**Title:** Combining multiple treatment comparisons with personalized patient preferences: a randomized trial of an interactive platform for statin treatment selection

Running Head (for journal reference only): Interactive platform for treatment selection

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# **Declaration of Competing Interests**

None.

#### Abstract

**Background.** Patients and clinicians are often required to make trade-offs between the relative benefits and harms of multiple treatment options. Combining network metaanalysis results with user preferences can be useful when choosing among several treatment alternatives.

**Objective.** Using cholesterol-lowering statin drugs as a case study, we aimed to determine whether an interactive web-based platform that combines network meta-analysis findings with patient preferences had an effect on the decision making process in a general population sample.

**Method.** This was a pilot parallel randomized controlled trial. Between December 2017 and January 2018, we used Amazon's Mechanical Turk to recruit participants over the age of 18 residing in the United States. 349 participants were randomly allocated to see either the interactive tool (intervention) or a series of bar charts (control). Randomisation was computer-generated by the Qualtrics online platform using a 1:1 ratio for allocation and investigators were blinded to group assignment. The primary endpoint was decisional conflict and secondary endpoints included decision self-efficacy, preparation for decision making, and the overall ranking of statins.

**Results.** 258 participants completed the trial and were included in the analysis. On the primary outcome, participants randomized to the interactive tool had significantly lower levels of decisional conflict than those in the control group (difference, -8.53; 95% CI, -12.96 to -4.11 on a 100-point scale; p=0.001). They also appeared to have higher levels of preparation for decision making (difference, 4.19; 95% CI, -0.24 to 8.63 on a 100-point scale; p=0.031). No difference was found for decision self-efficacy, although groups were statistically significantly different in how they ranked different statins.

**Conclusion.** The findings of our proof-of-concept evaluation suggest that an interactive webbased tool combining published clinical evidence with individual preferences can reduce decisional conflict and better prepare individuals for decision making.

### Introduction

When making decisions, patients and clinicians are frequently asked to consider the benefits and harms of multiple treatment options. Such decisions are complex and require obtaining, interpreting, and weighing large quantities of disparate sources of evidence about the efficacy and safety of alternative options. Although ultimate decisions should incorporate patient values and preferences about the relative importance of different outcomes, the extent to which patient preferences are integrated in practice remains unclear (1).

Decision aids are tools that can be used in routine clinical practice to increase the ability of patients and clinicians to make shared, collaborative and informed decisions that reflect the relative benefits and harms of treatment options (2). A recent systematic review including 105 studies (3) found that decision aids can be helpful in increasing a participant's knowledge, and decreasing decisional conflict and passivity in decision making. Decision aids may also allow patients to make decisions that are more reflective of their own preferences based on increased knowledge about the benefits and harms of alternative options. The majority of studies evaluating decision aids to date primarily focused on questions with a "yes" or "no" answer (e.g., proceeding with screening; initiating drug therapy; having surgery), and very few considered subsequent choices once these overarching decisions were made (e.g., choosing among several drug options). "What is the treatment of choice for condition x?" is among the most commonly asked questions in clinical practice (4). Hence, there is a clear need to develop and evaluate tools that effectively inform complex treatment selection decisions.

Statins are among the most widely prescribed classes of drugs due to their established benefits in reducing the risk of cardiovascular disease (5). Although they are often considered to be interchangeable, individual statins may differ in terms of their benefit and harm profiles. A recent series of network meta-analyses evaluated the relative benefits and harms of different statins (6,7). While some statins were shown to be more effective in reducing the risk of major coronary events, others were shown to have better tolerability. For patients to make informed choices and benefit fully from this evidence, the results of these comparative meta-analyses need to be presented in a way that is valid and understandable and also allows patients to reflect on how the performance of different statins interact with their own preferences (8).

We previously developed an interactive web-based tool that combines the results of network meta-analyses with the importance that individuals place on the different benefits and harms of individual statins (9). Our approach was informed by Subjective Expected Utility Theory (SEUT) which has been recommended and widely used in the development of other decision aids (10,11). According to SEUT, individuals have a personal preference for, or utility derived from, different outcomes. Their choices reflect expected utilities, which are a function of individuals' assumptions about the likelihood of outcomes and their preferences for those outcomes (12).

SEUT is especially relevant in the context of complex health care decisions that involve multiple choices with diverse benefits and harms. Such decisions present individuals with a situation that limits their ability to make well informed and considered decisions. In the case of statins, our interactive web-based tool was aimed at assisting individuals in choosing

which statin may be most appropriate for them. As the theory does not provide specific guidance about how best to present information (10), we chose not to present users with numerical estimates of outcome probabilities, and instead developed interactive visuals to communicate the likelihood of which statin is best on different outcomes. In most recent applications of SEUT to the development of patient decision aids, the process of deliberation and preference elicitation was externalized. We chose to have the deliberation process as a key component of the web-based tool by eliciting user preferences about different outcomes. The tool then combined these preferences with information (probabilities) from published network meta-analyses in an intuitive way.

This novel combination of data visualization with the fundamental components of SEUT may reduce the cognitive burden of decision-making, leading to meaningful improvements, and allowing users to feel more engaged with the process. Such improvements could subsequently increase the likelihood that patients are prescribed a statin that offers a unique match for their values and preferences. This emphasis on user preferences for different outcomes could ultimately help to improve primary medication adherence both in the short and long-term (13).

The aim of this study was to examine whether an interactive tool that combines published clinical information with user preferences had an impact on the decisional conflict, decision self-efficacy, and preparation for decision making that people felt when asked to choose among different statins. In addition, we aimed to determine if using the tool altered user preferences for statins. A general population sample was chosen for this proof-of-concept

evaluation in order to test and demonstrate the acceptability and usefulness of this interactive approach in decision-making.

### Methods

#### Study design and participants

The study was a randomized controlled trial. Participants were randomized to parallel groups to see either a set of bar charts showing rankings of benefits and harms of different statins (Supplementary Material Appendix 1) (control group), or the bar charts followed by an interactive tool for statins (intervention group). Allocation was carried out with a 1:1 ratio using the Qualtrics online platform. Participants were not aware of their group assignment. As randomization and data collection were completed centrally through an automatic web-based system, investigators also had no knowledge of group allocation, ensuring concealment of randomized allocation before and during the trial. To achieve the required sample size, responses were screened prior to analysis to ensure that all questionnaires had been completed, that uniform responses had not been given, and that participants had not participated previously. If this was the case, responses were excluded and recruitment was re-opened to ensure the predetermined sample size was met.

Participants were recruited via Amazon's Mechanical Turk (MTurk), which provides a general population sample of respondents from the United States. The task was posted online between December 2017 and January 2018. Participants had to be based in the United States, were over the age of 18 and had not completed the task previously. Each participant was remunerated according to Amazon's Mechanical Turk payment policy upon completion of the questionnaires.

The study was exempt from ethics review from the London School of Economics and Political Science Research Ethics Committee through the self-certification pathway and is reported in line with the CONSORT Statement as shown in the Supplementary Material (14). This proof-of-concept trial was not registered and no changes to the methods were made after trial commencement.

### Intervention

The intervention was an interactive web-based tool which synthesises key findings from published network meta-analyses on the benefits (6), and tolerability and harms (7) of the five most commonly used cholesterol-lowering treatments, statins (available at http://lse.live.kiln.digital/statins/)(9). The tool allows users to specify the importance of each benefit and harm outcome according to their own preferences and this information is combined with information on relative effects of the statins obtained from the network meta-analyses.

The ranking is therefore based on two components: (1) user preferences for different outcomes and (2) performance of individual statins on these different outcomes (9). While the former is directly entered by the user by moving the cursor from "Not important" to "Very important", the latter are obtained from published network meta-analyses.

As described previously, network meta-analyses forming the basis of the tool adopted a Bayesian framework and derived probabilities that each statin had a certain rank using the posterior distributions of all treatments (6,7). These findings were in turn used to estimate the surface under the cumulative ranking curve (SUCRA) for each statin, ranging from 0.0 to 1.0 (15,16).

These findings are incorporated into the tool's machinery as numeric summaries of the overall performance of each statin on each outcome (1.0 when a statin is certain to be the best and 0.0 when it is certain to be the worst). The tool then multiplies user weights applied to different outcomes by the performance on these of different statins. In other words, the overall ranking for each statin is a simple weighted average of its performance on different outcomes with the weight specified directly by the user. The tool ultimately shows users how the different statins rank according to their relative effects in combination with the users' own stated preferences.

## --- FIGURE 1 HERE ---

The control charts were seven bar charts which displayed the likelihood that each statin was the best option on each of the benefits and harms. Therefore, the control charts included identical information obtained from published network meta-analyses. The statin that scored most highly on each chart was indicated (Supplementary Material Appendix 1). Longer bars indicated more favourable benefit and harm profiles. These charts were not interactive, and participants were asked to visually compare how each statin performed on each outcome and reflect on the importance they placed on each independently. Prior to viewing the full set of charts, participants were shown one of the charts (coronary events) with an explanation of how to interpret the information which included highlighting the highest and lowest scoring statin on this outcome. To ensure that participants accurately interpreted the information presented in the bar charts, they were asked to identify which of the statins performed second best on the coronary events outcome before proceeding to the full set of bar charts. Participants could not proceed until the correct answer was selected. The control condition was chosen based on recommendations on presenting benefit-risk information from the IPDAS collaboration (17) and Innovative Medicines Initiative's PROTECT project (18).

#### Measures

### **Background Information**

A series of questions asked about participants' background and demographic characteristics (age, gender, ethnicity, education and income) and their cardiovascular health (whether they had cardiovascular disease, whether they were at high risk of cardiovascular disease, whether they were prescribed statins, whether they had spoken to a doctor about statins). Participants were also asked how important they judged the benefits (all-cause mortality, coronary events, cerebrovascular events) and harms (discontinuation, muscle pain, kidney problems, liver problems) of statins to be on a 5-point scale from "Not at all important" to "Very important".

### Primary outcome measure

#### Decisional Conflict Scale – 10-Item Format (19)

The pre-determined primary outcome of this study was the Decisional Conflict Scale (DCS). DCS measures perceptions of difficulty in making decisions, including lack of information to help choose between options, and feeling unclear about one's own preferences. It is a commonly used outcome in studies evaluating decision aids (3). This version of the scale has

10 items which are rated along a 3-point scale with options of "Yes", "Unsure", "No" and the combined scores are converted to a 0-100 scale with lower scores indicating lower levels of decision conflict. The scale has been validated previously (20) and had an acceptable alpha score of 0.76.

### Secondary outcome measures

#### Decision Self-Efficacy Scale (21)

The Decision Self-Efficacy (DSE) scale measures self-confidence and belief in one's ability to make a decision and to participate in shared decision making. The scale comprises 11 items rated along a 5-point scale from "not at all confident" to "very confident" and the combined scores are converted to a 0-100 scale with higher scores indicating higher self-efficacy. The scale has been validated previously (21) and had an acceptable alpha score of 0.82. Questions were slightly adapted for the purposes of this study to refer to statins.

### Preparation for Decision Making Scale (22)

The Preparation for Decision Making (PDM) scale measures a user's perception of how useful a decision support tool is in preparing them to talk to a health professional about a health decision. The full scale has 10 items but a single item ("Help you recognize that a decision needs to be made?") was omitted before data collection due to lack of relevance to this study. The items are rated along a 5-point scale from "not at all" to "a great deal" and the combined scores are converted to a 0-100 scale with higher scores indicating higher perceived level of preparation. The scale has been validated previously (23) and had an acceptable alpha score of 0.90.

#### Ranking of statins

Participants were asked to rank which of the five statins (atorvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin) would be their first, second and third choice on the basis of the information that they had seen in either the control charts or the interactive tool, while taking into account their preferences.

### Procedure

Participants were provided a link in Amazon's Mechanical Turk which directed them to the survey, hosted on the Qualtrics online platform. After participants were presented with information on the study, they were asked for their consent to take part. Participants were then asked to complete a series of questions about their background characteristics, cardiovascular health, and the importance they placed on each of the benefits and harms included in the control charts and the interactive tool.

After completing these questions, participants were randomized to either see the control charts only, or to see the control charts followed by the interactive tool. Both groups were then asked to indicate the statins that they would consider to be their first, second, or third choice. For participants randomized to the intervention arm, they were asked to rank the statins twice: first after seeing the control charts and second after seeing the interactive tool. After ranking the statins, all participants were asked to complete the DCS, and DSE and PDM scales. At the end of the survey, all participants were shown the interactive tool to seek qualitative feedback on its presentation and acceptability.

### Statistical analysis

Descriptive statistics were used for all variables using frequencies for categorical data and means and standard deviations for continuous data. Differences between the two groups in baseline characteristics, scores on the primary and secondary outcome measures and ranking of the statins with the control charts were analysed using t-tests and Fischer's exact tests. For participants randomized to see both the control charts and the interactive tool, the differences between their rankings of the statins was analysed using the Stuart-Maxwell test.

An *a priori* power calculation was completed to determine the required sample size. It suggested that 129 participants with complete responses in each of the two arms would give 80% power to detect a difference of seven points in the primary outcome on the DCS at the conventional 5% significance level. The standard deviation was assumed to be 20 based on the results of previous studies using the DCS (3).

All analyses were carried out using STATA 14 (24).

# Results

#### Characteristics of the sample

Three hundred and sixty-nine participants consented to take part in the study. Of these, 20 did not complete baseline information. 175 were randomized to the intervention group and 174 to the control group (**Figure 2**). No participants were excluded for taking part in the

study multiple times. After exclusions, there were complete data for 122 participants in the intervention group and 136 participants in the control group.

--- FIGURE 2 ABOUT HERE ----

The mean age of the sample was 32 years and most participants were white (181; 70.2%), had a bachelor degree (115; 44.6%) and the majority earned less than \$50000 per year (**Table 1**). Thirty-seven (14.3%) of the participants reported that they were at high risk for cardiovascular disease and 23 (8.9%) that they had cardiovascular disease. Thirty-nine (15.1%) reported that they had spoken to a doctor about statins and 21 (8.1%) were currently or had previously been prescribed statins. There were no significant differences between the two groups on any of these variables.

--- TABLE 1 ABOUT HERE ---

As shown in **Figure 3**, all-cause mortality, coronary events and cerebrovascular events were judged as the most important outcomes associated with using statins with most participants indicating that they saw these as 'very important'. Kidney and liver problems were next with participants indicating that they considered these as 'important'. Finally, muscle pain and discontinuation of treatment followed with participants indicating these were 'somewhat important.'

--- FIGURE 3 ABOUT HERE ---

Participants in the control and intervention groups reported broadly similar rankings when using the bar charts. Both groups indicated simvastatin was their first choice followed by atorvastatin and other statins (p=0.186). For the second choice, participants in the control group were most likely to choose pravastatin followed by atorvastatin whereas the intervention group reported the opposite (p=0.043). For the third choice, choices were more varied with differences between the groups (p=0.048) (Supplementary Material Appendix 3).

### Primary outcome

### **Decisional Conflict**

The mean total score on the DCS in the intervention group was 14.59 (SD = 15.04) compared to 23.12 (SD = 20.34) in the control group with a difference of -8.53 (95% CI -12.96; -4.11). This difference was significant with a moderate effect size (p=0.001; Cohen's d=0.48).

## --- TABLE 2 ABOUT HERE ---

#### Secondary outcomes

#### Decision Self-Efficacy

On the DSE scale, the mean score for participants in the intervention group was 82.86 (SD = 10.56) compared to 82.40 (SD = 9.96) in the control group with a difference of 0.46 (95% CI - 2.06; 2.98). This difference was not statistically significant (p=0.360; Cohen's d=0.04).

### Preparation for Decision Making

On the PDM scale, the mean score for participants in the intervention group was 96.11 (SD = 18.07) compared to 91.91 (SD = 18.04) in the control group with a difference in means of 4.19 (95% CI -0.24; 8.63). This difference was significant with a small effect size (p=0.031; Cohen's d=0.23).

The participants' reported ranks for the different statins are shown in **Figure 4**. When using the bar charts, most participants ranked simvastatin as their first choice (76; 62.3%). When using the interactive tool, even more participants reported ranking simvastatin as their first choice (101; 82.8%) (p<0.001). Participants were more likely to select atorvastatin as their second choice (43; 35.6%) when using the bar charts. When using the interactive tool, pravastatin (67; 54.9%) was more likely to be ranked second (p<0.001). For the third ranked statin, participants were most likely to choose pravastatin (38; 31.2%) when using the bar charts. When using the interactive toal, their third choice (60; 49.2%) (p<0.001) (Supplementary Material Appendix 3).

--- FIGURE 4 ABOUT HERE ----

#### Acceptability of the Statin Ranking Tool

The quality of the information that was presented in the interactive tool was reported to be good or very good for a series of considerations shown in **Table 3**. In addition, most participants reported that the tool gave the right amount of information (184; 71.3%), that it was balanced in its presentation of the benefits and harms (196; 76.0%) and the majority of participants indicated that they would be likely (112; 43.4%) or very likely (96; 37.2%) to use the tool if it was available.

----TABLE 3 ABOUT HERE ----

All but eighteen of the 258 participants made free text comments about what they liked

about the interactive tool and 187 made comments on what might be improved, with a

further 37 indicating they were unsure or had no suggestions. Thirty-four participants made

no comments on improvements. Examples of user comments are shown in the Box.

**Box**. Participant quotes on the tool.

In response to the question: "What did you like about the statin ranking tool?"

"It enabled me to make more personalized choices. I could really tell it what was important to me. I could readjust it to consider different situations and possibilities, and it gave me insights I didn't fully get with the other tool."

# (Participant 9)

"It was so easy to use and view the changes on the sliders. The information was informative and yet not too much information overload. It was simply put in easy to understand verbiage."

(Participant 16)

"It's very clear and easy to use. The sliders combined with the auto-updating graph makes it very easy to understand. The definitions are very useful. There is a decent amount of information given about each measure."

(Participant 41)

"It's colorful and simple, which makes it easy to process the information - and it allows you to move the sliders around to see how different choices change the rankings. It's a good tool - makes difficult information simple to understand."

(Participant 92)

"I like it, the graphics are easy to interpret and the information is presented in a well-organized way. I felt that I have the right information to make the right choice."

(Participant 137)

"I thought it was very easy to use. I liked that you put in your personal preferences of what is most important to you and it shows you in which order the statins are recommended based on those preferences. I think that gives you a great starting point to talk with your doctor about which one you think might be the right choice. It was very user friendly."

(Participant 165)

In response to the question: "What suggestions do you have to improve the statin ranking

tool?"

"I'd suggest adding more information, probably in the sidebar about the various side effects and other related topics. I felt the information provided was a bit too brief."

(Participant 86)

"The average cost for each could be helpful, or how much is usually covered by insurance. Also, I was wondering if the harms change based on age or gender and if information could be presented on this."

(Participant 164)

# Discussion

Our findings in this randomized controlled trial demonstrate that an interactive tool can have a positive effect on decisional conflict and preparation for decision making, as well as having an impact on the reported rankings of different treatments. Participants in our study judged the content of the tool to be appropriate, clearly presented, and balanced. The tool also had high acceptability: the vast majority of participants reported that they would be likely or very likely to use it if it was available. Individuals using the interactive tool reported considerably lower levels of decisional conflict and may have had higher levels of preparation for decision making, albeit with some lack of precision on this latter outcome. These findings suggest that the information presented in the tool provided the participants with greater certainty in terms of their own preferences. In addition, communication of network meta-analysis findings in an interactive and visually appealing format altered the way participants viewed the statins, resulting in different treatment rankings.

Recent systematic reviews showed that decision aids can effectively increase satisfaction with decision making and improve adherence (3). For example, the Statin Choice decision aid improves knowledge, reduces decisional conflict and increases trust (25,26). However, there is conflicting evidence on whether using the decision aid can improve adherence (25,26). Another statin decision aid, the Option Grid, provides a more interactive manner in which preferences are revealed and discussed. This decision aid shifts user preferences regarding treatment but improvements in satisfaction or adherence have not been documented (27). Both of these decision aids focus on whether to take statins and do not provide information on the comparative effects of statins and patients' preferences regarding these benefits and harms. The interactive tool evaluated in this study is therefore novel in combining the results of published network meta-analyses with user preferences.

Our findings are relevant for a wide range of decision contexts where multiple treatment options are available. Comprehensive network meta-analyses of the benefits and harms of treatment options are becoming more prevalent, with prominent recent examples in second-line treatment for diabetes (28), depression (29), and schizophrenia (30). For each of these conditions, it would be possible to develop tools that combine information on the comparative effects of treatment options with user preferences (31). This may be

particularly important when considering treatment options with more varied benefit or side effect profiles.

A key strength of this study is its relatively large sample size and randomized design. Nevertheless, our results should be interpreted in light of their limitations. The first set of limitations relate to the tool itself, as it shares the limitations of the clinical literature it summarizes. Network meta-analyses synthesized the findings of randomized trials. Patient populations included in randomized controlled trials may not be representative of those in actual clinical practice. There are also challenges when applying population-level average treatment effects to individuals.

The tool does not yet capture the full complexity of the range of factors that may be involved in the decision making process, such as out-of-pocket costs and the user's baseline risk for developing cardiovascular disease. In addition, we used the categories of outcomes commonly reported in systematic reviews and meta-analyses; however, some of the outcomes are overlapping (e.g., all-cause mortality and major coronary events). The current version of the tool does not account for the correlation between outcomes. Therefore, the tool does not allow for accurately trading off different benefit and harm outcomes. Future iterations of the tool should incorporate more complex methods, including multicriteria decision analysis (9). As described previously, the combination of network meta-analysis with multicriteria decision-analysis would provide a framework to accurately capture the trade-off between different benefit and harm outcomes associated with alternative treatment options (32,33).

The tool also reflects the limitations of the current methods to rank treatment choices. In the current tool, the ranking of statins is based on the surface area under the cumulative ranking curve obtained from published network meta-analyses. While such rankings offer a useful summary of the relative effectiveness of multiple treatments, they do not effectively communicate how much better or worse one treatment is compared to another (34). In real-world settings, a nuanced interpretation of treatment rankings may require input from clinicians with an understanding in combining point estimates with uncertainty intervals when comparing the effectiveness of multiple interventions.

Some further limitations relate to the study design. First, participants may have misinterpreted or had difficulty in understanding certain outcome definitions (e.g., myalgia and discontinuations due to adverse events). In some instances, the tool used non-standard terminology to define certain outcomes (e.g., kidney and liver enzyme elevations to refer to organ *damage*).

Second, while we observed a statistically significant difference on the primary endpoint, participants in both arms of the study had low levels of decision conflict and high levels of decision self-efficacy and preparation for decision making. This may be due to the hypothetical nature of the decisions in our study. Unlike the participants of earlier studies who were faced with actual treatment decisions and reported higher levels of decision conflict (3), most participants in our study did not have cardiovascular disease and had not previously considered statin therapy. Nevertheless, the magnitude of effect observed for the DCS in our study was comparable to the findings of studies reported in a recent systematic review of decision aids, including those using clinical samples (3).

Third, MTurk was used to recruit participants. Concerns have previously been raised that MTurk respondents may lack effort and not engage properly with the content of the questionnaires. However, past work has shown that responses from MTurk samples do have good internal validity and can provide better external validity than convenience or student samples (35). MTurk has been successfully used in other studies of decision aids and health communication (36–38). In this study, free text responses regarding what could be improved about the interactive tool were insightful, suggesting that participants effectively followed instructions and engaged with the tasks. It is possible that participants with lower levels of health literacy may require additional assistance when using the tool.

Fourth, we used a general population sample, which is unlikely to be representative of the real-world populations who constitute the target user audience of the tool. For example, approximately one third of participants reported either having or being at high risk of developing cardiovascular disease. They were also considerably younger than the population at risk of experiencing cardiovascular adverse events. Our sample therefore may have severely limited the generalisability of our findings to actual clinical practice.

Finally, the selection of the control charts could have influenced the results of the study. It remains a possibility that the bar charts used in this trial introduced decisional conflict that was subsequently resolved by the interactive tool. However, it is unclear to what extent this might have occurred and whether other approaches could provide lower decisional conflict while also attempting to ensure individuals' preferences were incorporated into decision making. To the best of our knowledge, no consensus exists on the preferred visual approach

to compare the benefits and harms of multiple treatment choices. It was reassuring that the participants answered the test question correctly, which indicates that they accurately interpreted the information conveyed in the bar charts. A multi-arm randomized experiment may be worthwhile to test the comparative effects of different visualization options in the future.

Despite these limitations, this randomized controlled trial offers compelling results from our proof-of-concept evaluation of the novel web-based interactive statin ranking tool. In the future, significant opportunities exist to advance the ranking machinery of the tool while maintaining its interactive and intuitive data visualization elements. As the web-based nature of the tool naturally lends itself to iterative development and improvement, it may be useful when communicating the findings of living systematic reviews and network meta-analyses which incorporate new evidence as it emerges (39,40). Future iterations of the tool should be evaluated among individuals who are eligible for statin therapy in real-world clinical settings. Feasibility of integrating our tool into existing decision aids and developing a comprehensive patient-facing platform should also be explored. Such a platform could assist patients when considering both "whether to take a statin" and "which statin to take".

### Conclusion

The findings of this randomized controlled trial suggest that interactive tools which combine information on the benefits and harms of treatment options with users' preferences can be

useful in decision making. In our proof-of-concept evaluation with statins, the interactive tool reduced decisional conflict and might have improved preparation for decision making when respondents from a general population sample were asked to choose among statins. The tool also effectively altered how trial participants ranked statins with larger numbers selecting the statins with more favourable benefit and harm profiles. Similar tools should be considered in other areas where value judgments are needed between the benefits and harms of treatment options.

## References

- Fowler FJ, Levin CA, Sepucha KR. Informing And Involving Patients To Improve The Quality Of Medical Decisions. Health Aff [Internet]. 2011 Apr 1;30(4):699–706.
   Available from: http://content.healthaffairs.org/cgi/doi/10.1377/hlthaff.2011.0003
- 2. Elwyn G, O'Connor A, Stacey D, Volk R, Edwards A, Coulter A. Developing a quality criteria framework for patient decision aids: Online international Delphi consensus process. Br Med J. 2006;333(7565):417–9.
- Stacey D, Légaré F, Lewis K, Barry MJ, Bennett CL, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev [Internet]. 2017 Apr 12; Available from:

http://doi.wiley.com/10.1002/14651858.CD001431.pub5

 Del Fiol G, Workman TE, Gorman PN. Clinical Questions Raised by Clinicians at the Point of Care. JAMA Intern Med [Internet]. 2014 May 1;174(5):710. Available from: http://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2014.36

 Krumholz HM. Treatment of Cholesterol in 2017. JAMA [Internet]. 2017 Aug 1;318(5):417. Available from:

http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2017.6753

- 6. Naci H, Brugts JJ, Fleurence R, Tsoi B, Toor H, Ades a E. Comparative benefits of statins in the primary and secondary prevention of major coronary events and allcause mortality: a network meta-analysis of placebo-controlled and activecomparator trials. Eur J Prev Cardiol. 2013;20(4):641–57.
- Naci H, Brugts J, Ades T. Comparative tolerability and harms of individual statins : A study-level network meta-analysis of 246 955 participants from 135 randomized, controlled trials. Circ Cardiovasc Qual Outcomes. 2013;6(4):390–9.
- Yudkin JS, Kavanagh J, McCormack JP. Guidelines for treating risk factors should include tools for shared decision making. BMJ [Internet]. 2016 Jun 14;i3147. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.i3147
- Naci H. Communication of Treatment Rankings Obtained From Network Meta-Analysis Using Data Visualization. Circ Cardiovasc Qual Outcomes [Internet]. 2016 Sep;9(5):605–8. Available from:

http://circoutcomes.ahajournals.org/lookup/doi/10.1161/CIRCOUTCOMES.116.00287

- Elwyn G, Stiel M, Durand M-A, Boivin J. The design of patient decision support interventions: addressing the theory-practice gap. J Eval Clin Pract [Internet]. 2011 Aug;17(4):565–74. Available from: http://doi.wiley.com/10.1111/j.1365-2753.2010.01517.x
- 11. Durand M-A, Stiel M, Boivin J, Elwyn G. Where is the theory? Evaluating the theoretical frameworks described in decision support technologies. Patient Educ

Couns [Internet]. 2008 Apr;71(1):125–35. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0738399107004880

- Fischhoff B, Goitein B, Shapira Z. Subjective Expected Utility: A Model of Decision-Making. In 1983. p. 183–207. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0166411508621998
- Polinski JM, Kesselheim AS, Frolkis JP, Wescott P, Allen-Coleman C, Fischer MA. A matter of trust: patient barriers to primary medication adherence. Health Educ Res [Internet]. 2014 Oct 1;29(5):755–63. Available from: https://academic.oup.com/her/article-lookup/doi/10.1093/her/cyu023
- Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ [Internet]. 2010 Mar 23;340(mar23 1):c332–c332. Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.c332
- 15. Salanti G, Ades AE, Ioannidis JPA. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. J Clin Epidemiol [Internet]. 2011 Feb;64(2):163–71. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0895435610001691
- Chaimani A, Higgins JPT, Mavridis D, Spyridonos P, Salanti G. Graphical Tools for Network Meta-Analysis in STATA. Haibe-Kains B, editor. PLoS One [Internet]. 2013 Oct 3;8(10):e76654. Available from: http://dx.plos.org/10.1371/journal.pone.0076654
- Trevena LJ, Zikmund-Fisher BJ, Edwards A, Gaissmaier W, Galesic M, Han PK, et al.
   Presenting quantitative information about decision outcomes: a risk communication
   primer for patient decision aid developers. BMC Med Inform Decis Mak [Internet].
   2013;13(Suppl 2):S7. Available from:

http://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/1472-6947-13-

S2-S7

- PROTECT Work Package 5 Group. Review of visualisation methods for the representation of benefit-risk assessment of medication: Stage 2 of 2. London; 2013.
- O'Connor AM. User Manual Decisional Conflict Scale (10 item question format).
   Ottawa; 1993.
- Linder SK, Swank PR, Vernon SW, Mullen PD, Morgan RO, Volk RJ. Validity of a low literacy version of the Decisional Conflict Scale. Patient Educ Couns [Internet].
   2011;85(3):521–4. Available from: http://dx.doi.org/10.1016/j.pec.2010.12.012
- 21. O'Connor AM. User Manual Decision Self-Efficacy Scale. Ottawa; 1995.
- Graham ID, O'Connor AM. User Manual Preparation for Decision Making. Ottawa;
   1995.
- Bennett C, Graham ID, Kristjansson E, Kearing SA, Clay KF, O'Connor AM. Validation of a Preparation for Decision Making scale. Patient Educ Couns [Internet]. 2010 Jan;78(1):130–3. Available from:

http://linkinghub.elsevier.com/retrieve/pii/S0738399109002328

- 24. StataCorp. Stata Statistical Software: Release 14. College Station, TX; 2015.
- 25. Weymiller AJ. Helping Patients With Type 2 Diabetes Mellitus Make Treatment Decisions. Arch Intern Med [Internet]. 2007 May 28;167(10):1076. Available from: http://archinte.jamanetwork.com/article.aspx?doi=10.1001/archinte.167.10.1076
- Mann DM, Ponieman D, Montori VM, Arciniega J, McGinn T. The Statin Choice decision aid in primary care: A randomized trial. Patient Educ Couns [Internet].
   2010;80(1):138–40. Available from: http://dx.doi.org/10.1016/j.pec.2009.10.008
- 27. Scalia P, Durand MA, Kremer J, Faber M, Elwyn G. Online, Interactive Option Grid Patient Decision Aids and their Effect on User Preferences. Med Decis Mak.

2018;38(1):56-68.

- Mearns ES, Sobieraj DM, White CM, Saulsberry WJ, Kohn CG, Doleh Y, et al.
   Comparative efficacy and safety of antidiabetic drug regimens added to metformin monotherapy in patients with type 2 diabetes: A network meta-analysis. PLoS One. 2015;10(4):1–28.
- 29. Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet [Internet]. 2018;1–10. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0140673617328027
- 30. Leucht S, Cipriani A, Spineli L, Mavridis D, Örey D, Richter F, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: A multiple-treatments meta-analysis. Lancet. 2013;382(9896):951–62.
- 31. Choi SE, Berkowitz S, Yudkin JS, Naci H, Basu S. Personalizing Second-Line Type 2 Diabetes Treatment Selection: Combining Network Meta-analysis, Individualized Risk, and Patient Preferences for Unified Decision Support. Medicial Decis Mak.
- Tervonen T, Naci H, Van Valkenhoef G, Ades AE, Angelis A, Hillege HL, et al. Applying Multiple Criteria Decision Analysis to Comparative Benefit-Risk Assessment. Med Decis Mak. 2015;35(7):859–71.
- 33. Naci H, Van Valkenhoef G, Higgins JPT, Fleurence R, Ades AE. Evidence-based prescribing: Combining network meta-analysis with multicriteria decision analysis to choose among multiple drugs. Circ Cardiovasc Qual Outcomes. 2014;7(5):787–92.
- 34. Mbuagbaw L, Rochwerg B, Jaeschke R, Heels-Andsell D, Alhazzani W, Thabane L, et al. Approaches to interpreting and choosing the best treatments in network meta-

analyses. Syst Rev [Internet]. 2017 Dec 12;6(1):79. Available from: http://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-017-0473-z

35. Berinsky AJ, Huber GA, Lenz GS. Evaluating Online Labor Markets for Experimental Research: Amazon.com's Mechanical Turk. Polit Anal [Internet]. 2012 Jan 4;20(03):351–68. Available from: https://www.cambridge.org/core/product/identifier/S1047198700013875/type/jour

nal\_article

- 36. Trenaman L, Munro S, Almeida F, Ayas N, Hicklin J, Bansback N. Development of a patient decision aid prototype for adults with obstructive sleep apnea. Sleep Breath [Internet]. 2016 May 8;20(2):653–61. Available from: http://link.springer.com/10.1007/s11325-015-1269-9
- Manigault AW, Handley IM, Whillock SR. Assessment of Unconscious Decision Aids Applied to Complex Patient-Centered Medical Decisions. J Med Internet Res [Internet]. 2015 Feb 5;17(2):e37. Available from: http://www.jmir.org/2015/2/e37/
- Rezai LS, Chin J, Bassett-Gunter R, Burns C. Developing Persuasive Health Messages for a Behavior-Change-Support-System That Promotes Physical Activity. Proc Int Symp Hum Factors Ergon Heal Care [Internet]. 2017 Jun 15;6(1):89–95. Available from: http://journals.sagepub.com/doi/10.1177/2327857917061020
- Elliott JH, Turner T, Clavisi O, Thomas J, Higgins JPT, Mavergames C, et al. Living Systematic Reviews: An Emerging Opportunity to Narrow the Evidence-Practice Gap. PLoS Med [Internet]. 2014 Feb 18;11(2):e1001603. Available from: https://dx.plos.org/10.1371/journal.pmed.1001603
- 40. Vandvik PO, Brignardello-Petersen R, Guyatt GH. Living cumulative network meta-

analysis to reduce waste in research: A paradigmatic shift for systematic reviews? BMC Med [Internet]. 2016 Dec 29;14(1):59. Available from: http://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-016-0596-4