OPTN Kidney Transplantation Committee
Meeting Summary
November 18, 2024
Teleconference

Jim Kim MD, Chair
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Introduction

The OPTN Kidney Transplantation Committee (the Committee) met via teleconference on 11/18/2024 to discuss the following agenda items:

1. Welcome and Objectives
2. Scientific Registry of Transplant Recipients (SRTR) Report: Non-Utilization Modeling Updates
3. Continuous Distribution Non-Utilization Metrics
4. 2-Year Race Neutral estimated Glomerular Filtration Rate (eGFR) Calculations Monitoring Report
5. Open Forum

The following is a summary of the Committee's discussions.

1. Welcome and Objectives

The Committee Chair welcomed the Committee members, and OPTN Contractor staff reviewed the meeting objectives.

Meeting objectives:

- Review SRTR report on non-utilization modeling updates
- Overview continuous distribution modeling research questions
- Review 2-year *Race Neutral eGFR Calculation* monitoring report

Summary of discussion:

There were no questions or comments.

2. SRTR Report: Non-Utilization Modeling Updates

A representative of the SRTR presented an update on the Kidney Committee's simulation model building request.

Presentation summary:

A simulator is a program designed to mimic a complex system like the organ allocation system. Such a simulator allocates organs as they become available while dynamically updating the waiting list of candidates. Simulations utilize inputs, such as candidates, donors, allocation rules, and the sub-models specifying features of the organ allocation system. A simulation is the concrete execution of the simulator using these inputs to generate data.

A simulation study begins with a set of research questions. Simulation sub-models need to be created to answer those research questions. The sub-models may not be able to adequately answer all research questions, and so it is important to ask both what the results are and whether they should be trusted.

This report looks at how well the models can replicate historical data in order to provide confidence in results shown in future requests.

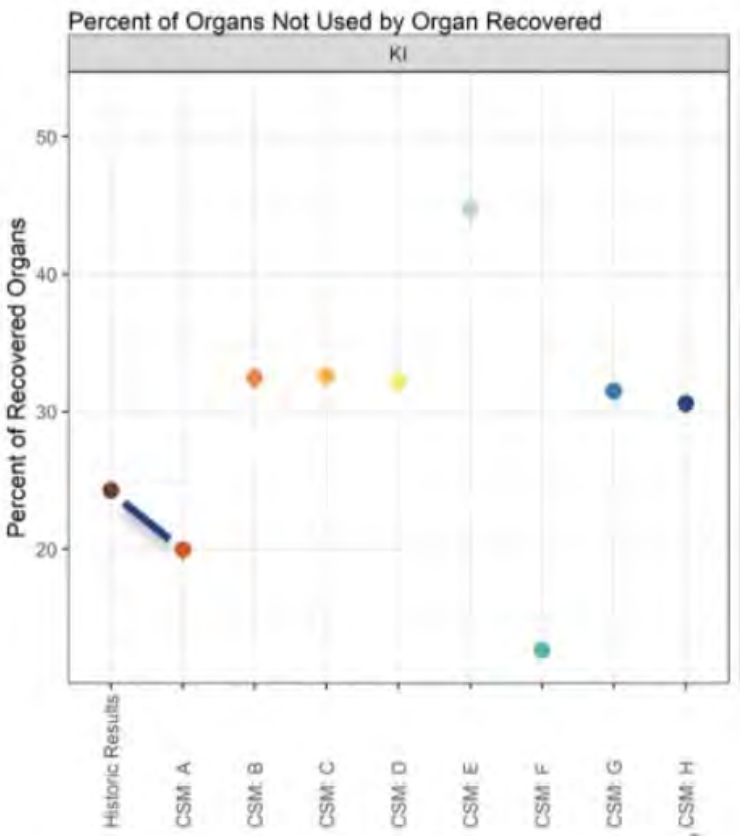
The Committee's research questions are related to how proposed allocation policies will impact access to transplant for various candidate subpopulations, utilization, efficiency, etc. Within this request, the purpose was to:

- Design and assess various collections of simulation sub-models
- Select which collection of sub-models will be used for future requests
- Place interpretative guardrails around the selected collection of sub-models and its ability to answer the Committee's research questions

The SRTR designed and assessed many different collections of sub-models, and selected which collection of sub-models would be used for future requests, when the Committee provide continuous distribution scenarios. For each collection of sub-models, the SRTR simulated historical eras of transplantation and compared the simulated results to historical results through various figures. Each collection of sub-models' ability to answer a research question was qualitatively assessed based on how closely the simulated and historical data matched. The selected collection of sub-models was the one which was judged to best replicate historical data across all of the research questions.

The SRTR presented an example utilizing the first research question - "how do the proposed policies impact non-use of donor kidneys overall?" The SRTR captured this in the simulated data by generating a figure showing percent of organs not used.

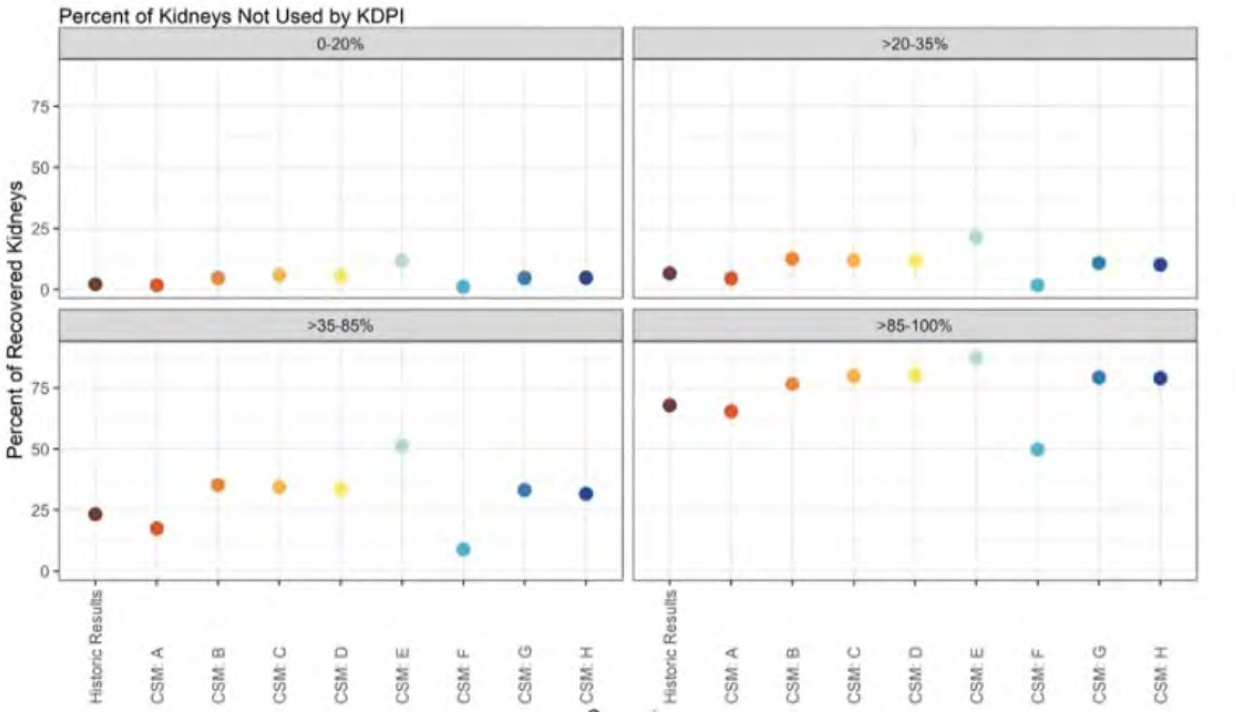
Figure 1: Percent of Organs Not Used by Organ Recovered



The dot on the far left represents the historical value for this metrics, which was at about 25 percent. All of the dots to the right represents a different collection of sub-models used to run the simulation; the corresponding dots represent the simulated non-use rate using that collection of sub-model over the same historical eras of transplantation. This allows the SRTR to qualitatively assess how closely each collection of sub-models replicates historical data. Here, the collection of sub-models labeled "A" (CSM: A) more closely replicates the non-use rate that any of the other collections, although it does slightly underestimate the historical non-use rate.

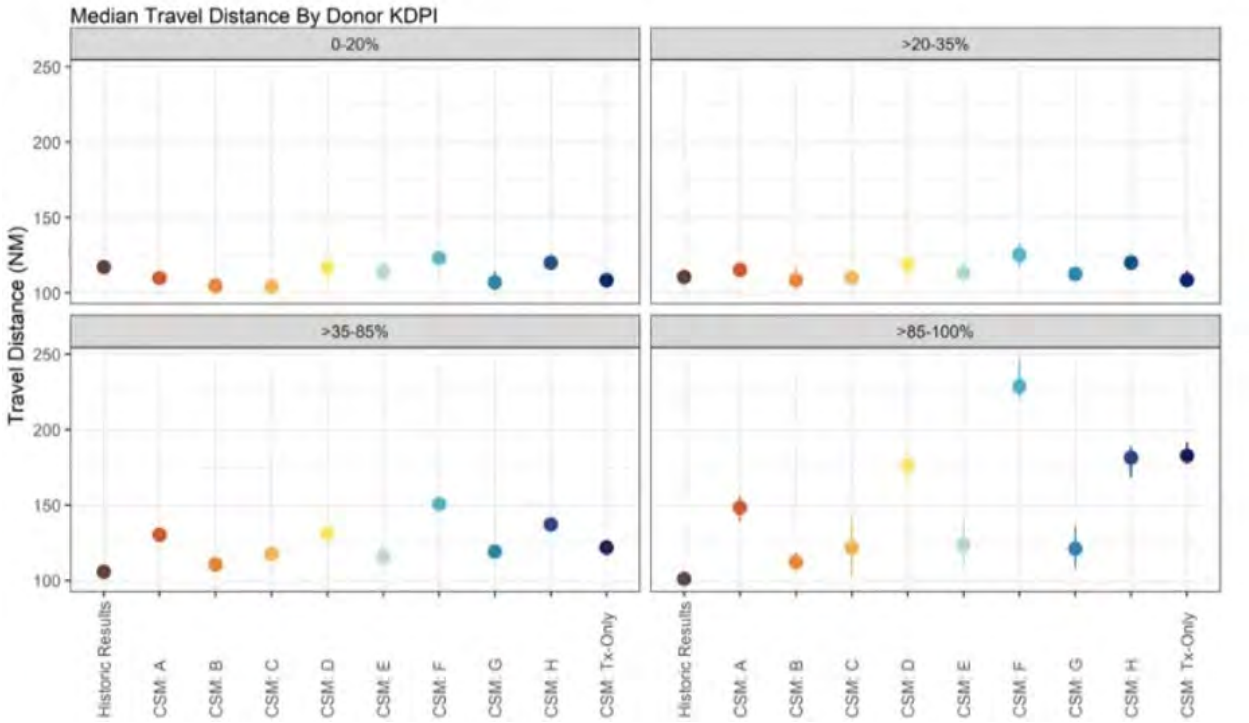
The SRTR described a second example, utilizing another research question: "how do the proposed policies impact non-use of donor kidneys by kidney donor profile index (KDPI)?" In looking at the performance of each collection of sub-models, CSM:A again most closely replicates the historical data across KDPI groupings, although it again slightly underestimates. CSM:A also replicates the relationship between non-use and KDPI, such that as KDPI increases, the simulated non-use increases, just as is shown in the historical data.

Figure 2: Percent of Kidneys Not Used by KDPI



The SRTR representative moved on to a third example, using the research question: "are higher KDPI kidneys traveling shorter distances?" In order to answer this question, the SRTR generated a figure showing the median travel distance by KDPI. As KDPI increases, historically, median travel distance increases. Looking at the collections of submodels, the median travel distance decreases as KDPI increases. This is an indication that the simulation is not quite able to capture the relationship between median travel distance and KDPI. This is a metric that should not be quite so closely evaluated when using the simulation to model continuous distribution policies, because the simulation is not able to accurately describe this relationship.

Figure 3: Median Travel Distance by Donor KDPI



The SRTR described a fourth and final example, using the research question: "how do the proposed policies impact cold ischemic time at acceptance?" When building and evaluating this collection of sub-models, the SRTR attempted to build one that could predict cold ischemic time at acceptance, based on information about the match run and where it was accepted on the match. However, those models were majorly deficient when evaluated against the historical data outside. The SRTR noted that those models were note sufficient enough to bring them into the simulation or present simulated results. The SRTR noted that this is an example of a question that the SRTR feels the simulation is not appropriate and able to adequately answer at this time.

For each figure and research question, the SRTR qualitatively assessed how well each collection of sub models replicated historical data. The selected collection of sub-models was the one which was judged to best replicate historical data across all of the research questions. For kidney, the collection of sub-models labeled "CSM:A" was judged to best replicate any deficiencies in other simulated kidney metrics compared to a transplant-only simulation. The selected collection of simulation sub-models which will be used in subsequent requests is "CSM:A."

The results in this report can help guide the committee when interpreting the results of future simulation requests. Some simulated metrics will not be presented in future simulation requests because this report indicated some deficiency in the ability to model that metric. The inclusion of simulated metrics in future simulation requests does not imply that results in future requests are accurate, but only that we don't have clear reason to doubt their validity. The reason for this is because there are a lot of assumptions that go into simulation requests, the most major of which is that acceptance behavior does not depend on policy, and that donor populations do not shit. These things obviously may very much change, and should be considered when interpreting future results.

Summary of discussion:

One member asked what considerations compose "CSM:A," and whether this sub-model is linked to a particular set of policies. The SRTR representative explained that each collection of sub-models are simulating the same set of policies and eras, and that the only thing shifting from one collection to another is the details about the mathematical models used to run the simulation. The SRTR representative further explained that in some cases, it's the variables that are different, while in other cases, it's the actual form of the model that is different. This allowed the SRTR to test different ways to model utilization in simulation.

The Chair thanked the SRTR for their presentation, and noted that this report is like an addendum to the Organ Allocation Simulation model (OASIM). The SRTR confirmed this, noting that OASIM is the simulator, meaning that it is a software and set of mathematical models that can be used to run simulations. The SRTR representative continued that the OASIM is effectively useless without inputs, which are typically policy scenarios, candidate and donor information, and mathematical sub-models, in order to run the simulation. The SRTR representative noted that this analysis tweaked the internals of the models or the mechanisms in order to see how well the simulation can replicate historical data. The SRTR has done this kind of work in the past, but has not typically presented it as such. This report allows the SRTR to share more of the methodology and decision making before the Committee and the public.

One member remarked that the Committee and community may need to hear this information a few times in order to fully appreciate the nuances. The SRTR representative noted that the report is largely technical, but that the main takeaway from this report is that the SRTR can incorporate utilization modeling without negatively impacting the ability to simulate other metrics. The SRTR noted that these figures provide some interpretive guidelines, and that it is important to understand where the simulator may over or under-estimate some figures. The SRTR also noted that this report describes which questions the simulation can't answer, which ensures the Committee will not be drawing conclusions from unreliable data. The Chair noted that this may make more sense later on when there is data to evaluate different policies, but this report informs on the process and helps the Committee understand and trust the simulation results.

An SRTR representative provided additional context, remarking that simulations are an imperfect reflection of what we understand to have happened in the past in system, let alone a counter factual of a different policy. The SRTR representative noted that this additional information is not intended to see a change in how the results are interpreted, but rather as a more data driven way to communicate the same idea. The SRTR representative explained that this report provides more information about the ways in which simulations are imperfect, to help guide interpretation of just one component of the Committee's decision making.

A member asked how the center level covariates fit into the model. An SRTR representative explained that some of the acceptance models tested accounted for differences in center level behavior, which is the center level covariate. The center covariate means that the probability of acceptance can depend on where that candidate is listed, so a candidate can be more or less likely to accept depending on their program. One member asked if the SRTR was using the offer acceptance ratios currently published. The SRTR noted that the offer acceptance ratios were not used, but the center level covariate was a simpler and potentially better way to capture that data.

3. Continuous Distribution Non-Utilization Metrics and Research Questions

OPTN Contractor staff reviewed the Committee's research questions, highlighting which ones the Committee is able to use simulation to answer.

Presentation summary:

The Committee has posed the following research questions; those that are struck through are *not* able to be adequately modeled in simulation:

- Non-use:
    - How do the proposed policies impact non-use of donor kidneys, overall and by:
        - KDRI and KDPI
        - The factors used to calculate KDPI: age, height, weight, history of hypertension, history of diabetes, serum creatinine, and donation after circulatory death (DCD) status
- Patient access:
    - Do the proposed policies maintain the high level of access that pediatric candidates receive in the current system?
    - Do the proposed policies maintain a high level of access for the extremely highly sensitized (calculated panel-reactive antibody (cPRA) 99.9+)?
    - Do the proposed policies have those with the highest qualifying times undergoing transplant at a rate equal to or higher than current policy?
    - Does patient access differ by OPTN region (transplant rates by OPTN region)?
    - How does median qualifying time at transplant differ between proposed policies?
    - Do the proposed policies impact the distribution of KDPI by estimated post-transplant survival (EPTS)? In other words, are low-EPTS patients appropriately prioritized for low-KDPI kidneys?
- Placement efficiency
    - On average, how far are organs traveling?
    - What is the distribution of travel distance?
    - Are higher KDPI kidneys traveling shorter distances? In other words, is the increased donor modifier having the intended effect?
    - When organs travel farther are they traveling farther to reach vulnerable populations (i.e., pediatrics, extremely highly sensitized)?
- Candidate biology
    - Do the proposed policies maintain access for blood type O and type B candidates? Committee expressed that decreased access for type B and type O candidates would not be tolerable.
        - Do the proposed policies result in fewer disparities in access to transplant across blood types?
    - How do the proposed policies impact the percent of recipients by DR mismatches (0, 1, or 2)?
- Post-transplant outcomes
    - Do the proposed policies result in decreased graft failure and higher survival (short and long term)?
    - Do the proposed policies balance longevity matching and qualifying time? In other words, are we able to have candidates with EPTS of 0-20% undergo transplant with low-KDPI kidneys without dropping their access while still having those with the longest qualifying times undergo transplant?
- Other
    - Do the proposed policies help diminish any disparities in access to transplant for subpopulations:

        - Sex, race, ethnicity, age, rural/urban, geography, CPRA, blood type, EPTS, medical urgency, time on dialysis groups, safety net candidates
    - The proposed policies aim to balance priority for patient access groups but may inadvertently result in decreased access for some subpopulations in an effort to prioritize others. Are there any unintended consequences on waitlist outcomes (additional time waiting, access to transplant, higher cumulative incidence of death, etc.) for any subpopulations:
        - Sex, race, ethnicity, age, rural/urban, geography, CPRA, blood type, EPTS, medical urgency, time on dialysis groups, safety net candidates

Summary of discussion:

One member asked if this was meant to inform efforts to identify hard to place kidneys, or develop a continuous distribution policy. OPTN Contractor staff noted that these questions are meant to help inform the development of the continuous distribution project. OPTN Contractor staff explained that this should provide the Committee a sense of what modeling tools are available to them, and that SRTR and MIT are going to be working together to share tools so that the Committee is able to optimize policies with new metrics.

4. 2-Year Race Neutral eGFR Calculations Monitoring Report

The Committee reviewed the 2-year monitoring report for the *Race-Neutral eGFR calculation* policy.

Presentation summary:

This policy's purpose was to prohibit the use of eGFR calculations that include a race-based variable in OPTN policies. This requirement for race-neutral calculations intended to increase equity in access to transplantation for Black kidney candidates by more accurately estimating their GFR values.

This monitoring report utilizes the following cohorts for waitlist additions, transplants, and waitlist mortality analyses:

- July 26, 2020 – July 26, 2022 ("Pre-policy," 2 years pre-implementation)
- July 27, 2022 – July 26 2024 ("Post-policy," 2 years post-implementation)

This monitoring report utilizes the following cohorts for probability of transplant, to allow 1 year of follow-up:

- July 26, 2021 – July 26, 2022 ("Pre-policy," 1 year pre-implementation)
- July 27, 2022 – July 27, 2023 ("Post-policy," 1 year post-implementation)

In the pre-policy era, kidney waitlist additions were 41.7 percent White, 29.3 Black, 19.2 percent Hispanic/Latino, and 7.7 percent Asian. In the post-policy era, kidney waitlist additions were 39.3 percent White, 30.1 percent Black, 20.7 percent Hispanic/Latino, and 7.3 percent Asian.

In the pre-policy era, the 25.4 percent of black kidney waitlist additions were listed pre-dialysis; this increased to 28.6 percent in the post-policy era. Furthermore, the proportion of black kidney waitlist additions who qualify for waiting time by maintenance dialysis decreased from 63.1 percent pre-policy to 51.7 percent post-policy. The proportion of black kidney waitlist additions who qualify for waiting time by eGFR or creatinine clearance increased from 34.8 percent pre-policy to 46.1 percent post-policy.

The overall kidney transplants by race were composed of 42.6 percent White, 28.4 percent Black, 19.7 percent Hispanic/Latino, and 7.3 percent Asian in the pre-policy era. In the post-policy era, the overall kidney transplants by race was 40 percent White, 30.2 percent Black, 20 percent Hispanic/Latino, and 7.6 percent Asian.

The number of transplants to Black Kidney Recipients listed pre-dialysis increased from 11.5 percent in the pre-policy era to 15 percent in the post-policy era. The number of transplants to Black Kidney Recipients listed while on dialysis decreased from 88.5 percent to 85 percent.

The kidney waitlist death rate per 100 patient years decreased for candidates of all races; Black kidney candidates did have an improved mortality rate on the waiting list.

The probability of a deceased donor kidney transplant within 1 year of listing increased significantly from the pre-policy to the post-policy era. The probability of receiving a transplant within 1 year of listing also increased slightly for most of the other racial groups.

In summary:

- Overall, we observed a greater proportion of black kidney candidates in waitlist additions, and a greater proportion of kidney transplants to Black recipients
- After the policy implementation, both Black kidney candidates' waitlist additions and their transplants also shifted towards being done pre-dialysis vs. on dialysis
- Black kidney candidates' waiting list qualifying source shifted towards a qualifying eGFR or tiebreaker date, and away from dialysis
- Waitlist mortality declined for Black kidney candidates, but also for all other race/ethnicity groups after the policy
- The probability of receiving a transplant within 1 year of listing increased for Black kidney candidates

Summary of discussion:

The Chair thanked the presenter and asked if this data represented the waitlist as of the cohort period, not just new waitlist additions. OPTN contractor staff noted that the waitlist additions were just the nw additions to the waitlist, while the mortality analysis looked at all candidates ever waiting for the two year periods before and after implementation. OPTN contractor staff noted that it is important to remember that the first eGFR policy was implemented in July of 2022, and then the eGFR based waitlist modification policy was implemented in January of 2023. Thus, this data shows some of a combined effect of these two policies; it is difficult to distinguish the effect of one versus another.

One member noted that most of the changes post-policy seem mild or marginal, or else also seen in other demographic groups. The member remarked that, anecdotally, it seemed like the waiting time modification policy made a huge difference, and so it is surprising that the differences are not drastic. OPTN contractor staff noted that this is a two year monitoring report, so it only evaluates within two years, when on average, candidates wait for years. OPTN contractor staff noted that some of these effects may be larger if looking at a longer period. An SRTR representative noted that another explanation for these trends not being as large could be that this analysis examines Black candidates overall, not just those Black candidates who received the waiting time modification. The SRTR representative noted that the waiting list itself is huge, and that there are many Black candidates who did not qualify for waiting time modifications. A member remarked that this makes a lot of sense, and noted that one of the limitations of this policy is that candidates who have never seen a physician and end up in emergency rooms in kidney failure may not have data to qualify for waiting time modifications. The member continued that candidates who may benefit from the waiting time modification policy are those with greater access to care and medical records indicating prior qualification.

A member expressed support for decreasing mortality rates, noting that efforts to reduce inequities seem to be working. Another member noted that increased efforts by the transplant community in

general to transplant patients and get them off of dialysis earlier may also contribute to these trends. The member noted that the transplant community has been working harder to get everyone transplanted faster. OPTN contractor staff noted that the limitation of these monitoring reports is that these trends could be partially due to other, external factors.

Upcoming Meetings

December 16, 2024

Attendance

- **Committee Members**
  - Jim Kim
  - Arpita Basu
  - Eloise Salmon
  - Jason Rolls
  - John Lunz
  - Marc Melcher
  - Patrick Gee
  - Prince Anand
- **SRTR Staff**
  - Bryn Thompson
  - Grace Lyden
  - Jon Miller
  - Jodi Smith
  - Nick Wood
  - Josh Pyke
  - Peter Stock
- **UNOS Staff**
  - Kayla Temple
  - Kaitlin Swanner
  - Keighly Bradbrook
  - Meng Li
  - Lauren Motley
  - Carly Layman
  - James Alcorn
  - Joann White
  - Sarah Booker
  - Thomas Dolan