaging required by protocol, to be performed at an ACRIN-qualified facility.
- ____ 3.1.5 Patients must be willing and able to provide a written informed consent.
- ____ 3.1.6 Patients must not have symptoms or signs of benign or malignant breast disease (eg, nipple discharge, breast lump) warranting a diagnostic rather than a screening mammogram, and/or other imaging studies (eg, sonogram). Patients with breast pain are eligible as long as other criteria in 3.1.6 are met.
- ____ 3.1.7 Patients must not have had a screening mammogram within the last 11 months prior to date of randomization.
- ____ 3.1.8 Patients must not have previous personal history of breast cancer including ductal carcinoma in situ.

- _____ 3.1.9 Patients must not have breast enhancements (e.g., implants or injections).
- _____ 3.1.10 Annual Screening Regimen Eligibility Check
- To be eligible for inclusion in the annual screening regimen one of the following three conditions must be met in addition to the eligibility criteria above:
- Patients are pre-menopausal; **OR**
- Post-menopausal aged 45-69 with any of the following three risks factors:
- Dense Breasts (BIRADS density categories c-heterogeneously dense or d-extremely dense), or
 - Family history of breast cancer (first degree relative with breast cancer), or, positive genetic testing for any deleterious genes that indicate an increased risk for breast cancer, or
 - Currently on hormone therapy; **OR**
- Post-menopausal ages 70-74 with either of the following two risk factors:
- Dense Breasts (BIRADS density categories c-heterogeneously dense or d-extremely dense), or
 - Currently on hormone therapy
- Postmenopausal women are defined as those with their last menstrual period more than 12 months prior to study entry. For the purpose of defining menopausal status for women who have had surgical cessation of their periods, women who no longer have menses due to hysterectomy and oophorectomy will be considered postmenopausal. Women who no longer have menses due to hysterectomy without oophorectomy will be considered premenopausal until age 52 and postmenopausal thereafter.
- All other postmenopausal women are eligible for inclusion in the biennial screening regimen.
- For those women who cannot be assigned to annual or biennial screening at the time of study entry and randomization because they are postmenopausal, have no family history or known deleterious breast cancer mutation, are not on hormone therapy AND have not had a prior mammogram, breast density will be determined by the radiologist's recording of it at the time of interpretation of the first study screening examination, either DM or TM. For those who are randomized to TM, radiologists will assign BI-RADS density through review of the DM or synthetic DM portion of the TM examination. Such women cannot be part of the planned stratification by screening frequency and are expected to represent far less than 1% of the TMIST population.
- Breast density will be determined by prior mammography reports, when available. All other risk factors used to determine patient eligibility for annual or biennial screening will be determined by subject self-report.