Value of Echo in Research:
Use of Echocardiography in Clinical Trials Research

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Many Uses of Echocardiography in Clinical Trials Research

- Improving echo as a test: Technology development, diagnostic capabilities and test performance
  - Examples: New scanners, Contrast agents
- Improving application of echo: Diagnostic strategies
  - PROMISE: 10,000 pt w CP randomized to either functional testing or CTA; MACE is 1◦ endpoint, Cost 2◦
- Harnessing the power of echo: Delineate disease pathophysiology or therapeutic mechanism of action
  - Example: Reverse remodeling in HF trials
- Use information derived from echo as a 1◦ or 2◦ endpoint for efficacy or safety of a new therapeutic

Echo Endpoints in Clinical Trials: General Principles

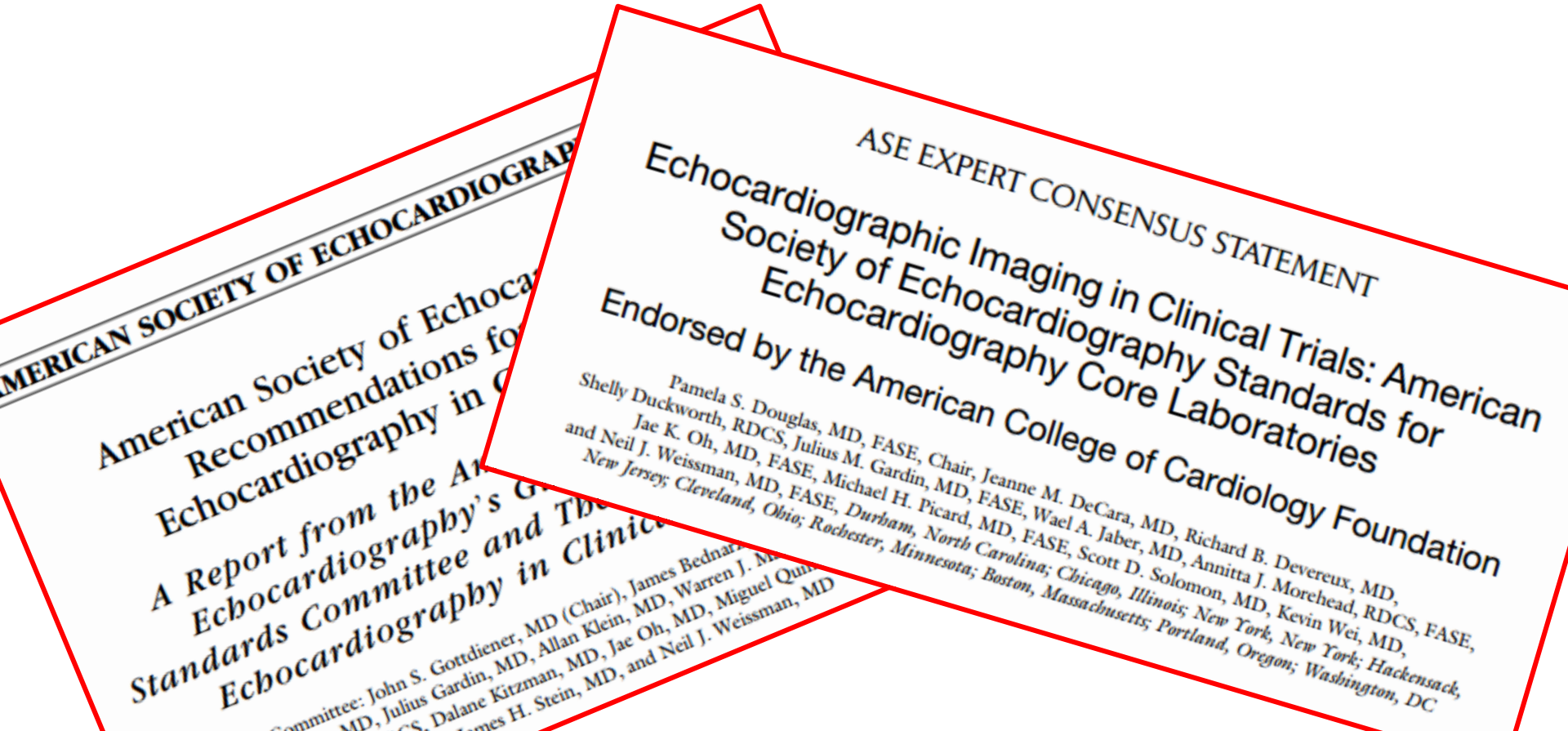
- Endpoints can serve many possible clinical trial roles:
  - Efficacy, effectiveness, utility, efficiency, mechanistic, exploratory and/or safety
- Echocardiography can address all of these
- In RCTs, both echo and trials expertise required throughout
  - Design: Endpoints, Assessments, Timing, Sample size calculations, etc
  - Trial structure: Site vs core lab(s)
  - Image acquisition
  - Image transmission and archiving
  - Image analysis
  - Results analysis and interpretation

Echo Endpoints in Clinical Trials: Advantages

- Structure, function, hemodynamics
- Noninvasive
- Longitudinal assessments
- Safe; No ionizing radiation
- Available at most centers
- Relatively inexpensive
- Well tolerated (no claustrophobia)
- Substantial investigator experience
- Robust national best practice standards in place

ASE Standards Documents for Use of Echo in Clinical Research

- Gottdiener et al. J Am Soc Echocardiogr 2004;17:1086-1119
- Douglas et al. J Am Soc Echocardiogr 2009;



Echo Endpoints in Clinical Trials: Disadvantages

- Most echo research requires quantitation
- All image measurements have variable reproducibility and precision
- If not done well study results can be invalid
- High data quality requires strenuous attention to quality at both site and core lab
- Trial leadership and operations must be supportive
- Regulatory compliance can require more resources and time than anticipated

Echo in Clinical Trials Research: Future Directions

- Echo technology will continue to evolve and improve
- Growing need to understand and provide evidence to support the role of echo in clinical care algorithms
- Increasing importance of translation and robust Quality Improvement
- Increasing incorporation of echo endpoints in clinical trials: Diagnostic strategies, new drugs and devices
- Increasing importance of safety signals in development (eg Cardio-oncology)
- Research infrastructure is improving
  - Transthoracic echo data elements in development
    - FDA, now ACC/AHA/ASE effort
    - Intended use: Clinical care and research reporting
  - Ongoing ASE initiatives to improve echo reproducibility assessment methodology and practice