International Study of Comparative Health Effectiveness with Medical and Invasive Approaches – Chronic Kidney Disease
Primary Report of Quality of Life Outcomes

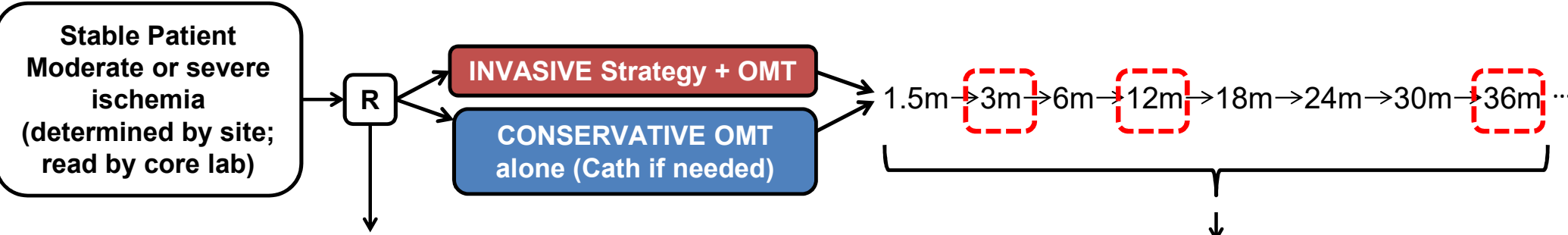*Funded by National Heart, Lung, and Blood Institute*

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Scientific Sessions 2019   #AHA19

ISCHEMIA-CKD QoL Research Question

In a stable patient with advanced CKD and at least moderate ischemia, does an invasive strategy improve patients' health status (symptoms, function and quality of life)?

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Study Design

Stable Patient Moderate or severe ischemia (determined by site; read by core lab)

R

INVASIVE Strategy + OMT

CONSERVATIVE OMT alone (Cath if needed)

1.5m → 3m → 6m → 12m → 18m → 24m → 30m → 36m ···

Brief QoL Assessment

Brief QoL Assessments

Brief QoL Assessment:
- Seattle Angina Questionnaire – 7
  - Angina Frequency**
  - Quality of Life**
  - Physical Limitations

SAQ Summary Score*

Completion Rates

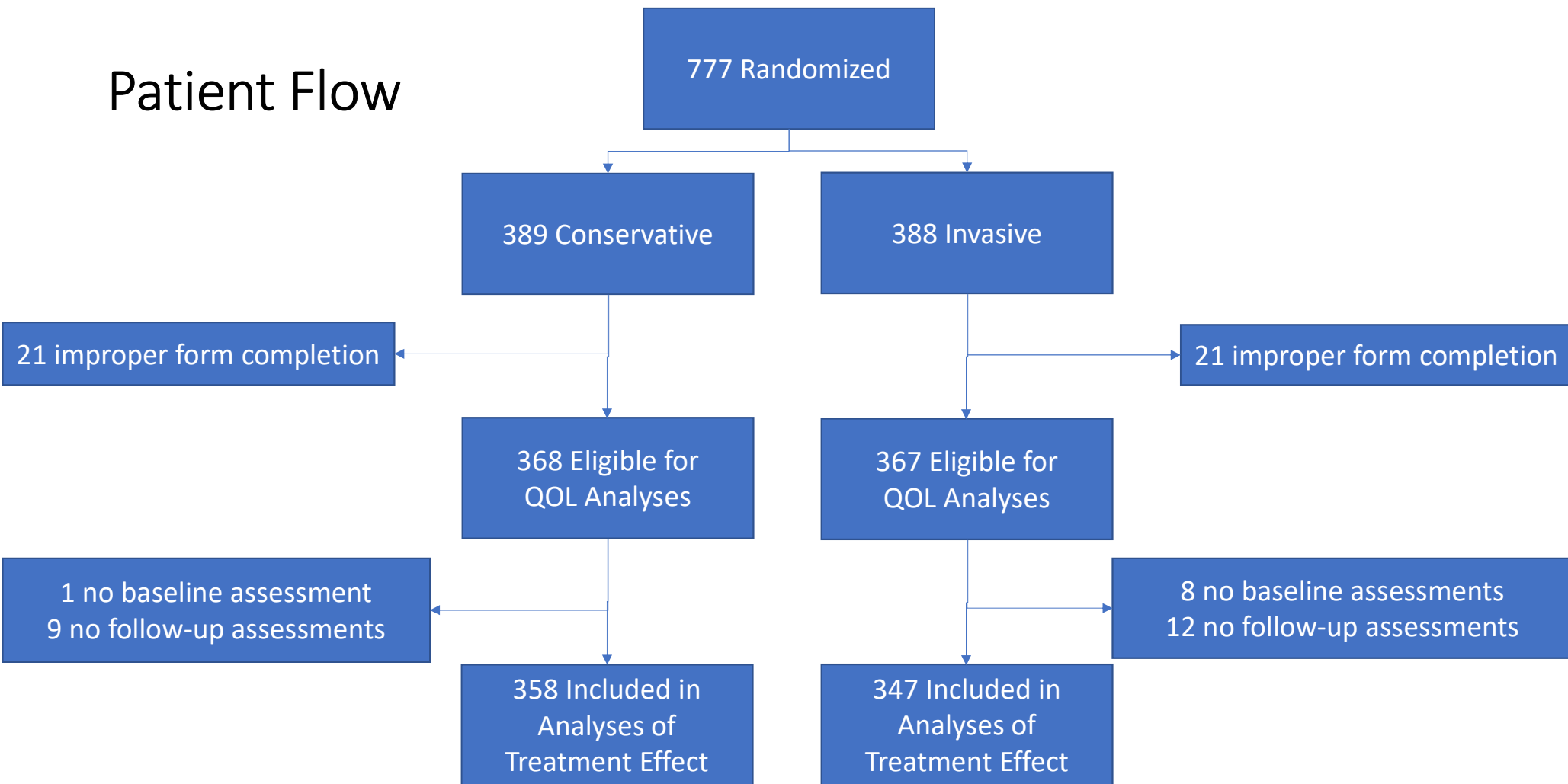|	1.5m	3m	6m	12m	18m	24m	30m	36m
Con:	92%	90%	91%	89%	90%	87%	85%	88%
Inv:	88%	85%	90%	85%	87%	86%	82%	80%

*Primary QoL Outcome
**Secondary QoL Outcome

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Statistical Methods

- Simple descriptive statistics of observed mean scores

- Mixed-effect proportional odds models for all QOL scales
  - Treatment effect = Odds ratio for QOL ≥ X, at each time point
  - Results transformed to individual SAQ scales

- Bayesian methods used for all models to directly estimate probability of treatment effect with posterior means and 95% posterior density intervals
  - Joint models to account for drop-outs due to death as a secondary analysis

- Analyses performed for all patients and stratified by baseline angina
  - e.g. daily/weekly vs. several times per month vs. no angina

Patient Flow

777 Randomized

389 Conservative

388 Invasive

21 improper form completion

21 improper form completion

368 Eligible for QOL Analyses

367 Eligible for QOL Analyses

1 no baseline assessment
9 no follow-up assessments

8 no baseline assessments
12 no follow-up assessments

358 Included in Analyses of Treatment Effect

347 Included in Analyses of Treatment Effect

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Baseline Health Status

Scale	Invasive	Conservative
SAQ Summary Score	75.7±20	76.0±19
SAQ Quality of Life Score	65.3±28	66.2±27
SAQ Angina Frequency Score	86.7±18	86.9±18
Daily/Weekly Angina	11.9%	11.7%
Several Times per Month	38.2%	40.2%
No Angina	50.0%	48.0%

Description of Observed Data – All Patients

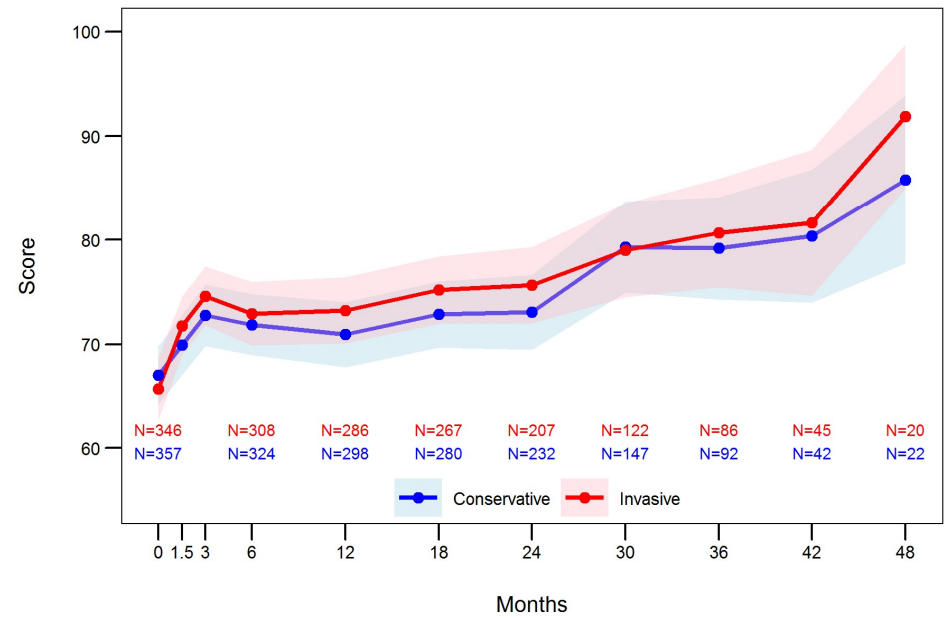## SAQ Summary Score

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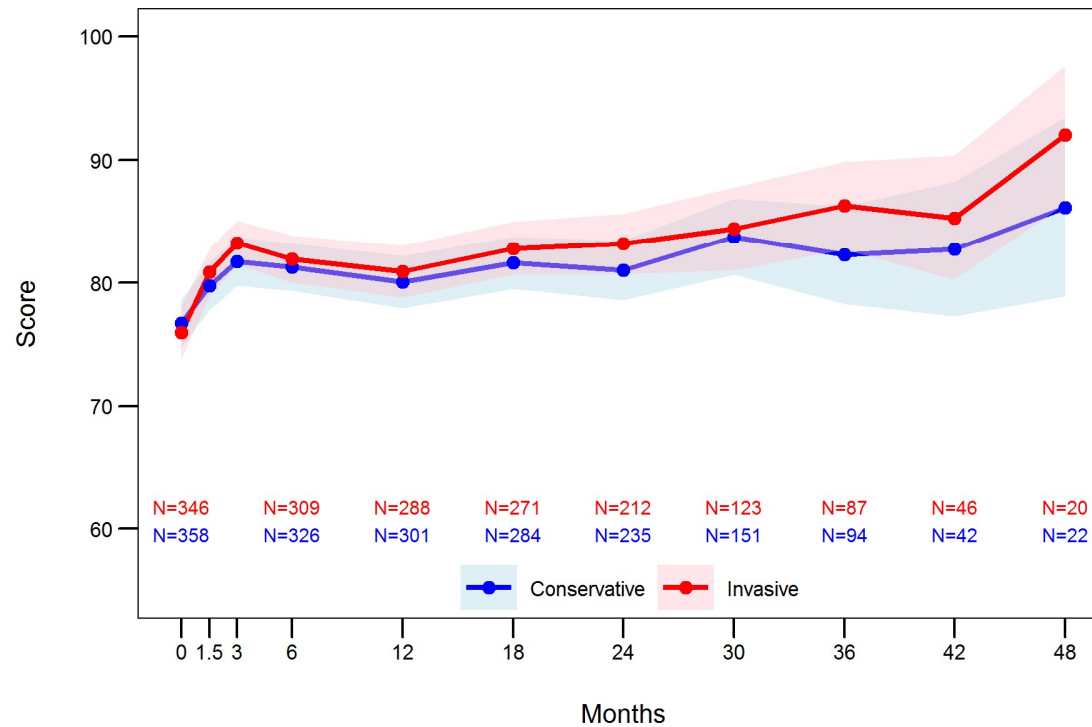
Description of Observed Data – All Patients
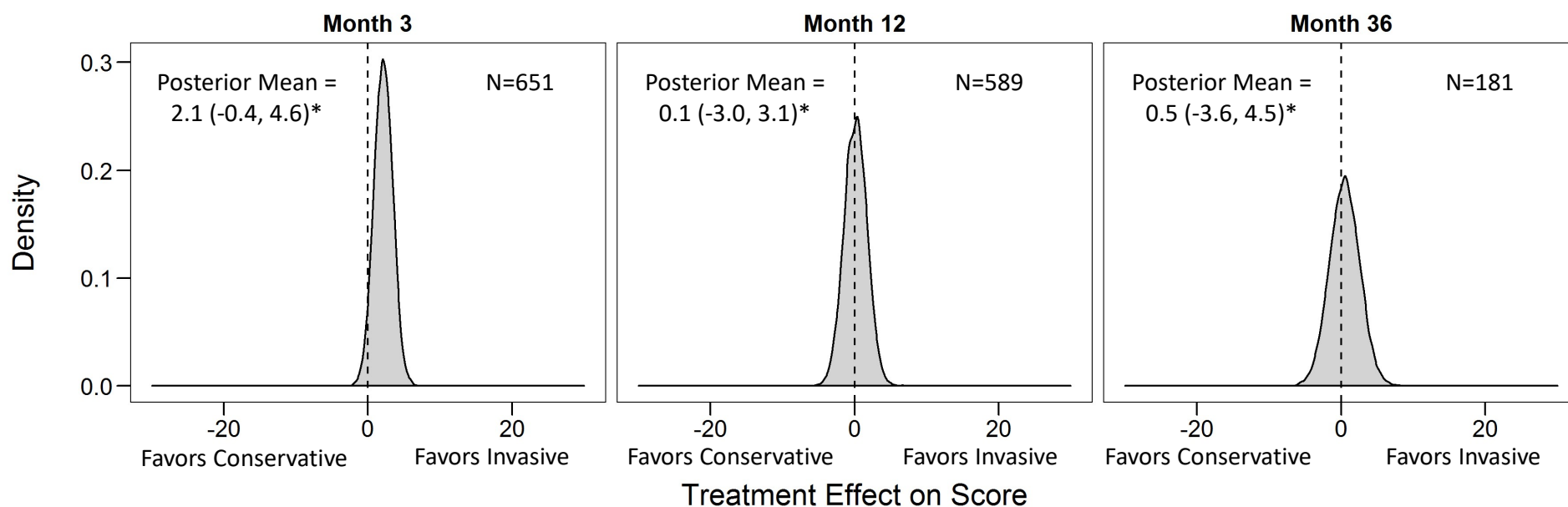

SAQ Angina Frequency Score

SAQ Quality of Life Score

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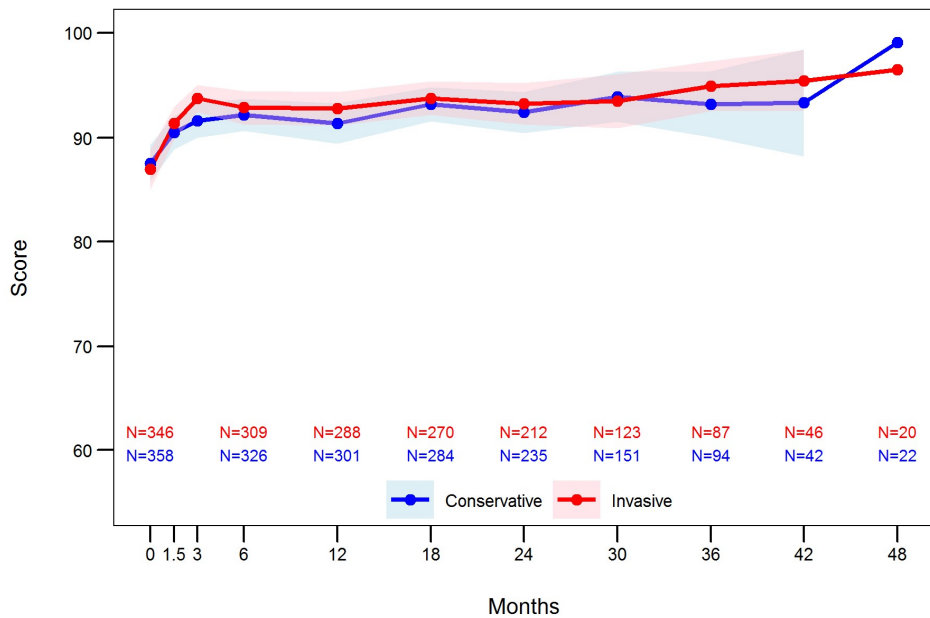
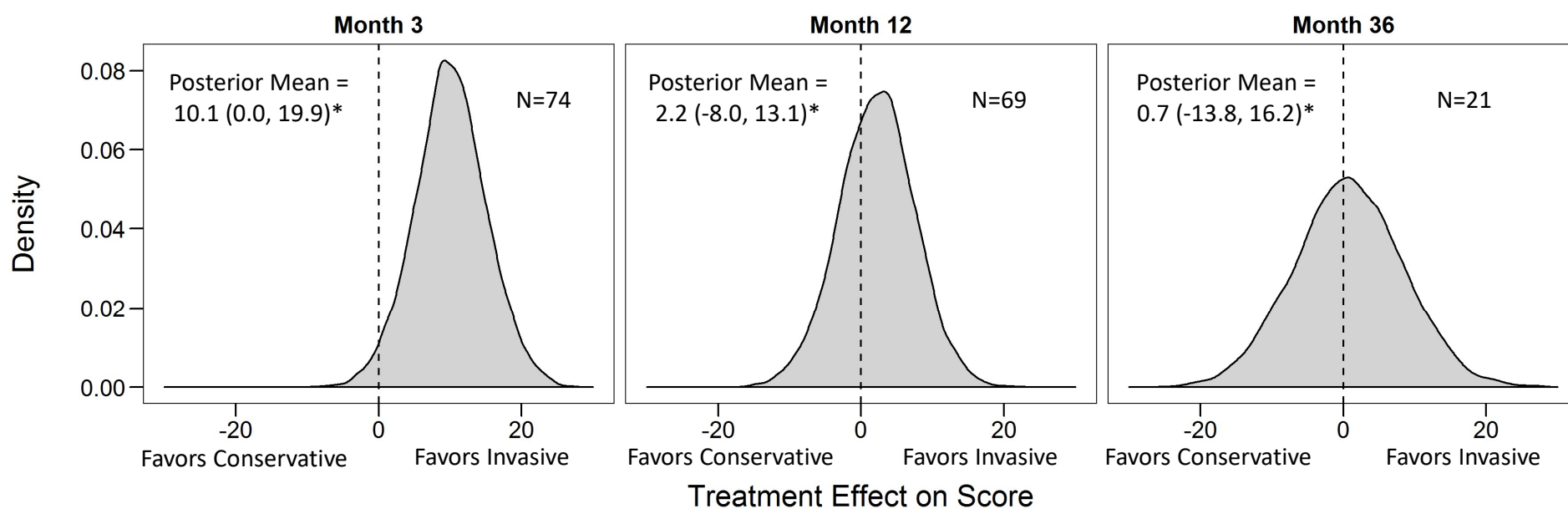# Probability Distribution of Treatment Benefit from Bayesian Analyses

All Patients

Month 3

Posterior Mean = 2.1 (-0.4, 4.6)*   N=651

Month 12

Posterior Mean = 0.1 (-3.0, 3.1)*   N=589

Month 36

Posterior Mean = 0.5 (-3.6, 4.5)*   N=181

Density — Treatment Effect on Score

Favors Conservative / Favors Invasive

*95% Highest Posterior Density Interval

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Probability Distribution of Treatment Benefit on SAQ Summary Score

Daily/Weekly Angina

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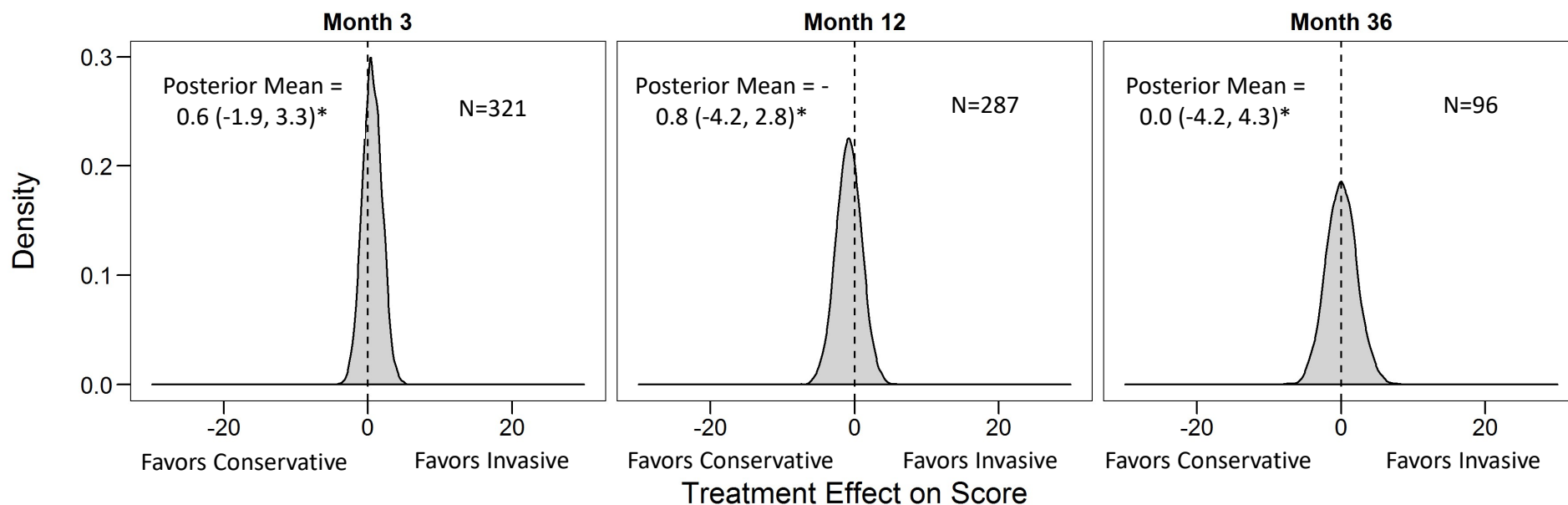# Probability Distribution of Treatment Benefit on SAQ Summary Score

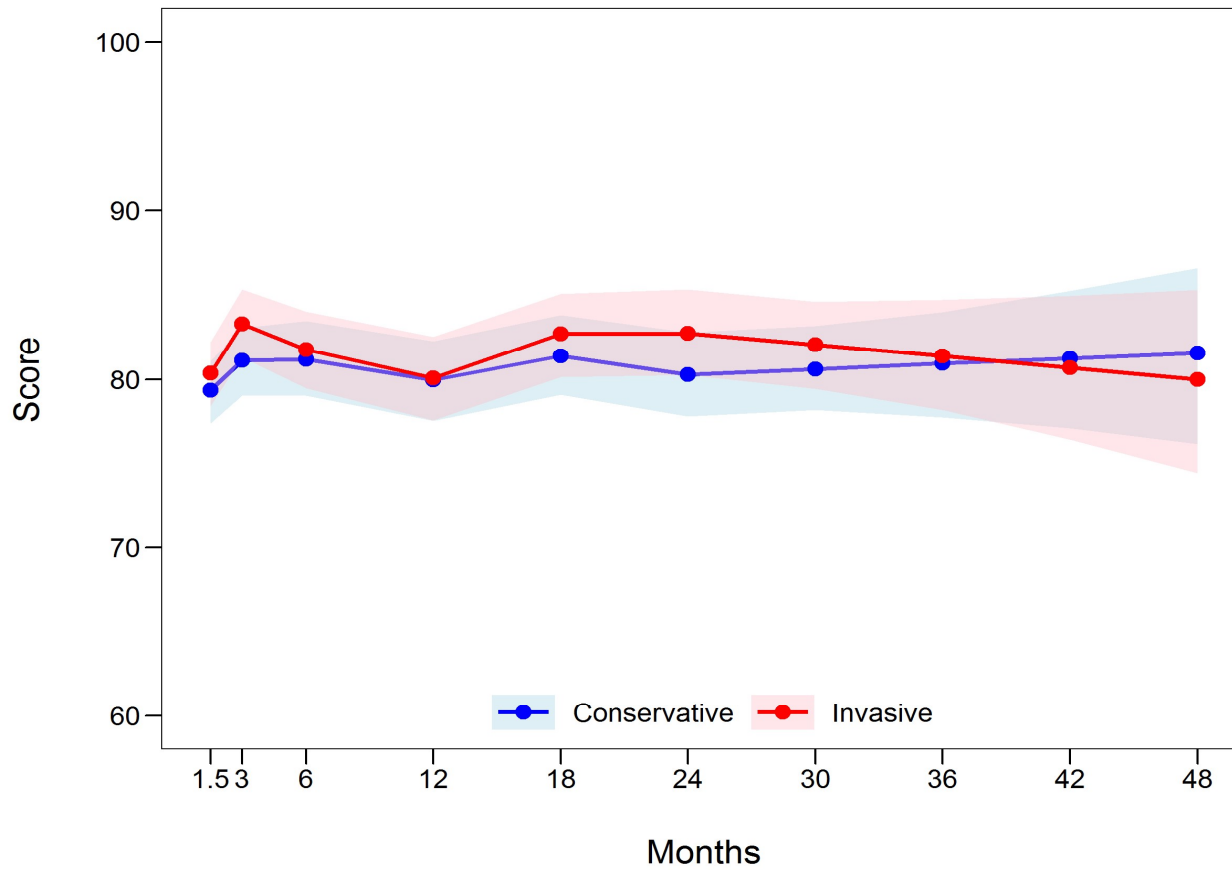At Least Monthly Angina
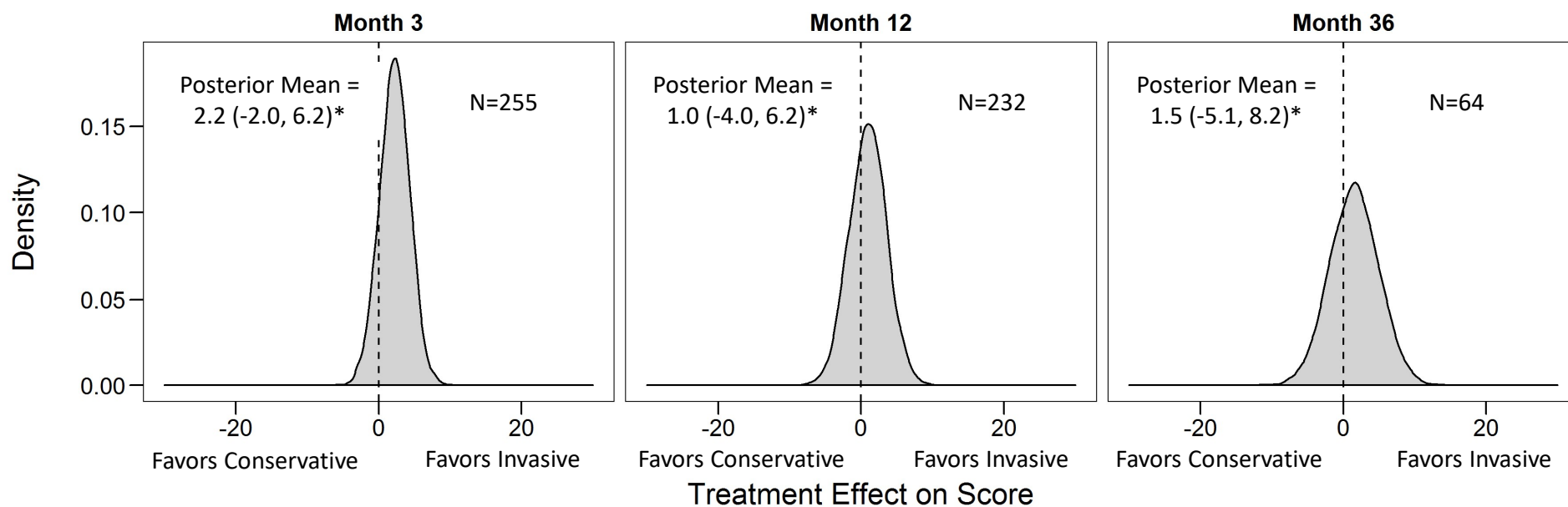
*95% Highest Posterior Density Interval

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Probability Distribution of Treatment Benefit on SAQ Summary Score

No Angina

Month 3	Month 12	Month 36
Posterior Mean = 0.6 (-1.9, 3.3)*	Posterior Mean = -0.8 (-4.2, 2.8)*	Posterior Mean = 0.0 (-4.2, 4.3)*
N=321	N=287	N=96

Favors Conservative — Favors Invasive

Treatment Effect on Score

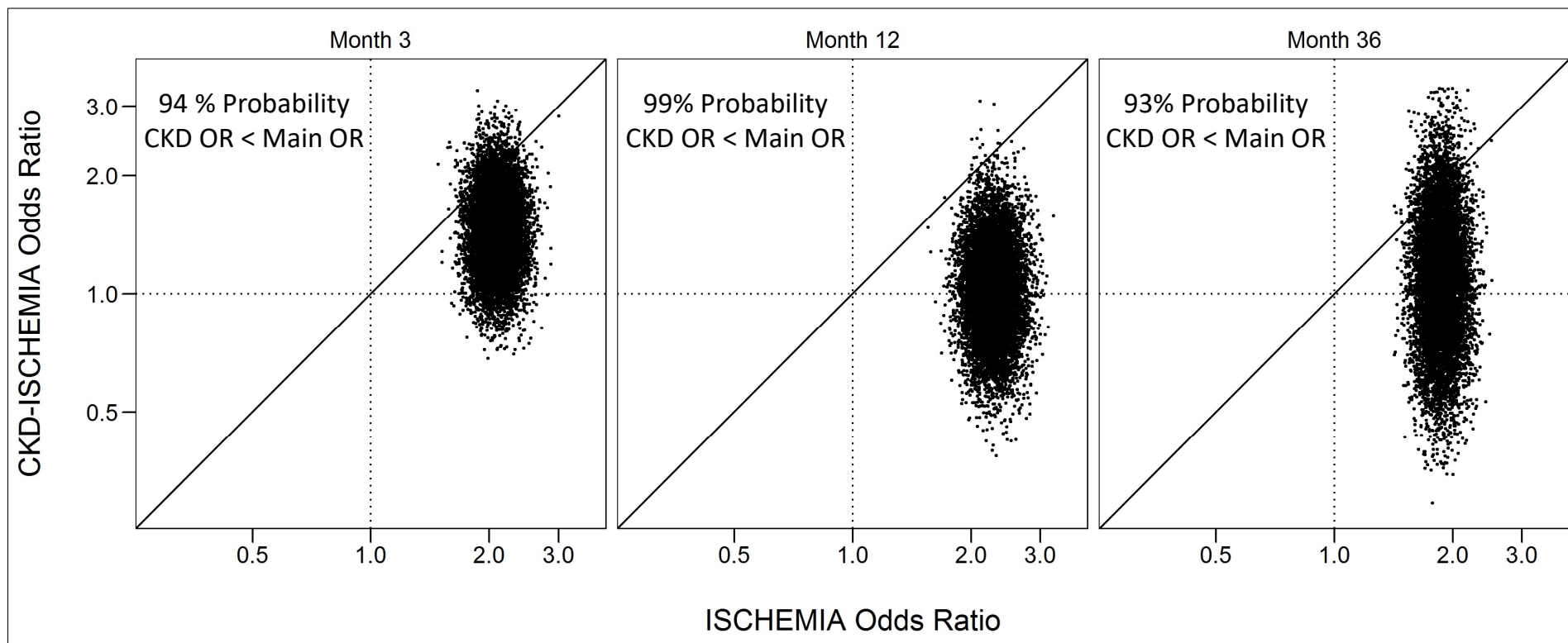*95% Highest Posterior Density Interval*

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Predicted Means of SAQ SS with Joint Models

SAQ-7 Summary Score Odds Ratios

Month	Odds Ratios (95% CrIs)	Probability (%) of *Any* Benefit
1.5	1.20 (0.76, 1.66)	81%
3	1.48 (0.90, 2.16)	95%
6	1.13 (0.61, 1.69)	65%
12	1.06 (0.55, 1.62)	53%
24	1.59 (0.77, 2.49)	93%
36	1.16 (0.45, 2.03)	59%

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Posterior Distribution of ORs for Main and CKD Trials

Limitations

- Missing SAQ data, although small (<15%)

- Very skewed enrollment towards less symptomatic patients; may not have been able to discern a QoL benefit in more symptomatic patients

- Large mortality rate, but little difference in joint models due to similar mortality in both arms

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Conclusions

- In patients with stable CAD, advanced CKD and moderate to severe ischemia, we did not observe a substantial improvement in angina control and quality of life over time

- However, given the large proportion of asymptomatic patients at baseline, we cannot exclude the possibility of a small benefit in symptomatic patients

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Thank you….

- Quality of Life Core Lab: Philip Jones, Dan Mark, Khaula Baloch, Lisa Hatch

- ISCHEMIA-CKD PI: Sripal Bangalore

- ISCHEMIA-CKD Analytic Center and DSMB: Sean O'Brien, Frank Harrell

- ISCHEMIA-CKD Site PIs and Data Coordinators

- ISCHEMIA Trial Chair & Co-Chair: Judith Hochman, David Maron

- The Patients volunteering to participate in ISCHEMIA-CKD

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Backup Slides

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