

Checklist of Voluntary Actions¹ for Company Sponsors to Consider to Improve Recruitment, Enrollment and Retention of Women in Cardiovascular Medical Device Clinical Trials

While there has been some progress, gender bias and under representation of women in cardiovascular medical device trials continues to be a challenging issue. The reasons for under representation are multi-factorial. For example, independent research conducted in Canada showed that physicians rated men as more likely than women to benefit from cardiac catheterization.² Physicians also refer women to trials less often than men.³ Gender gaps in diagnosis of women with heart disease are also a factor. Only 8% of primary care doctors, 13% of gynecologists and 17% of cardiologists were aware of heart disease as a greater cause of mortality in women than men.⁴ In addition, cardiovascular classification schemes may fail to appropriately capture women. One in eight young women are unclassified by the universal definition of myocardial infarction.⁵

This Checklist of Actions is intended to provide cardiovascular medical device companies and others with a menu of options and ideas they can consider on a voluntary basis to improve the recruitment, enrollment and retention of women and other minorities in the clinical trials that they conduct. This document is not intended to be a list of requirements to be applied to every cardiovascular medical device trial. For additional resources please see the AdvaMed [Take Her Health To Heart](#) (THHTH) website.

To improve the recruitment, enrollment and retention of women and minorities, companies may consider the following voluntary options:

Internal Sponsor Actions

- Create a Clinical Trials website on the company website which includes women and diversity in clinical trials information with the Take Her Heart to Health materials and links to other relevant information.
- Ensure all clinical trial material is diverse (women and people of color are included) in posters, pamphlets, patient facing materials, trial recruitment materials, etc.
- Expand screening logs for clinical trials to capture data around why human subjects choose not to participate as well as their perceptions around research.
- Brand the AdvaMed Take Her Heart to Health (THHTH) materials with the Sponsor logo. Train Sponsor staff for awareness.

¹ The information and perspectives represented in this document are not intended to represent a standard and do not represent legal or compliance advice.

² Sloane D, et al. Referrals in Acute Coronary Events for CARDiac Catheterization: The RACE CAR trial. Canadian Journal of Cardiology 2010; 26(8):e290-e296.

³ Dhruva, SS et al. Cardiovasc Qual Outcomes 2011; 4:165-171.

⁴ Mosca L., et al. National Study of Physician Awareness and Adherence to Cardiovascular Disease Prevention Guidelines. Circulation. 2005 Feb 1; 111(4):499-510.

⁵ Spatz, E, et al. The VIRGO Classification System: A Taxonomy for Young Women with Acute Myocardial Infarction; Circulation. 2015; 132:1710-1718.

External Sponsor Actions

- Participate in industry-supported initiatives such as AdvaMed's THHTH initiative and create strategic partnerships.
- Conduct market research (including cultural or other barriers) with patients and physicians to understand more about the barriers to women and minority human subject participation and incorporate learnings into patient-facing and physician training educational materials.
- Actively seek opportunities to share information on women and minorities in medical device trials at industry, clinical or other public events.
- Develop patient advocacy programs.
- During disease awareness presentations, or in company disease awareness materials, ensure women and minorities are represented in pictures, text, statistically, and in leadership

Study Strategy and Site Selection Strategy/Support

- Actively seek women and diverse principal investigators and co-investigators and site research staff.
- Ensure that clinical trial Steering Committees or Advisory boards include female and minority physicians.
- During the clinical trial site screening and selection process, prioritize sites with recruitment programs for women and minorities or sites willing to implement them.
- Encourage clinical trial sites to develop specific recruitment programs for women and minorities (e.g., provide transportation, childcare, etc.).
- Include patient outreach funding in clinical trial budgets for sites to use to attend health fairs, church events, women's groups, etc. All-comers are welcome but the emphasis is on diversity.
- Include wording considerations in the research agreement and wording in the protocol that sets expectations for enrollment of women and minorities.
 - Periodically review progress towards meeting those expectations (e.g., actively monitor the gender mix on monthly clinical trial dashboards).
 - Review prior performance of centers for enrollment of women and minorities and/or ask them to project how many and the percentage of women and minorities they can enroll when selecting centers for new trials.

Protocol Design Considerations

- Include women and minorities in patient engagement activities on clinical trial design.
- Assess numbers of women, men and racial and ethnic minorities with the disease state being studied and include in protocol background section.
- Perform a critical review of inclusion and exclusion criteria (e.g., pregnancy, age, lactation, menopausal status, etc.) to identify and eliminate barriers to enrollment of women such as:
 - Review timeframes to prevent arbitrary timeframes with respect to previous cardiovascular disease diagnosis.
 - Consider whether a requirement for previous chest pain is needed (i.e., women's CD may present differently (e.g., shoulder or jaw pain, stomach pain). Consider all patterns of and diverse and atypical CD presentations and assure they are represented in inclusion criteria.
- Identify alternative follow-up requirements that may encourage participation of women and minorities such as:
 - Minimize required follow up visits where possible
 - Phone follow up by the nurse coordinator
 - Home visits by nurse coordinator
 - On-line or telehealth follow up visits
 - Permit the human subject's primary care provider to perform some of the follow up requirements and be reimbursed for such
 - Allow some follow-up visits at local networked facility
- Include wording considerations in the protocol that sets expectations for enrollment of diverse patient populations inclusive of women and minorities.
 - Periodically review progress towards meeting those expectations (e.g., actively monitor the gender mix on monthly clinical trial dashboards).
 - Review prior performance of centers for enrollment of women and minorities and/or ask them to project how many and the percentage of women and minorities they can enroll when selecting centers for new trials.

Recruitment and Retention Tactics

- Where challenges with diagnosis are a contributing factor (e.g., failure to evaluate, inadequate evaluation, methodologies for diagnosis), work to address the ability for patients to be appropriately evaluated for potential enrollment. This could include strategies such as:
 - Working with referral clinicians and sites
 - Educational programs
- Use multiple tactics to recruit and retain women and minorities such as:
 - Consider flexible hours and days for required follow up visits
 - Posting trial on ClinicalTrials.gov

- Partnering with patient advocacy groups (e.g., to publicize trial or to target geographic areas for study sites)
- Use of live speakers and presentations
- Use of advertisements
- Use of social media to recruit and/or provide updates on clinical trial
- Use of Email
- Use of Clinic flyers
- Reimbursement for participation, transportation and/or childcare
- Develop Newsletters or similar written updates of clinical trial
- Provide investigator tools (e.g., call scripts for patient follow-up, letter or email templates)
- Use of e-consent to help simplify and shorten the informed consent process or simplify informed consent language as much as possible.
- Ensure patient engagement activities include a diverse range of women (e.g., age ranges and racial and ethnic minorities)
- Extra or ongoing patient education on consent or risks and benefits of the trial
- Extra or ongoing patient education on insurance versus study coverage