

## DISCO: A Patient Intervention to Reduce the Financial Burden of Cancer

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## **1.0. Objectives:**

Our overall goal of this American Cancer Society-Funded project is to **address the burden of financial toxicity and work toward health equity** by testing the effectiveness of an electronic, highly scalable, and tailorable education and communication intervention on patient outcomes in a population of economically and racially/ethnically diverse patients from all age groups. We will do this by accomplishing the following 3 aims and testing the following hypotheses:

**Aim 1: Using a RCT, determine the effectiveness of the Discussions of Cost App (DISCO App) on short-term outcomes at three levels:**

- a. **patient** (treatment cost knowledge, self-efficacy for managing cost and physician interactions, and perceived financial toxicity [cost distress, material hardship]);
- b. **patient-oncologist interaction** (patient active participation; frequency and quality of patient-initiated cost discussions with oncologists; oncologists' patient-centered communication as observed in video recordings); and
- c. **healthcare utilization** (social work/financial navigation referrals, social work/financial navigation referral uptake).
  - a. **H1a:** We hypothesize that the DISCO App will improve outcomes for all intervention patients, and
  - b. **H1b:** Black patients will experience greater improvement than White patients, lower-income patients will experience greater improvement than higher-income patients, and younger patients will experience greater improvement than older patients.

**Aim 2: Determine the effectiveness of the DISCO App on longer-term outcomes (financial toxicity, treatment adherence, and clinic appointment adherence).** We will compare longer-term outcomes across arms.

- a. **H2a:** We hypothesize that: patients receiving the DISCO App + booster will experience the greatest improvement in outcomes, followed by patients receiving the DISCO App, and last, usual care; and that
- b. **H2b:** Black patients will experience greater improvement in outcomes than White patients.

**Aim 3: Test potential mediators and moderators of the relationship between the short-term and longer-term outcomes of the DISCO App.**

- a. **H3:** We hypothesize that the DISCO App will increase the frequency and quality of patient-initiated cost discussions, which will increase social work/financial navigation referrals, social work/financial navigation referral uptake, and patient self-efficacy for managing treatment cost, which in turn will reduce financial toxicity and improve adherence.
- b. **H4:** We hypothesize that this relationship will be moderated by patient socio-demographic characteristics.

## **2.0. Background:**

**Financial toxicity, the severe material and psychological burden of the cost of cancer treatment, affects an estimated 30-50% of patients.**<sup>1-5</sup> As cancer treatment costs escalate<sup>6</sup> and the cost burden increasingly shifts to the patient,<sup>7-10</sup> more patients are experiencing severe material economic consequences. Across cancer types, patients are, on average, responsible for \$16,000 annually for out-of-pocket direct and indirect treatment costs.<sup>11</sup> People with cancer are 2.6 times as likely to file for bankruptcy as people without cancer.<sup>12,13</sup> Recent studies of breast cancer survivors found that 24% used all of their savings over a six-month period to pay for treatment,<sup>14</sup> and 62% of colorectal cancer survivors incurred debt to pay for treatment with an average liability of \$26,860.<sup>15</sup> Financial toxicity can also result from indirect costs, such as loss of income. Breast cancer survivors reported losing an average of 42 work days per year, which translated to an average of \$8,236 in lost wages.<sup>16</sup> Treatment costs can also have deleterious psychological effects, with almost half of survivors reporting significant, even catastrophic, levels of cost-related distress.<sup>17-19</sup> We emphasize that the material and psychological consequences of financial toxicity can be experienced both short-term during diagnosis and treatment and longer-term into survivorship.<sup>1,19,20</sup>

**The burden of financial toxicity is a health equity issue, disproportionately affecting patients who are racial/ethnic minorities,<sup>15,21-24</sup> have lower incomes,<sup>13,15,18,22</sup> and/or are <65 years of age.<sup>13,22,25</sup>** Compared to White cancer patients, Black cancer patients are twice as likely to deviate from treatment, have utilities turned off, and move out of their homes because they cannot afford to pay for treatment and living expenses.<sup>21</sup> Black survivors are more likely to report treatment-related debt (15%) than White survivors (9%). Lower-income Black breast cancer patients spend a greater proportion of their income (27-31%) on treatment expenses than lower-income Whites (9-13%).<sup>22</sup> Survivors are 1.4 times as likely to be unemployed (often due to extended time off for treatment/recovery) as people without cancer; racial/ethnic minority survivors are twice as likely to be unemployed as White cancer survivors.<sup>26</sup> The disproportionate burden of financial toxicity experienced by racial/ethnic minorities remains even when controlling for employment status and insurance status at diagnosis.<sup>22,23</sup> Younger patients (<65) are also at greater risk for financial toxicity and bankruptcy than older patients, mainly due to insurance status (i.e., Medicare).<sup>25</sup> A study of colon cancer patients found being younger, nonwhite, and/or having a low annual income increased the risk of financial toxicity.<sup>15</sup> A study of breast cancer survivors found the burden of financial toxicity was higher for younger patients with lower incomes.<sup>27</sup>

**Cancer treatment costs and related material and psychological burden influence treatment recommendations,<sup>28</sup> treatment decisions,<sup>29-32</sup> adherence,<sup>1,3,20,32</sup> and mortality.<sup>25</sup>** A majority of oncologists report that cancer drug costs (56%) and patient out-of-pocket costs (84%) influence their treatment recommendations.<sup>28</sup> Costs also influence patients' treatment decisions,<sup>29-32</sup> including whether to participate in clinical trials.<sup>30,33</sup> Patients with lower incomes are more likely to choose treatments with lower costs **even if those treatments have lower survival and higher toxicity.**<sup>31</sup> To offset cost, patients may deviate from treatment (including treatment for side effects)<sup>3,34,35</sup> and/or forgo treatment altogether.<sup>32</sup> A study of 254 patients being treated with either chemotherapy or hormonal therapy found that 20% of patients took less than the prescribed amount of medication, partially filled, or avoided filling prescriptions due to the out-of-pocket costs.<sup>3</sup> Another study of patients being treated for solid tumors found that 45% of patients were non-adherent to treatment due to cost.<sup>20</sup> A study of 1556 cancer survivors found that those who reported financial problems were more likely to delay (18.3% vs. 7.4%) or forgo treatment (13.8% vs. 5.0%) compared to respondents without financial problems.<sup>36</sup> In a study of more than 22,000 women with early-stage breast cancer, higher copayments were associated with greater non-adherence to treatment by Medicare and non-Medicare patients. Indirect costs (e.g., travel distance) also reduce the likelihood of receiving or completing treatment.<sup>37</sup> Severe financial distress resulting from cancer treatment may itself be a **mortality risk factor.**<sup>25</sup>

**Health insurance, whether public or private, does not protect patients against financial toxicity.**<sup>14</sup> The American Cancer Society conducted a national poll of 1,000+ adults who reported they or a member of their household had cancer or a history of cancer.<sup>4</sup> Regardless of insurance, 20% of respondents had difficulty paying for basic necessities, 15% used up all or most of their savings, and 11% incurred thousands of dollars of debt due to treatment expenses. This survey found that 26% of respondents who were insured during their cancer diagnosis and treatment experienced problems with their coverage.<sup>4</sup> A study of 10,000 patients with Medicare or private insurance found higher copayments were related to prematurely stopping oral chemotherapy.<sup>38</sup>

**Including costs as part of patient-oncologist treatment discussions could help raise awareness and prepare patients to manage treatment costs.** A major contributor to the burden of financial toxicity is patients' lack of awareness of potential costs they may incur during treatment and survivorship and how to manage those

costs.<sup>2,39-42</sup> Patients are often unprepared when out-of-pocket costs arise.<sup>43</sup> Patient-oncologist treatment cost discussions could improve patients' knowledge of what costs to anticipate<sup>2,39,41,42,44</sup> and connect patients with vital financial resources.<sup>43</sup> **Most patients express a desire to discuss cost with their physicians.**<sup>45-47</sup> However, a rich body of research, including our own, shows that **cost discussions occur infrequently.**<sup>48-50</sup> In a study of video-recorded treatment discussions (n=103), we (Hamel et al. 2017) found that cost discussions occurred in only 45% of treatment discussions. When cost was discussed, it was mostly patient-initiated (63%) and focused more on indirect costs (e.g., time off work) than on direct costs (e.g., copayments).<sup>48</sup>

In an attempt to increase patient awareness and communication about cost, the American Society of Clinical Oncology (ASCO) developed tools, including ASCO Answers: Managing the Cost of Cancer Care;<sup>51</sup> ASCO's Value Framework;<sup>2</sup> and ASCO's Patient-Clinician Communication Consensus Guidelines.<sup>52</sup> These materials are intended to educate patients on the types of treatment costs they may incur, to encourage physicians to discuss patient cost concerns directly, and refer patients to a social worker or financial navigator, if needed. *Unfortunately, ASCO's current materials are static, text-heavy, and do not provide patients with specific actions they can take to manage cost. Though they encourage discussions, the guidelines are overly general and do not provide patients and physicians with specific strategies to initiate such discussions.*

Despite these professional recommendations, a debate remains about whether cost discussions should be part of patient-oncologist treatment visits. Some argue physicians should focus only on medical aspects, while others counter that cost should be considered as a side effect.<sup>41,42,53,54</sup> Others argue that cost is better discussed with social workers, although social workers report difficulty identifying patients who need assistance without a referral from a physician.<sup>43</sup> Patients worry that such discussions may negatively affect their relationship with their physician,<sup>55</sup> but research shows that discussing cost does not negatively affect the patient-physician relationship.<sup>56</sup> Some physicians report discomfort discussing cost<sup>42,57,58</sup> but a survey of 167 oncologists found that **most oncologists believe it is important to be explicit with patients about cost (80%),** that it is their responsibility to consider the impact of treatment on a patient's finances (86%), and that they should consider cost when recommending treatment (66%).<sup>57</sup> Recent work has identified physician engagement in discussions of treatment costs as a critical **unmet need** for cancer patients.<sup>47</sup> Furthermore, physicians are the most important and preferred source of information for patients and also the most central and proximal influence on treatment decisions.<sup>59</sup> To be sure, addressing the costs of cancer care likely requires changes across national, state, and hospital systems. However, we, and other experts, argue that the most efficient and direct point of intervention to reduce patients' burden of financial toxicity is at the patient-provider level. **Education and communication about treatment cost needs to occur at the time that patients and oncologists discuss treatment options and make decisions.** In current practice, cost discussions are a critical yet missing component of treatment decision-making interactions.<sup>47,49,60</sup> Without a cost discussion at the initial clinical interaction, patients are unlikely to be referred for guidance or assistance in a timely manner, thereby missing out on early financial planning for treatment and psychological support, which are critical steps in reducing longer-term financial toxicity.<sup>43,61</sup>

**The premise of this application is that patient-oncologist treatment cost discussions could improve psychological and cost-related outcomes for patients, thus addressing financial toxicity and health equity.** Our conceptual model suggests the intervention will improve short-term outcomes during the interaction (patient active participation, patient-initiated oncologist treatment cost discussions) and, following the interaction (patient cost knowledge, self-efficacy for managing both cost and physician interactions, referrals, distress, perceived material hardship); in turn, these will affect longer-term outcomes (financial toxicity, adherence).

**Increasing patient active participation during oncology interactions has the potential to improve the frequency and quality of patient-oncologist treatment cost discussions.**<sup>62,63</sup> Research on clinical interactions in many medical settings shows patient active participation (e.g., asking questions, expressing concerns, making assertions) plays an important role in short-, intermediate-, and long-term outcomes.<sup>64,65</sup> Patient active participation influences the amount of information physicians provide,<sup>66-68</sup> the treatment physicians recommend,<sup>69</sup> topics patients and physicians discuss,<sup>63</sup> patient healthcare decisions,<sup>70</sup> and patient psychosocial and physical health outcomes.<sup>71,72</sup> In this proposal, we build on prior research on patient active participation by providing education along with prompting for active participation in clinical interactions. Research shows that, in the short term, cost education and patient-oncologist discussions can improve patient self-efficacy for managing cost,<sup>44,73</sup> increase referrals for support (e.g., social work),<sup>43</sup> and reduce cost distress and perceived material hardship.<sup>74</sup> Longer-term effects include improved financial toxicity<sup>74</sup> and treatment adherence.<sup>75</sup>

**There is a great need for tools to improve patient treatment costs education and to prompt patient-oncologist treatment cost discussions.** Question prompt lists (QPLs) are communication tools designed to

enhance patient active participation in interactions with physicians. QPLs are lists of questions that patients might consider asking their healthcare provider during a clinical interaction,<sup>76-79</sup> and have been shown to improve patient active participation in interactions,<sup>62</sup> psychological outcomes (e.g., anxiety), cognitive outcomes (e.g., information recall),<sup>76</sup> patients' report of their role in treatment decisions,<sup>77</sup> and trust in their oncologist.<sup>76,78,79</sup> Our own research demonstrated the success of QPLs in increasing patient active participation among Black patients with cancer discussing treatment with oncologists.<sup>62</sup> **We improve upon the effectiveness of currently published QPLs** in three ways: 1) we include education on issues of costs, so patients are aware of the need to ask questions about cost to gain information and support; 2) we specifically address treatment costs; and 3) we use an electronic format that can be tailored to a specific patient's needs. **We propose to address the limitations of current ASCO tools** by increasing knowledge of costs and discussions through an intervention comprised of a "app"-based educational video and QPL focused on treatment cost. This tailorable<sup>76</sup> app, **DIS**ussions of **CO**st (DISCO)<sup>80</sup> was developed in collaboration with survivors, clinicians, and a software development firm, and pilot-tested in two outpatient oncology clinics. Patients receive the app on an iPad provided to them before a clinical interaction. Using the app, patients view a brief educational video on treatment costs they may incur, ways to manage them, and are advised that starting a discussion with their oncologist is a good way to start managing costs. They are then asked to select questions related to their financial needs (e.g., employment, insurance, financial navigation, etc.), and provided with an individualized list of questions to ask their oncologist during the clinic visit.

**We believe this app-based intervention may be particularly effective in a diverse patient population.** Smartphone/tablet technology use is highly prevalent across racial/ethnic groups, ages, and income levels,<sup>81-85</sup> as is willingness to use these technologies for health interventions.<sup>86,87</sup> Interventions tailored to an individual are also more effective at prompting behavior change in diverse populations, compared to static interventions.<sup>88-90</sup>

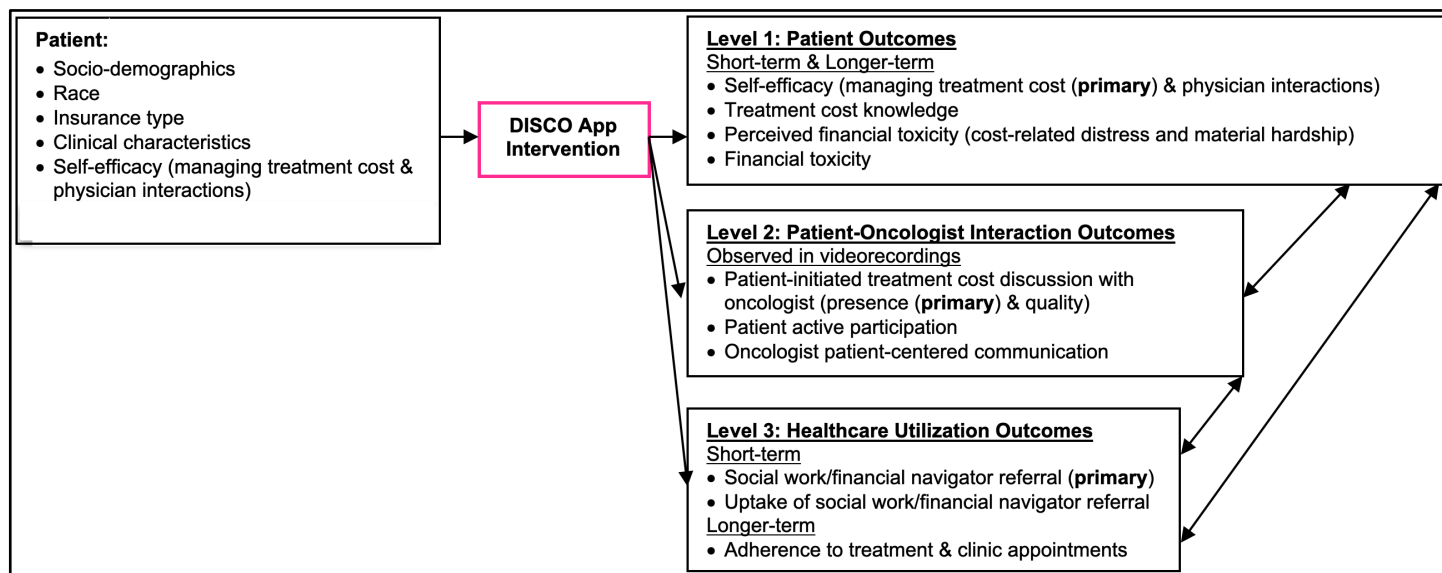
**Study overview.** We build upon our previous success with paper-based QPLs for use with diverse groups of patients<sup>62,91,92</sup> in the oncology clinic setting<sup>62</sup> testing the effectiveness of an electronic, cost-focused QPL.<sup>93,94</sup> The **DISCO App**<sup>80</sup> is an electronic communication intervention provided to patients on an iPad prior to a patient's second visit with an oncologist to finalize treatment plans. The app opens with a brief educational video summarizing the types of treatment costs patients may incur, specific ways to proactively manage cost, and why discussing cost with an oncologist may be helpful. Then, patients are invited to respond to specific questions about their medical and financial situation. Finally, patients are presented with a QPL with cost-related questions tailored to their specific situation. The DISCO App is designed to improve, during the interaction, patient active participation and patient-initiated oncologist treatment cost discussions, and, in the short term, patient's treatment cost knowledge, self-efficacy for managing both cost and physician interactions, referrals, perceived financial toxicity (i.e., distress and material hardship); in turn, these will affect longer-term outcomes of financial toxicity and adherence. Our pilot test demonstrated the acceptability and feasibility of the QPL of the DISCO App, so **we now propose to test its effectiveness on short- and longer-term patient outcomes through a randomized controlled trial (RCT)**. We will compare outcomes in patients who receive the DISCO App and those who receive usual care. We will recruit a diverse sample of patients newly diagnosed with breast, lung, colorectal, or prostate cancer (stages I-IV) who have an initial appointment with a participating oncologist to discuss oral or IV systemic therapy (e.g., chemotherapy, hormone, immunotherapy - referred to throughout as "systemic therapy"). We chose these cancers as their treatments are roughly equivalent in terms of cost.<sup>95</sup> We expect the DISCO App to influence important short-term outcomes, but, given the long-term and multifaceted nature of financial toxicity, we also expect it may need reinforcement to influence longer-term outcomes (e.g., financial toxicity, treatment adherence). Thus, we will also explore the effects of a booster for a sub-set of patients who receive the intervention. The booster is comprised of an individually tailored e-mail with information from patients' use of the DISCO App (e.g., treatment cost management information and the questions they selected).

**Conceptual model.** Financial toxicity is comprised of psychological and material economic burden, both of which can contribute to poor treatment adherence and mortality. **Our overall goal is to address the burden of financial toxicity and work toward health equity through a tailorable education and communication intervention.** Our conceptual model (Figure 1) illustrates our expectation of patient baseline characteristics (e.g., socio-demographics, race, insurance type, clinical characteristics, self-efficacy in managing treatment cost and physician interactions, treatment cost knowledge) and the DISCO App intervention, provided just prior to the second patient-oncologist interaction, will improve short- and longer-term **outcomes at three levels**. At the **patient level, short and longer-term** outcomes include: self-efficacy for managing cost and physician interactions, treatment cost knowledge, perceived financial toxicity [cost distress, material hardship], and actual financial toxicity. At the **patient-physician interaction level** outcomes include: patient active participation,

frequency and quality of patient-initiated cost discussions with the oncologist,<sup>48</sup> and oncologists' patient-centered communication. At the **healthcare utilization level** short-term outcomes include: SW/FN referrals and SW/FN referral uptake. Longer-term outcomes include adherence to treatment and to clinic appointments.

In **Aim 1**, we will determine the effectiveness of the DISCO App on short-term outcomes at three levels: the patient level, patient-oncologist interaction level, and the healthcare utilization level, using a RCT. In **Aim 2**, we will examine the effectiveness of the DISCO App on longer-term outcomes. We will do this by comparing outcomes between patients in the usual care and the

**Figure 1: Conceptual Model**



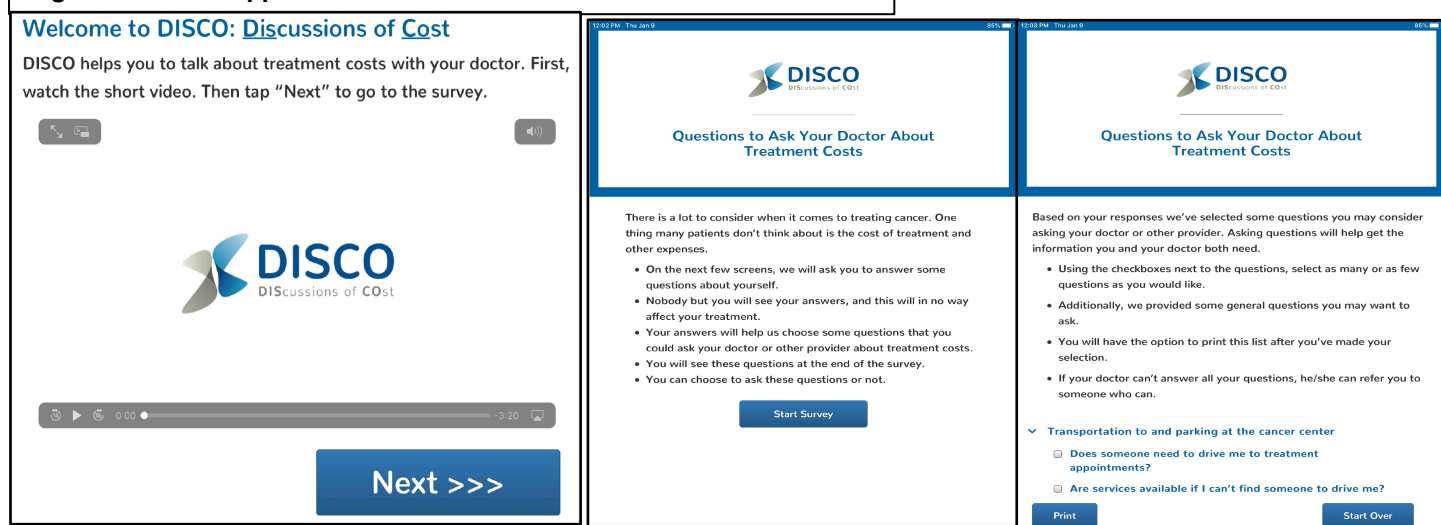
two intervention arms (i.e., DISCO App and DISCO App + booster). We will examine the influence of patient demographics (e.g., race, age, income level) on all outcomes. In **Aim 3** we will test models to examine the likely moderators and mediators of the short-term and longer-term outcomes.

**Summary.** This work is based on our **core scientific premise** – that **increasing patient active participation and the frequency and quality of treatment cost discussions will decrease the short- and longer-term burdens of financial toxicity through their influence on self-efficacy for managing treatment cost.** We focus on patient self-efficacy for managing treatment cost because we expect improved treatment cost education and patient-oncologist treatment cost discussions prompted by the DISCO App will directly improve the self-efficacy needed for patients to proactively manage treatment costs,<sup>44,73</sup> thus reducing the material and psychological burden of financial toxicity.<sup>74,75</sup> The DISCO App is not designed to increase patients' ability to pay or reduce the cost of treatment, but it may benefit patients by increasing: their knowledge of treatment costs, their self-efficacy for managing cost, and the likelihood they receive financial and psychological assistance and support.<sup>39,42,43,49,56,60,74,96</sup> This research is **significant** because, if successful, reducing the material and psychological burden of financial toxicity will improve the quality of care and work toward achieving health equity. We have already tested the DISCO App for feasibility and acceptability. We are now prepared to test its effectiveness in a diverse population of people with solid tumors treated with IV and oral chemotherapies. The intervention can easily be adapted to other cancers, where expensive treatments are emerging (e.g., chimeric antigen receptor T-cell therapy). This work should also contribute to our understanding of the mechanisms through which treatment cost discussions and other aspects of clinical communication improve patient outcomes related to financial toxicity. Our methods are based on prior research, including our own, and a collaboration with stakeholders, suggesting they are **rigorous** and **reproducible**. Given that the **American Cancer Society and the National Cancer Institute are encouraging research to address the pervasive and distressing issue of financial toxicity**,<sup>97</sup> this research is timely and significant.

**DISCO App<sup>80</sup> Development.** We leveraged institutional funds and other resources to develop and test the DISCO App (Figure 2). We established partnerships with Karmanos Cancer Institute's (KCI) Detroit Healthlink Cancer Action Councils (CACs) funded through PCORI (2971-WSUSM Thompson, PI),<sup>98</sup> oncologists and social workers from KCI and the Dana-Farber Cancer Institute; the University of Michigan's (UM) Tech Transfer Program, and CrossComm, a mobile application development firm that builds apps. The CACs are racially diverse groups of community members and include many cancer survivors. With feedback on content and format

from CAC members, oncologists and social workers, Dr. Hamel worked with UM's Tech Transfer and CrossComm to build the DISCO App.

**Figure 2. DISCO App Educational Video & QPL Introduction Screens**

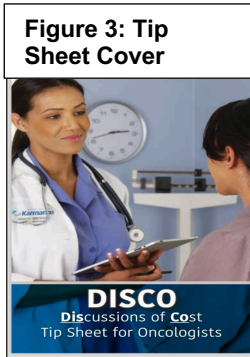


The DISCO App (Figure 2) is displayed on an iPad provided to intervention patients in a private room just prior to their second interaction with their oncologist to discuss and finalize treatment plans. The DISCO App opens with an introduction screen. **First**, patients watch a 3-minute educational video featuring a communication scientist (Hamel, PI), a medical oncologist (Dougherty, Consultant) and a patient using the DISCO App. The video summarizes the types of treatment cost patients may incur (e.g., copayments, transportation/parking costs, time away from work) and ways to manage those costs (e.g., talk with an oncologist or social worker, contact pharmaceutical companies, seek clarification from insurance provider). The video ends by emphasizing to patients that the best way to start managing treatment costs is to discuss them with their oncologist who can answer their questions or refer them to someone who can assist. **Second**, after the video, the QPL is introduced with the following text: "There is a lot to consider when it comes to treating cancer. One thing many patients don't think about is the cost of treatment and other expenses." The text continues to explain that the DISCO App includes a short survey, which will lead to some cost-related questions the patient can consider asking the oncologist. This section asks patients to enter their demographic information and their financial characteristics. Specifically, patients respond to 17 questions (e.g., "How much do you know about your insurance coverage?"; "Are you currently employed?"; "Is there anyone who helps you when you're sick or need help of any kind?"). Based on patient responses, an individually-tailored QPL with up to 18 cost-related questions in 7 categories is generated. For example, patients who indicate they are employed will be prompted to ask: "Can I schedule my treatment around my job?"; patients who indicate transportation concerns will be prompted to ask: "are services available if I can't find someone to drive me?"; Patients who indicate they are unfamiliar with their insurance coverage will be prompted to ask: "Is there someone I can talk to about my insurance and treatment cost questions?" All patients will be provided with four diagnosis questions (e.g., "What is my diagnosis?"), have the option of **adding in any of their own questions**, and then either take the iPad or a **printed** question list into the meeting with the oncologist. Thus, the **DISCO App arms patients with concrete information about the types of out-of-pocket and indirect costs they may incur while undergoing treatment, specific actions they can take to begin to address those costs, and a list of individually tailored cost-focused questions they can take with them to the clinic visit to ask their oncologist. This information and individualized prompting is something few patients with cancer currently receive, on any topic.**

**DISCO App Booster.** Financial toxicity is multifaceted and long-term. We expect the DISCO App to influence short-term outcomes, but we expect it may need reinforcement to influence longer-term outcomes (e.g., financial toxicity, treatment adherence). Thus, we will explore the effects of a booster to reinforce the effects of the DISCO App. Patients in arm three will receive the booster two months after receiving the DISCO App. The booster will be a tailored email or text message reminding patients of 1) the content in the educational video, 2) the questions they selected, and 3) that treatment costs are something they can discuss with their oncologist.



**DISCO App<sup>80</sup> testing.** To test acceptability, Dr. Hamel invited an expert panel of 12 cancer survivors, oncologists, and social workers to use and critique the DISCO App. The panel members felt the DISCO App would be useful for patients to prompt treatment cost discussions with their oncologist and gain important information for their treatment. However, they expressed the concern that oncologists may be unprepared to answer cost questions. In response, we designed an oncologist “tip sheet,” which emphasizes oncologists’ role in cost discussions (as recommended by ASCO) and provides ways to overcome identified barriers to cost discussions (Figure 3).<sup>55,99</sup> For example, oncologists report concern that they will be unable to answer questions about treatment costs. It is impractical to expect oncologists to know the complexities of treatment cost so the tip sheet provides language, including “if a patient asks about cost and you do not know the answer, you can simply say: ‘I’m glad you brought this up, because it’s important for me to know what concerns you have about your treatment. I’m not an expert in this area, but if you have questions about costs I can arrange for you to meet with a social worker who can help after we’re done here.’”<sup>104</sup>



**Feasibility and preliminary effectiveness testing of the DISCO App** occurred in two KCI outpatient clinics (these clinics are among those we propose to conduct the RCT in), using institutional funds. Oncologists (n=3) and 32 patients newly diagnosed with breast (94%) or lung (6%) cancer agreed to participate. Upon consent, and prior to the clinic visit, patients were invited to use the DISCO App on an iPad and printed their QPLs while they waited to see their oncologist. The visits were video recorded and patients completed pre- and post-interaction surveys of the outcome variables and their perceptions of the DISCO App. Findings show significant pre- to post-intervention increases in patients’ self-efficacy for managing treatment costs ( $p=.01$ ) and self-efficacy for interacting with their oncologists ( $p=.001$ ). There is also a promising trend toward decreased patient distress. Most (94%) interactions were video recorded (in two cases technical difficulties prevented recording). **All 30 (100%) of the video-recorded interactions included a cost discussion, and 23 included multiple cost topics.** The most frequently discussed topics were: insurance, time off from work, and SW/FN referrals, suggesting an immediate and direct benefit of the DISCO App. Further, patients reported the DISCO App was easy to understand ( $M=4.5$  out of 5) and useful as they talked with their doctor ( $M=4.0$ ); 84% of patients reported needing less than 15 minutes to use the DISCO App, and all patients were able to use the DISCO App in the time they were waiting for their oncologist. On average, patients selected 6.5 out of 18 possible questions to print. Findings suggest that the DISCO App is feasible, acceptable, and effective in improving outcomes at all three levels including: greater self-efficacy for managing treatment cost (patient), more frequent and high-quality cost discussions (patient-oncologist), and more social work/financial navigation referrals (healthcare utilization).<sup>100</sup>



### **3.0 Methods and patient selection:**

**Study overview.** We propose to conduct a 3-arm RCT of a patient education and communication intervention, the DISCO App, which is comprised of 1) a brief treatment cost educational video and 2) an individually tailorable QPL. We will recruit medical oncologists and their Black and White patients newly diagnosed with breast, lung, colorectal, or prostate cancer who will likely be treated with systemic therapy via IV infusion from outpatient clinics of Wayne State University (WSU)/Karmanos Cancer Institute (KCI), a NCI-designated comprehensive cancer center located in Detroit, Michigan, and one of its network sites, all which serve a highly diverse population. The patient population for this study will be diverse in terms of race, gender, age and socioeconomic status. All patients will provide baseline socio-demographic information at the time of consent. Just prior to the second patient-oncologist visit to finalize treatment plans, but before treatment begins, patients will be randomized to receive usual care, the intervention, or the intervention + booster. Patients in the two intervention arms will receive the DISCO App. Patients in the intervention arm + booster will receive the DISCO App and a booster provided two months later. The booster will be an individually tailored e-mail that reminds patients 1) of the content of the educational video, 2) of the questions they selected in the QPL, and 3) that they can discuss treatment costs their oncologist. For all patients, we will video record the second patient-oncologist interactions using our established, unobtrusive video recording system.<sup>48,62,101,102</sup> Video recording will allow us to use our validated coding systems<sup>48,62,103</sup> to assess outcomes that occur during the interaction. We will also assess outcomes through patient self-report measures at baseline, after the video-recorded interactions, at 1, 3, 6, and 12 months after the video-recorded interaction, and from patients' medical charts.

#### **A. Eligibility or how subjects will be selected:**

Using successful procedures from our prior studies,<sup>59,62,104,105</sup> we will recruit up to 25 medical oncologists and medical oncology fellows and 240 (120 men, 120 women) of their White and Black patients from various socioeconomic statuses, and ages. Please see Section 4.4 for power analysis and sample size justification.

**Oncologists** are eligible if they treat patients with breast, prostate, lung, or colorectal cancers at KCI Detroit and/or Farmington Hills. Data from oncologists will include their self-report data and video-recorded treatment discussions with participating patients.

**Patients** are eligible if they are  $\geq 18$  years of age; are able to read and write in English; have an email account; and are newly diagnosed with breast, prostate, lung or colorectal cancer (stage I-IV) for which systemic therapy is a likely recommended treatment. Data from patients will include their self-report data, video-recorded treatment discussions with participating oncologists, and medical record data.<sup>59,62</sup>

Based on past studies,<sup>59,62,101</sup> we expect oncologists will participate with minimal attrition and we assume approximately 20% patient attrition, reducing the number of patients to 192. Oncologists will receive a \$30 gift card for their participation, following completion of the baseline survey.

#### **B. Description of disease and stage as applicable:**

We are focused on patients newly diagnosed with breast, prostate, lung, or colorectal cancers (Stages I-IV) for which systemic therapy is likely a recommended treatment. This is also a health equity project due to the fact that burden of financial toxicity is disproportionately experienced by patients who are racial/ethnic minorities, have lower incomes, and are younger (<65 years of age). Thus, we will be recruiting a patient sample that is diverse in terms of race, income level, and age.

#### **C. Method(s) to be used in the study:**

This study is a RCT to test a patient education and communication intervention. Oncologists and patients will complete self-report measures through an online survey service (Qualtrics) on an iPad with the assistance of research staff. All patients will have up to two interactions with their oncologist video recorded. Qualtrics randomization software will randomly assign patients (1:1:1, within oncologist) to one of the intervention or usual care arms. Patients randomized into the intervention arms will receive the DISCO App in the clinic between the first and second interaction with the oncologist, but before treatment begins. This timing is based on feedback from stakeholders who agreed that discussing treatment cost early is important, but the first patient-physician interaction may not be ideal due to the number of other issues (e.g., prognosis, side effects) that are being discussed.<sup>93</sup>

**Oncologists recruitment.** Drs. Hamel and Heath will explain the study at clinic program meetings and meet with interested oncologists to obtain consent. Oncologists who consent will agree to 1) complete a baseline survey; 2) inform their eligible new patients (via a phone call, e-mail, or face-to-face conversation with the oncologist or another clinical member of the study team (e.g., nurse, nurse practitioner)) about the study prior to their initial appointment to discuss treatment; 3) have interactions with participating patients video recorded; and 4) complete a brief survey following interactions with participating patients. Upon recruitment, oncologists will receive a “tip sheet” to help prepare them for patient treatment cost discussions with patients.

**Patients recruitment.** Eligible patients will be identified by research staff who will review participating oncologists’ schedules weekly. Patients will be contacted via phone call, face-to-face, or email from the participating oncologist’s clinical staff to inform the patient of the study and assess interest. If interested, patients will be contacted by research staff via a phone call or in person in the clinic prior to a scheduled appointment. The research staff member will explain the study and obtain consent and collect baseline data. The option to consent patients and collect baseline data over the phone has been put in place to accommodate the clinic procedures put in place due to the COVID-19 pandemic. Then, patients who consent will agree to 1) arrive 30 minutes early to their next scheduled appointment with their oncologist; 2) be randomized to one of the study arms; 3) complete a brief survey following the video-recorded interactions with a participating oncologist; 4) have up to two of their clinical interactions video recorded; and 5) complete up four follow-up surveys at 1, 3, 6, and 9 months after their last video-recorded interaction. All follow-up surveys will be, depending on the patient’s preference, administered either over the phone or via a secure link delivered via email. This will also reduce the time patients and staff will be in the clinic.

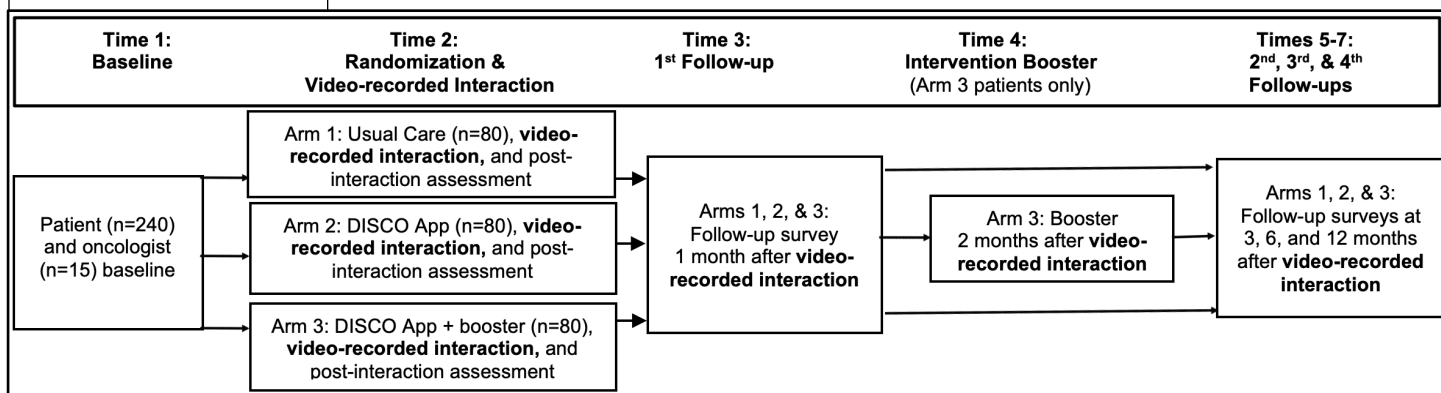
We will ask patients for their preferred method of contact for follow-up surveys. Strata will be created to ensure recruited patients vary by race, income, age, and sex. Given the multiple patient follow-ups, attrition is a concern. We will employ several strategies to keep attrition to a minimum.<sup>59,62,65,105</sup> First, we will compensate patients up to \$150 in gift cards, which they will receive in increments. Patients will receive \$20 after each video recorded interaction and after the first three follow-up surveys. As a further incentive, they will receive \$50 after they complete the final follow-up survey. Second, patients will receive email and text reminders two days before each survey, depending on their preference for contact. Third, because of concern about patient burden, we will keep measures to a minimum. Last, we will monitor for attrition and adjust our methods if needed. These recruitment and retention procedures have been quite successful in our prior studies.<sup>59,62,101</sup>

**Procedure.** Just before the second patient-oncologist interaction, patients in the intervention arms will access the DISCO App<sup>80</sup> on an iPad. Our research demonstrates that patients are comfortable with iPads, especially if they are assisted.<sup>62,93</sup> Research assistants will show patients the DISCO App with an explanation, instructions, and demonstration. Staff will be trained NOT to answer questions nor discuss cost, but encourage patients to ask questions during their clinical interaction. These meetings will be audio-recorded to assess fidelity to the protocol. The DISCO App begins with a brief educational video followed by a section asking patients to enter their financial information (e.g., employment, insurance status, etc.) and their financial concerns. That will result in a list of questions tailored to patients’ needs, and patients can select which questions they would like to ask. Patients will have the option to either print a list of their questions from a mobile printer or take the iPad into the interaction. Based on feasibility data, we anticipate that using the DISCO App will take <20 minutes. Since patients in the intervention arm may bring the print out and/or iPad into the interaction, oncologists will not be blind to study arm. Thus, we will give patients in the usual care arm treatment information on a printout for their meeting with their oncologist. Immediately after the recorded interactions, patients and oncologists will complete brief surveys assessing any cost discussions that occurred. Patients in the intervention arms will also complete assessments of the DISCO App (e.g. “The app helped me ask my treatment cost questions”) after the second interaction.

**Intervention booster.** Two months after receiving the DISCO App, patients in the intervention + booster arm (Arm 3) will receive an intervention booster. The booster will be an email or text message (depending on patient preference) to remind patients 1) of the content in the education video, 2) the questions they selected from the DISCO App, and 3) that treatment costs are something they can discuss with their oncologist or other providers. The email or text message will include a “Read Receipt” so we can track whether patients view the email or text message.

All patients will be contacted via their preferred method of contact to complete follow-up measures including questions about their disease and treatment status, whether they received a referral for financial support, if they followed up on that referral, self-efficacy managing treatment cost, perceived short-term financial toxicity (perceived material hardship and cost distress) in the first follow

**Figure 4. Study Design**



up, actual financial toxicity in the remaining follow ups, and treatment adherence. Follow ups will occur at 1, 3, 6, and 12 months after the second recorded interaction. Patients who receive the intervention booster will also complete booster assessments.

**Measures.** Most of the measures in this study have been used with cancer patients, including in the DISCO App's feasibility pilot, with high completion rates and few complaints about burden. However, the first ten patients who complete all measures will be specifically queried about burden. Measures will be adjusted if necessary.

**Baseline measures.** Baseline measures from patients and oncologists will be used as moderators and covariates in analyses of the intervention's effects. Patients: After providing consent, patients will provide socio-demographics including age, race/ethnicity, gender, education, marital/personal status, income, employment, and financial situation (e.g., *It is difficult for me to live on my total household income right now?*).<sup>15</sup> They will also complete measures of their diagnosis; their recommended treatment (if known); insurance type; their self-efficacy in patient-physician interactions (PEPPI  $\alpha=.91$ ; e.g., *How confident are you in your ability to know what questions to ask your doctor?*); patient-practitioner orientation (e.g., *The doctor is the one who should decide what gets talked about during a visit*); their self-efficacy in managing cost of treatment (adapted from a validated scale; e.g., *I am confident I can pay for the direct costs of my treatment*);<sup>126</sup> their level of treatment cost distress (e.g., *I am concerned about how much my cancer treatment will cost me*), and their anticipated material hardship due to their cancer treatment (e.g., *I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment*).<sup>106</sup> Oncologists: After providing consent, oncologists will complete a one-time assessment of their socio-demographic and professional information, including race/ethnicity, gender, age and years in practice. Oncologists will also complete measures of patient-practitioner orientation (e.g., *The doctor is the one who should decide what gets talked about during a visit*); their perceptions of the oncologists' role in treatment cost discussions (e.g., *Oncologists should be discussing treatment cost with their patients*), and their self-efficacy with discussing treatment cost. Medical records: We will use patients' medical records to abstract information on the clinical characteristics of patients' cancer diagnosis, if they have any co-morbidities, and their zip code.

**Level 1: Patient Outcome Measures:** Immediately after the video-recorded interactions, patients will complete the following measures: self-efficacy in patient-physician interactions;<sup>127</sup> self-efficacy in managing cost of treatment;<sup>126</sup> knowledge of types of treatment cost (e.g., *Cancer treatment may cost me in the following ways*), and ways to manage those costs (e.g., *The following are ways I can manage treatment cost*); perceived financial toxicity, comprised of treatment cost distress (5-items; e.g., *I am worried about how much my cancer treatment will cost*) and perceived material hardship (7-items; e.g., *Do you anticipate having to borrow money to pay for cancer treatment? Do you anticipate having to take unpaid time off from work for treatment?*).<sup>15</sup> Intervention patients will also provide perceptions of the DISCO App after the interaction (5 items; e.g., *The DISCO App helped me ask my doctor my cost questions*).<sup>91</sup>

At the 1, 3, 6, and 12 month follow-ups, patients will be contacted via their preferred method by research staff to complete measures on their disease and treatment status (e.g., diagnosis, stage, type of treatment) to help account for any differences observed in the outcome measures. Patients will also complete measures assessing self-efficacy in patient-physician interactions;<sup>127</sup> self-efficacy in managing cost of treatment;<sup>126</sup> their employment status; and actual financial toxicity using the 11-item COST scale ( $\alpha=.90$ ; e.g., *My out-of-pocket medical*

expenses are more than I thought they would be).<sup>128</sup> At the three month follow-up, patients who received the booster will be asked if they received the booster and their perceptions (e.g., *The reminder email or text message was helpful with my cost questions and concerns*).

**Level 2: Patient-Oncologist Interaction Outcome Measures:** Immediately after the video-recorded interactions, patients and oncologists will complete measures of perceived presence of treatment cost discussion(s) (3 items; e.g., *Did you and your oncologist (patient) discuss the cost of your (his/her) cancer treatment today?*) and satisfaction with treatment cost discussion(s) (3 items; e.g., *I am satisfied with how my oncologist (patient) and I discussed treatment cost today*).

**Observational measures:** Trained research assistants (RAs), blind to research questions, will observe and rate video-recorded interactions using our established procedures to ensure acceptable inter-rater reliability.<sup>48,59,62,107,108</sup> To assess the frequency and quality of a cost discussion, RAs will determine if a treatment cost discussion occurred (e.g., *any verbal expression of perceived direct or indirect costs for the patient for cancer treatment*); who initiated the cost discussion (e.g., *patient, oncologist*); and what topics were discussed (e.g., *insurance, transportation, etc.*).<sup>48</sup> RAs will also rate the quality of the interaction through assessing patient active participation (e.g., *the patient asked a lot of questions*)<sup>103</sup> and oncologists' patient-centered communication (12 items,  $\alpha=.75$ ; e.g., *the doctor encouraged the patient to express concerns and worries*).<sup>103</sup> Another team of trained RAs will assess if the DISCO App or printout is present and/or used<sup>62</sup> and interaction length.<sup>62</sup>

**Level 3: Health Utilization Outcomes:** Immediately after the video-recorded interactions, patients will complete measures of: whether they wanted and/or received a SW/FN referral, and, if so, if they followed up on the referral. Oncologists will complete measures on whether they made a SW/FN referral for the patient.

At the 1, 3, 6, and 12 month follow ups, patients will be contacted by their preferred method of contact by research staff to complete measures, including whether they wanted a SW/FN referral, and if so, whether they followed up on that referral; treatment adherence (Medical Outcomes Study General Adherence; e.g., *I had a hard time doing what the doctor suggested I do for treating my cancer*) and treatment-cost related adherence (e.g., *Was there a time in the past 12 months when you needed to see a doctor for your cancer but could not because of cost?*),<sup>131</sup> and clinical appointment adherence.

**Using medical records,** we will assess whether the oncologist made a SW/FN referral for the patient, and, if so, if the patient followed up on the referral, treatment adherence, and clinic appointment adherence.

#### **D. How data will be handled and kept confidential:**

All files will be stored on a network server at the Karmanos Cancer Institute/Wayne State University in the Department of Oncology. Only the Wayne State University staff listed in the application will have access to the files and at no time will data files be shared with collaborators outside the institution. The Karmanos Cancer Institute/Wayne State University network server utilizes hardware-based encryption at the level of the hard drives. Approved domain users are granted project specific permission on the server folders. The server is backed up to an off-site software encrypted disk-based backup solution. The PI's PC and the network server are protected under the same CISCO firewall. The recordings will be kept in a locked file cabinet in KCI's Behavioral and Field Research Core's editing suite (which is also locked whenever unoccupied). Patient medical record numbers will be assigned a study ID number in a master key, and study IDs will be used on all research documents. Only the principal investigator, co-investigators, and data manager will have access to the master key, which will be locked in password protected computers as described. We assure that any publications and presentations of the data will not allow for the identification of patients, hospitals or physicians.

## 4.0. Statistical Considerations:

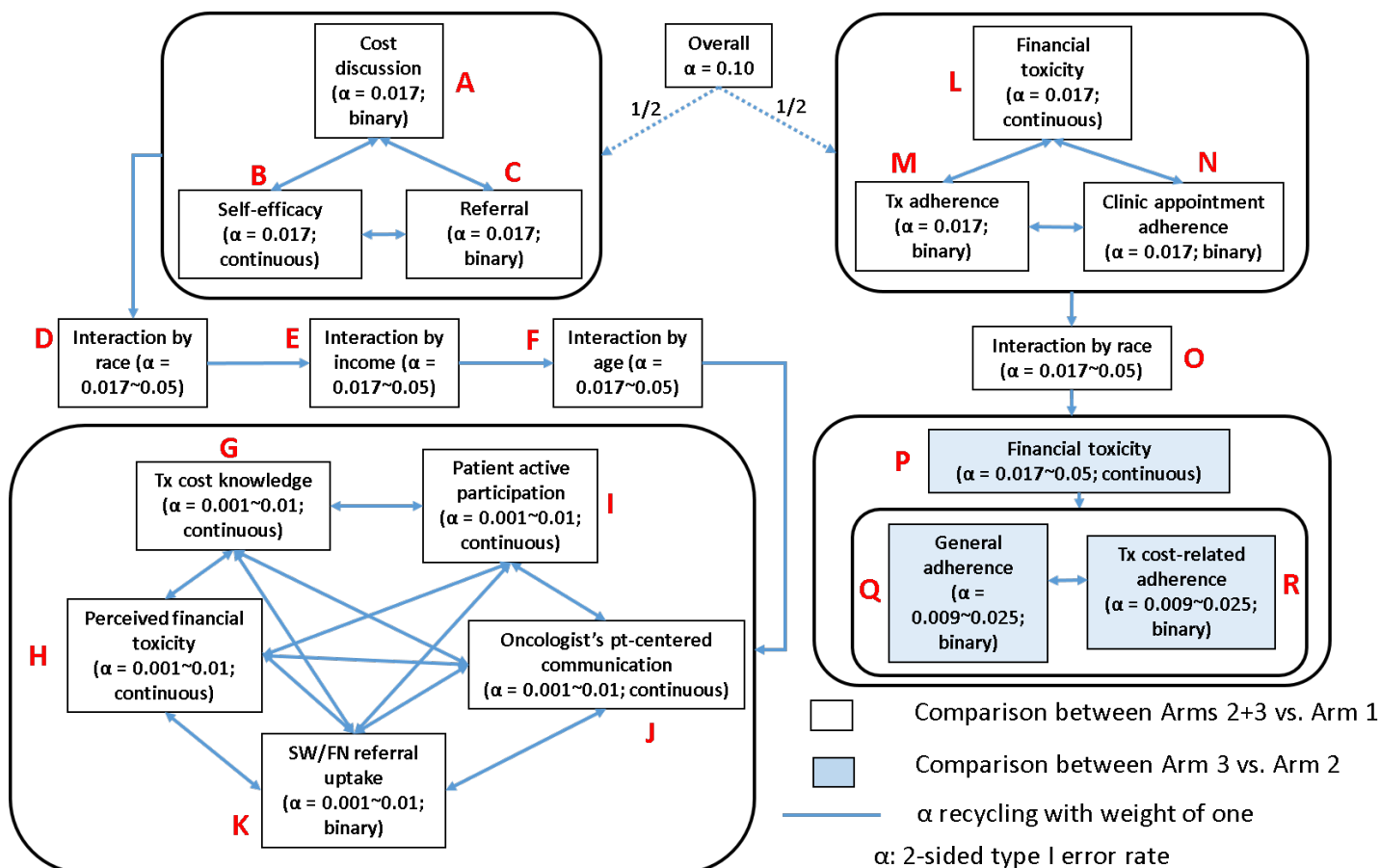


Fig. 4 Graphical representation of hierarchical Holm's testing.

## 4.0. Statistical Considerations:

### 4.1. Objectives

#### Primary objectives

1. To assess the effectiveness of the DISCO App on short-term outcomes of cost discussion, self-efficacy in managing treatment costs; self-efficacy in physician interactions, and social work/financial navigation (SW/FN) referral between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**A, B, C** in Fig. 4).
2. To assess the effectiveness of the DISCO App on longer-term outcomes of financial toxicity, general adherence, and treatment cost-related adherence between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**L, M, N** in Fig. 4).

#### Secondary objectives

1. To assess the interaction between patient race and the effectiveness of the DISCO App on short-term outcomes of cost discussion, self-efficacy in managing treatment costs, self-efficacy in physician interactions, and SW/FN referral between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**D** in Fig. 4).
2. To assess the interaction between patient income and the effectiveness of the DISCO App on short-term outcomes of cost discussion, self-efficacy in managing treatment costs, self-efficacy in physician

interactions, and SW/FN referral between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**E** in **Fig. 4**).

3. To assess the interaction between patient age and the effectiveness of the DISCO App on short-term outcomes of cost discussion, self-efficacy in managing treatment costs, self-efficacy in physician interactions, and SW/FN referral between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**F** in **Fig. 4**).
4. To assess the effectiveness of the DISCO App on short-term outcomes of treatment cost knowledge, perceived financial toxicity, patient active participation, oncologists patient-centered communication, and SW/FN referral uptake between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**G, H, I, J, K** in **Fig. 4**).
5. To assess the interaction between patient race and the effectiveness of the DISCO App on long-term outcomes of financial toxicity, general treatment and clinic appointment adherence, and treatment cost-related adherence between patients in the usual care and those in intervention arms [DISCO App and DISCO App + booster] (**O** in **Fig. 4**).
6. To assess the effectiveness of the booster on longer-term outcomes of financial toxicity, general treatment and clinic appointment adherence, and treatment cost-related adherence between patients in the usual care and those in each intervention arm [DISCO App and DISCO App + booster] (**P, Q, R** in **Fig. 4**).

#### Exploratory objectives

1. To explore the potential moderators and mediators of the short-term outcomes.
2. To explore the potential moderators and mediators of the longer-term outcomes.

#### **4.2. Measurable variables**

For the short-term outcomes, the primary endpoints are self-efficacy for managing cost at the patient level (continuous outcome), the presence of cost discussion at the patient-oncologist interaction level (binary outcome, present or not)<sup>48</sup>, and social work/financial navigation referrals at the healthcare utilization level (binary outcome, referred or not). The secondary endpoints are the treatment cost knowledge (continuous), perceived financial toxicity (continuous), patient active participation (continuous), oncologists patient-centered communication (continuous), and social work/financial navigation (SW/FN) uptake (binary).

For the long-term outcomes, the primary endpoints are financial toxicity (continuous), treatment adherence (binary), and clinic appointment adherence (binary).

Other measurable variables are patient baseline, demographic and clinical characteristics as well as oncologist baseline and demographic characteristics.

#### **4.3. Analysis**

Patient baseline and clinical characteristics will be summarized by count and frequency for categorical variables and mean and standard deviation (SD) (or median and range) for continuous variables, separately by arms. Oncologist baseline characteristics will be also summarized by these descriptive statistics. For all statistical testing, the distributional assumptions will be checked and, if needed, either data transformation or nonparametric approach will be applied.

The first primary and fourth secondary objectives will be assessed using logistic and continuous multi-level models (MLM) with patients nested within oncologists between intervention (DISCO App [Arm 2] and DISCO App + booster [Arm 3]) vs. usual care (Arm 1).

The second primary objective will be assessed using longitudinal logistic and continuous MLM with patients nested within oncologists between Arms 2+3 vs. Arm 1.

The first, second, and third secondary objectives will be assessed using logistic and continuous MLM with each of race (Black vs. White), income (high vs. low), and age (<65 years vs. ≥ 65 years) by arms (Arms 2+3 vs. Arm 1) interaction factors.

The fifth secondary objective will be assessed using longitudinal logistic and continuous MLM with a race (Black vs. White)-by- arm (Arms 2+3 vs. Arm 1) interaction factor.

The sixth secondary objective will be assessed using longitudinal logistic and continuous MLM with patients nested within oncologists between Arm 3 vs. Arm 2.

The first and second exploratory objectives will be explored using multi-level structural equation models (MSEM)<sup>109,110</sup> to test the predicted mediations and moderations.

The overall type I error rate is 1-sided 5% level (i.e., 2-sided 10% level) and the family-wise error rate (FWER) was controlled using hierarchical Holm's procedures as depicted in **Fig. 4**.<sup>111</sup> The overall type 1 error rate will be split equally into two primary objective with a 2-sided 5% level.

For the first primary objective, each of three endpoints will be further tested at a 2-sided 1.7% level while allowing the type I error rate to be reallocated to each other if a null hypothesis is rejected regardless of the order of testing (**A, B, C** in **Fig. 4**). If at least one endpoint is positive, then the interaction with race will be evaluated minimally at a 2-sided 1.7% level (up to a 5% level at maximum) for the endpoint that is positive (**D** in **Fig. 4**; the first secondary objective). If the interaction with race is positive, the interaction with income followed by age will be evaluated at a 2-sided 1.7% level (up to a 5% level at maximum) (**E, F** in **Fig. 4**; the second and third secondary objectives). If the interaction with income is positive for at least one endpoint, each of five endpoints for the fourth secondary objective will be tested minimally at a 2-sided 0.1% level (up to a 1% level at maximum) while allowing the type I error rate to be reallocated to each other if a null hypothesis is rejected regardless of the order of testing (**G, H, I, J, K** in **Fig. 4**).

For the second primary objective, each of three endpoints will be tested at a 2-sided 1.7% level while allowing the type I error rate to be reallocated to each other if a null hypothesis is rejected regardless of the order of testing (**L, M, N** in **Fig. 4**). If at least one endpoint is positive, then the interaction with race will be evaluated minimally at a 2-sided 1.7% level (up to a 5% level at maximum) for the endpoint that is positive (**O** in **Fig. 4**; the fifth secondary objective). If the interaction with race is positive for at least one endpoint, the effect of the booster on financial toxicity will be evaluated at a 2-sided 1.7% level (up to a 5% level at maximum) between Arm 3 vs. Arm 2 (**P** in **Fig. 4**; the sixth secondary objective). If financial toxicity is positive, each of two additional endpoints for the sixth secondary objective will be tested minimally at a 2-sided 0.9% level (up to a 2.5% level at maximum) while allowing the type I error rate to be reallocated to each other if a null hypothesis is rejected regardless of the order of testing (**Q, R** in **Fig. 4**).

In the hierarchical testing, if a parent testing is negative, there is no further formal statistical testing and the following analyses will be deemed as descriptive analyses.

The primary analyses will be based on complete data without missing values. As a sensitivity analysis, we will also perform the hypothesis testing after multiple imputation. For time-independent variables (e.g., baseline attributes), multiple imputation will be performed using chained equations (MICE)<sup>112</sup> and for the time-dependent variables, Amelia II will be used to consider time trends of a variable.<sup>113,114</sup>

#### 4.4. Sample size and power justification

For the first primary objective (**A, B, C** in **Fig. 4**), we expect that the presence of a cost discussion will influence the other outcomes. Thus, the presence of cost discussions was first considered to estimate the sample size and power justification for other outcomes. The rates of occurrence for cost discussions and social work/financial navigation referrals will be calculated and the outcomes will be compared between usual care (Arm 1) vs. both DISCO App and DISCO App + booster (Arms 2+3). The sample size ratio was assumed to 1:2 since Arms 2 and 3 will be the same in the intervention evaluation. We employ a between-subjects design with patients nested



within oncologists (e.g., accounting for oncologists seeing multiple patients). Given that the unit of analysis is the patient-oncologist interaction and data from these interactions will likely be more similar within oncologists than between oncologists, we used MLM with the binary outcome to conduct the sample size justification and power analyses using an MLM cluster-randomized design for two proportions<sup>115,116</sup>. The effect of intra-cluster correlation (ICC) was further examined using ICC estimation from the random intercept logistic model.<sup>139</sup> Based on our previous observational study,<sup>48</sup> we assume that the ICC will be  $\leq 0.04$  (hereafter, for the sake of the worst scenario and the sample size estimation, we assumed that ICC is zero, which produce the largest sample size) and the rate of cost discussions without the DISCO App will be 45%. Our pilot study found that the cost discussion rate with the DISCO App is 100% (95% CI, 0.86 to 1). Based on findings from the pilot and the observational study, in this study, we expect that the rate of cost discussions will be at least 75% with the DISCO App, and the minimally meaningful difference between two groups will be 30%.<sup>48,100</sup> We consider each oncologists a “block” and assume a Bonferroni-corrected 2-sided 1.7% level (= 5%/3 primary endpoints). Thus, 180 patients (10 oncologists X 3 arms x 6 patients) will achieve at least 90% power to detect 30% difference in the rate between two arms. This is also what we will need to detect a difference in the primary outcome at the healthcare utilization level (social work/financial navigation referral). A total of 180 patients will allow us to detect an effect size of  $\geq 0.58$  for the patient-level outcome (self-efficacy for managing treatment cost) with 90% power at a 2-sided 1.7% level. With 20% attrition, we will need 240 (10 oncologists x 3 arms x 8 patients) patients to maintain a balanced design.

For first, second, and third secondary objectives (i.e., interactions by each of race (Black [B] vs. White[W]), income (high vs. low), and age (<65 vs.  $\geq 65$ )) (**D, E, F** in **Fig. 4**), 180 patients will produce more than 89% power to detect any of three interactions for binary outcomes when the group proportions under the alternative hypothesis are 0.45, 0.45, 0.45, and 0.75 (e.g., for Arm1-W, Arm 1-B, Arms 2-3-W, Arms 2-3-B, respectively) using a z-test from a GEE analysis of a logistic model at a 2-sided 1.7% level. These patients will allow us to detect an interaction difference of at least 1.64 for continuous outcomes with 90% power at a 2-sided 1.7% level when an estimated SD of subjects is one.

For the fourth secondary objective (**G, H, I, J, K** in **Fig. 4**), 180 patients will allow us to detect a difference of at least 0.23 between two proportions for binary outcomes as well as to detect an effect size of at least 0.72 for continuous outcomes with 90% power at a 2-sided 0.1% level.

For the second primary objective (**L, M, N** in **Fig. 4**), outcomes will be measured at 5 time points (baseline, 1, 3, 6, 12 months post intervention) and the power was justified using longitudinal logistic and continuous MLM. 180 patients will have 90% power to detect a difference of 0.18 in slopes for continuous outcomes as well as to detect a difference of at least 0.13 for binary outcomes between Arms 2+3 vs. Arm 1 at a 2-sided 1.7% level when the autocorrelation is assumed to be zero.

For the fifth secondary objective (**O** in **Fig. 4**), 180 patients will allow us to detect an interaction between race and slope of at least 0.52 for continuous outcomes with 90% power at a 2-sided 1.7% level. 180 patients will produce more than 90% power to detect an interactions with race for binary outcomes when the group proportions under the alternative hypothesis are 0.45, 0.45, 0.45, and 0.75 (e.g., for Arm1-W, Arm 1-B, Arms 2-3-W, Arms 2-3-B, respectively) using a normal test from a GEE analysis at a 2-sided 1.7% level when the autocorrelation is assumed to be zero.

For the sixth secondary objective (**P, Q, R** in **Fig. 4**), 180 patients will have 90% power to detect a difference in slopes for continuous outcomes between Arm 3 vs. Arm 2 of 0.21 at a 2-sided 1.7% level. These patients will allow us to detect a difference of at least 0.16 for binary outcomes between Arms 3 vs. Arm 2 at a 2-sided 0.9% level when the autocorrelation is assumed to be zero.

All sample size and power justifications were performed by PASS 2020 (NCSS LLC, Kaysville, UT, USA).

#### 4.5. Expected accrual and study durations

Based on the current practice at KCI Detroit and Farmington, we expect that each oncologist will see at least 3 patients per month regardless of cancer type. In addition, we expect that the consent rate is about 35% based

on our previous experiences (i.e., the expected lowest accrual rate is one patient per oncologist per month). Thus, it will take about 24 months to accrue 240 eligible and consented patients by 10 oncologists. Considering the durations of IRB approval (5 months) and data collection/analysis (7 months), the expected study duration is about 36 months.

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