Breakout Session Discussion Questions

To foster conversation, participants will automatically be placed in breakout rooms after brief presentations for small group live discussion.

After the break-out sessions, participants will automatically rejoin the main session for report-outs.

SESSION 1: SCIENTIFIC, CLINICAL, AND TECHNOLOGICAL CONSIDERATIONS

Group 1:

Moderator: M. Kittleson

Group Members: M. Baffoe-Bonnie; A. Bhatt; J. Grazzini Frantz; Y. Kim; V. Le; F. Urnov

ACC Staff: A. Shinkar; A. Dearborn

Discussion Questions: *Clinical Applications and Emerging Research in Gene Editing*

1. Which emerging therapies in cardiology are poised for imminent approval and use?
2. What future areas offer potential for clinical applications of gene editing in cardiology?
3. What challenges remain in translating innovations in gene editing into clinical practice?

Group 2:

Moderator: J. Januzzi

Group Members: N. Bhave; R. Cook-Deegan; M. Fontana; E. Pardee; R. Rocha

ACC Staff: A. Covington

Discussion Questions: *Advancements in Delivery Mechanisms and Technologies*

1. What are the key challenges in improving the efficiency and specificity of delivery systems for gene editing tools, and how can these challenges be overcome to enhance clinical applications?
2. How do different delivery mechanisms compare in terms of safety, effectiveness, and scalability for therapeutic gene editing, and which appears most promising for widespread clinical use?
3. What role do advancements in nanotechnology play in enhancing the precision and targeting of gene editing therapies, and how might this influence future treatment options for genetic diseases?

Group 3:

Moderator: M. O'Donoghue

Group Members: R. Escandon; C. Gersbach; D. Landup; P. Natarajan; S. Solomon

ACC Staff: S. Bhatia

Discussion Questions: *Integration with Existing Cardiovascular Interventions*

1. How could gene editing be used to address genetic risk factors for cardiovascular diseases, and what challenges exist in integrating these therapies with current treatments?
2. What are the ethical and clinical implications of using gene editing to prevent or treat cardiovascular diseases in patients with early-stage or asymptomatic conditions, particularly when genetic alterations could have long-term, unpredictable effects?

Group 4:

Moderator: K. Brummel

Group Members: A. Choi; D. Dixon; D. Dudzinski; D. Judge; J. Weissmann

ACC Staff: S. Chavez

Discussion Questions: *Evaluating Safety, Efficacy, and Long-Term Outcomes*

1. How should clinical trials be designed to rigorously assess the long-term safety of gene editing therapies, and what specific markers or indicators should be monitored over extended periods to detect potential adverse effects?
2. Given the complexity of gene editing and its potential for off-target effects, what standardized metrics or benchmarks should be used to assess the precision and accuracy of gene editing tools in clinical applications?
3. Is there a role for whole genome sequencing as a routine part of clinical trials to assess off-site integration/effects?
4. Should therapy approvals be staggered to account for long-term safety concerns—for example, by initially approving them only for older populations, who would have shorter cumulative exposure to potential off-target effects?
5. Should approvals be linked to long-term data collection registries to monitor long-term safety?

Group 5:

Moderator: A. Ambardekar

Group Members: S. Cuddy; D. Erion; M. Gulati; A. Khera; W. Parker; R. Thakar

ACC Staff: M. Arobo

Discussion Questions: *Clinical Applications and Emerging Research in Gene Editing*

1. Which emerging therapies in cardiology are poised for imminent approval and use?
2. What future areas offer potential for clinical applications of gene editing in cardiology?
3. What challenges remain in translating innovations in gene editing into clinical practice?

Group 6:

Moderators: A. Caplan

Group Members: G. Fishman; H. Gaggin; R. Kovacs; K. Musunuru; N. Patel

ACC Staff: M. Reynolds

Discussion Questions: *Integration with Existing Cardiovascular Interventions*

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Group 7:

Moderators: R. Barrangou

Group Members: C. Ballantyne; R. Hershberger; C. Rogers; J. Vaishnav

ACC Staff: M. Poblete

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SESSION 2: ETHICAL, REGULATORY, AND SOCIETAL CHALLENGES OF GENE EDITING

Group 1:

Moderator: M. Kittleson

Group Members: M. Baffoe-Bonnie; A. Bhatt; J. Grazzini Frantz; V. Le; Y. Kim

ACC Staff: A. Shinkar; A. Dearborn

Discussion Questions: *Regulatory and Guidance Frameworks for Safe Implementation*

1. What safety measures and regulatory frameworks should be established to ensure that gene editing is safely incorporated into cardiovascular treatment protocols?
2. What role should international regulatory bodies play in establishing universal guidance for gene editing therapies, and how can they ensure consistency in safety and efficacy standards across different countries?
3. How can regulators effectively balance innovation and safety in the fast-evolving field of gene editing, ensuring that therapies are both groundbreaking and thoroughly vetted before being approved for widespread clinical use?
4. What should be the role of ethics committees or advisory panels in overseeing clinical trials for gene editing therapies, and how can they ensure that patient safety and informed consent are prioritized throughout the development process?

Group 2:

Moderator: J. Januzzi

Group Members: N. Bhave; R. Cook-Deegan; M. Fontana; E. Pardee; R. Rocha

ACC Staff: A. Covington

Discussion Questions: *Ethical and Economic Considerations in Cardiovascular Care*

1. How can researchers ensure that delivery methods for gene editing are not only effective but also ethical, considering issues such as potential misuse, environmental impact, and unintended consequences in the body?
2. What are the key ethical challenges in assessing the efficacy of gene editing therapies, particularly when dealing with vulnerable patient populations or rare genetic disorders where the benefits and risks are not fully understood?
3. Should there be limits on how gene editing technologies are applied in cardiovascular care, such as restrictions on editing non-disease-related traits, and who should be responsible for setting these ethical boundaries?
4. What specific ethical guidance should be put in place to govern gene editing in human germline cells, particularly in terms of acceptable applications for therapeutic versus non-therapeutic purposes?
5. What role should public-private partnerships play in advancing gene editing research, and how can they help balance innovation with ethical responsibility?

Group 3:

Moderator: M. O'Donoghue

Group Members: R. Escandon; C. Gersbach; D. Landup; P. Natarajan; S. Solomon

ACC Staff: S. Bhatia

Discussion Questions: *Addressing Access, Equity, and Societal Concerns*

1. How can policymakers ensure that gene editing therapies for genetic diseases are accessible to diverse populations, particularly marginalized or underprivileged communities, without exacerbating existing health disparities?
2. How can health systems balance the potential cost-effectiveness of gene editing for cardiovascular diseases, such as preventing costly heart failure treatments, with the significant upfront costs of developing and implementing these therapies?
3. How can society navigate the potential social consequences of gene editing, such as the creation of "genetic class" divisions, where certain genetic traits may be considered more desirable or valuable than others?
4. What strategies can address the economic disincentives for private insurers to cover gene editing therapies? Given that individuals often change insurance plans, insurers may be reluctant to pay for high-cost, one-time treatments that offer long-term benefits, preferring instead to defer the expense to future insurers.

Group 4:

Moderator: K. Brummel

Group Members: A. Choi; D. Dixon; D. Dudzinski; D. Judge; J. Weissmann

ACC Staff: S. Chavez

Discussion Questions: *Public Education, Informed Consent, and Managing Expectations*

1. How can researchers and clinicians ensure that the long-term outcomes of gene editing therapies are effectively communicated to patients, especially regarding potential risks, genetic implications for future generations, and the possibility of unintended health consequences?
2. How should gene editing companies, regulators, and clinicians collaborate to provide transparent and accurate information to patients and the public, ensuring that expectations are grounded in scientific evidence and ethical considerations?
3. How can public education campaigns be designed to effectively communicate the complexities, risks, and benefits of gene editing therapies, ensuring that the general population understands both the potential and limitations of these technologies?

Group 5:

Moderator: A. Ambardekar

Group Members: S. Cuddy; D. Erion; M. Gulati; A. Khera; W. Parker; R. Thakar

ACC Staff: M. Arobo

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Group Members: C. Ballantyne; R. Bhattacharya; R. Hershberger; C. Rogers; J. Vaishnav

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