Title of Project: Treating Comorbid Depression In Care Transitions with Relational Agents

Principle Investigator and Team Members:

Dr. Suzanne Mitchell (PI) of Boston Medical Center,
Ms. Katie Krizman LMHC of Boston Medical Center
Ms. Jenna Bhaloo, Ms, Mary Cawley and Ms. Michelle Welch all of Boston Medical Center were the study research assistants and conducted qualitative analysis.
Dr. Bickmore of Northeastern University and Lazlo Ring (PhD candidate) were subcontracted for the development efforts on behalf of NEU.
Ms. Crystal Alvarez, a graduate student at the Boston University School of Public Health conducted the statistical analysis on the survey data.

Organization: Boston Medical Center
                    One Boston Medical Center Pl, Boston, MA 02118

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A. **Abstract**

Purpose: The aim of this study was to demonstrate the usability, feasibility and acceptability of using a relational agent system to deliver cognitive behavioral therapy (CBT) to treat comorbid depression in adults with chronic disease.

Scope: We designed a 6 module CBT intervention delivered by a relational agent, a novel animated, computer-based embodied character scripted to administer a structured CBT program for patients with depression. We then tested the feasibility, acceptability and usability of the system to gather preliminary evidence to support implementation of a fully powered clinical trial of the system called The Sophie CBT System.

Methods: An RA system was designed and developed to deliver 6 modules of cognitive behavioral therapy for comorbid depression and chronic disease (RA-CBT). We recruited 22 adults with a history of a chronic disease and comorbid depression to test the RA-CBT program and provide feedback and survey responses on character attributes, character script, module navigation and working alliance. Qualitative interviews were completed with each participants. Interview data was coded and analyzed using thematic analysis.

Results: A total of 21 participants completed testing of the Sophie RA-CBT system. Key themes from qualitative interviews included: Sophie system addresses barriers to mental healthcare, Participant response to character attributes and forming a working alliance with the RA, and Usability of CBT system and curriculum. The average score of the Working Alliance Inventory scale was 149 (+/-35) out of a possible score of 201 or approximately the 50th percentile.

Key Words: comorbid depression, cognitive behavioral therapy

B. **Purpose:** The purpose of this study was to design and develop a technology-driven relational agent system to deliver cognitive behavioral therapy (RA-CBT) to support patients with chronic illness including chronic pain and comorbid depression. The study aimed to demonstrate that self-administered RA-CBT will be feasible and acceptable to patients within the target population. The study also sought to gather feedback on the usability of the system components. Before implementing an RA system in standard practice, it is important to determine the credibility of using a RA to address chronic illness including chronic pain and comorbid depression.

Note: Due to the major delays in programming as specified in prior reports, we were not able to obtain data on the RA-CBT system's potential efficacy for treating depression. As a result, the pilot study was revised from a randomized controlled pilot study to a feasibility study.

C. **Scope:** Comorbid depression among individuals with chronic illness such as heart failure (CHF) or chronic pulmonary disease (COPD) is a strong predictor of poor clinical outcomes and high rates of avoidable 30-day readmissions.[1,2] While depression is a treatable condition, less than 36% of people with depression receive effective treatment.[3] Cognitive behavioral Therapy (CBT) is an effective approach to depression treatment for people with chronic disease but attending treatment sessions can be challenging.[4,5] An alternative to computerized and face-to-face cognitive behavioral therapy (CBT) is CBT delivered by novel health technology known as the relational agent (RA).[6] The RA is a human animation program that interacts with patients, integrates best practices from provider-patient communication theory, emulating the face-to-face conversational behavior of an empathic provider emphasizing nonverbal communicative behavior such as gaze, posture, gestures, etc.[6] To date, RAs have been studied for use in hospital discharge education, medication adherence, risk assessment, lifestyle modification and more.[6,7,8,9] The study team designed and developed a technology-driven RA system to deliver a 6 module cognitive behavioral therapy intervention (RA-CBT) to support patients with comorbid depression and chronic illness including chronic pain. The data reported provides preliminary assessment of the feasibility of using the RA-CBT system for depression therapy in a self-paced setting within the target population. This data will inform further development of an

RA-CBT system to treat comorbid depression and expand access and scalability for post-discharge mental health support in the care transition.

D. **Methods:** A technology-driven relational agent system was designed and developed to deliver cognitive behavioral therapy (RA-CBT) to participants with chronic illness and comorbid depression. Phase one of this project involved design and development of the RA-CBT system and phase two involved pilot testing the feasibility, acceptability and usability of the system with a cohort of target participants with a diagnosis of major depression.

D.1. Sophie System Development: The software architecture used to develop the RA was drawn directly from previous projects using state-of-the-art software engineering practices. The RA was named "Sophie". Scripts were developed for the RA-CBT system using audio recorded sessions between a mental health therapist and a study participant with moderate to severe depressive symptoms and chronic disease. These sessions were administered as part of a clinical trial (RED-D AHRQ R01HS019700) testing telephonic CBT versus usual care for treating depressive symptoms in recently hospitalized patients with moderate to severe depressive symptoms. The CBT curriculum is based on the standard CBT session outline adapted from Beck A, Rush J, Shaw, B, and Emery, G's "Cognitive Therapy of Depression", along with Safren, S., Gonsales, J., and Sourudi, N.'s "Coping with Chronic Illness : A Cognitive-Behavioral Therapy Approach for Adherence and Depression". Scripts were then programmed by the subcontractors at Northeastern University to be delivered by the animated Sophie relational agent using standard programming and animation software and development protocols.[9]

D.2. Description of the RA-CBT curriculum: Each module began with a personalized greeting, using the patient's name and inquiring about the participant's current emotional state. Screening questions were then verbally administered by the RA to assess for depressive and pain symptoms. The screening tools used were PHQ-8 and Brief Pain Inventory, Short Form. CBT activities targeted skills to reframe thinking, boost mood, and change behaviors. The following six modules were developed: 1.) Intro to CBT – the first module offered an introduction to acquaint the patient with the basics of CBT. This educational section was written to inform on the cognitive model of depression and provide instruction for utilizing CBT within the virtual platform. 2.) Stress and Pain Management – the second module offered education on stress and pain management within the context of comorbid depression. The activities (mediation, chair yoga, and progressive muscle relaxation) offered concrete interventions to help manage stress and pain. 3.) Thought-Feeling Connection – the third module explores the relationship between thoughts and emotions. The activity, thought record, was introduced to help participants begin to identify automatic thoughts. 4.) Transforming Thoughts- the fourth module builds upon the third module by explaining unhelpful thinking patterns and instructing the essential CBT skill of cognitive restructuring. The activity continues use of the thought record while identifying healthy thinking patterns and practicing cognitive restructuring. 5.) Behavior Activation/Pacing- the fifth module was designed to increase engagement with activities that are limited by symptom burden through the use of the CBT skill, pacing. Pacing is a technique that is used to help patients accomplish tasks and activities in a sensible and thoughtful way. 6.) Wrap Up – the sixth and final module was intended to review completed modules and reinforce continued practice of CBT skills.

D.3. Pilot testing: A feasibility study was then conducted among participants with chronic illness and comorbid depression to explore their experience with the RA-CBT. The target audience was recruited from a list of 166 patients recently hospitalized for exacerbation of a chronic illness and had also screened positive for depressive symptoms with a PHQ-8 score greater or equal to 10.[10] We used convenience sampling to comprise a cohort of 21 study participants. Letters were sent to the target audience explaining the RA-CBT study with an invitation to enroll. Follow-up calls were made within one week of the letters being sent. Interested participants were consented and enrolled over the phone and scheduled for an in-person RA-CBT session and key informant interview. A total of 21 participants enrolled in the study and completed testing. The testing sessions lasted 4 hours in duration. The participants were introduced to the RA character, "Sophie", and provided instructions for use of the technology. The participants were interviewed after completing 2 modules to gather feedback on their experience with the RA. Near the end

of the session, participants engaged in a recorded semi-structured key informant interview and completed an exit survey.

D.4. Outcomes Measures and Data Collection: The primary outcome measure was the score on the Working Alliance Inventory scale, a 36-item validated questionnaire which was used to measure how participants relate with the Sophie character.[11] Possible scores range from lowest score of 44 to highest score of 201, with higher scores correlated with higher therapeutic alliance. In addition, we surveyed participants on their satisfaction with, and the acceptability of, the Sophie system as a mode for accessing depression treatment. To further elucidate the participants' experience using the Sophie system and their views on the character's attributes, we conducted semi-structured key informant interviews during and following the CBT module testing. All interviews were audio recorded and transcribed verbatim. Thematic analysis was used for coding and analysis of the qualitative data.[12] A codebook was created based on initial coding and analysis of first 2 transcripts. This codebook was used to code and analyze the remaining transcripts. New codes were added to the codebook as needed. Two research assistants were assigned to each transcript to conduct line by line data coding and analysis. Discrepancies in coding were discussed and resolved by a third qualitative researcher or the PI. Initial codes were consolidated into broader codes and finally into overarching themes based on the research aims and data analysis. Data analysis was ongoing throughout the study period, and ended when new salient themes ceased to surface and data saturation was attained.[13]

E. Results: A total of 21 participants completed the pilot testing of the Sophie RA-CBT system. The average as of study participants was 54 years old, the majority were female (76%) and 67% self-identified as racial/ethnic minority. All participants had a medical diagnosis of major depression and 67% were on medication for depression. The mean score on the PHQ 8 depression screen prior to testing was 11 ($\pm$ 5), correlating with a moderate depressive symptom burden.

E.1. Survey Results on Feasibility, Acceptability and Usability of Sophie System

E.1a. Acceptability: The Working Alliance Inventory (WAI) scoring of the bond between the relational agent, Sophie, and the subjects was based on a Likert scale, where 1 was never and 7 was always. People scored 5.29 $\pm$ 1.82 (mean $\pm$ SD) when asked if they felt confident in Sophie's ability and 5.33 $\pm$ 1.80 when asked if there was good understanding between the subject and Sophie. Additionally, participants scored 5.33 $\pm$ 2.00 when asked if there was mutual trust between Sophie and subject and 4.90 $\pm$ 2.32 when asked if they felt that Sophie trusted and cared about them. Furthermore, when participants were asked if they trusted Sophie, the score was 1.76 $\pm$ 1.22, where 1 was equal to very much and 7 was equal to not at all. When asked if subject would have rather talked to a healthcare provide than Sophie, we see a score of 4.05 $\pm$ 1.75, where 1 equals definitely prefer my provider and 7 equals definitely prefer Sophie.

E.1.b. Feasibility: The subjects found Sophie easy to talk to, with a score of 1.76 $\pm$ 1.22 (mean $\pm$ SD) on a scale of 1 equal to easy and 7 equal to difficult. When asked if they would like to speak with Sophie again based on the modules they answered, we see a score of 2.10 $\pm$ 1.64, where 1 was equal to definitely yes and 7 equal to definitely no. Finally, when subjects were asked if they would seek health care from Sophie, 15 (23.81) subjects said yes and 6 (28.57) said they would not (n (%)).

Table 1. Participant characteristics N=21

Age in years, *mean ± SD*	54.10 ± 11
Sex, *n (%)*	
Female	16 (76.19)
Male	5 (23.81)
Race, *n (%)*	
Non-Minority	7 (33.33)
Racial/Ethnic Minority	14 (66.75)
Language spoken at home, *n (%)*	
English	19 (90.48)
Other	2 (09.52)
Highest level of education obtained, *n (%)*	
Some and/or high school graduate	6 (28.57)
Some college	9 (42.86)
College graduate (B.A. or B.S.)	6 (28.57)
Medically diagnosed depression, *n (%)*	20 (95.24)
On medication for depression, *n (%)*	15 (71.43)
***PHQ8 Total Score**, *mean ± SD*	11 ± 5

*where PHQ8 total score equal to or greater than 10 serves as an indicator of depression

E.1.c. Usability: Subjects found the modules for Sophie to be timely, with a score of 4.05 ± 1.16 (mean ± SD) on a scale of 1 equal to too short and 7 equal to too long. When asked about how well Sophie listened to the subjects, 12 (57.14) individuals answered great, 5 (23.81) answered good, 1 (4.76) answered fair, and 3 (14.29) subjects said Sophie's listening was okay (n (%)). Finally, when asked if they felt Sophie spent enough time on them, 7 (35.00) subjects said the time spent was good, 10 (50.00) said the time spent on them was great, and 3 (15.00) said the time Sophie spent on them was okay.

E.2. Qualitative Themes on Feasibility, Acceptability and Usability of the Sophie System

Three key themes emerged from the key informant interviews including addressing barriers to care, response to character attributes and forming a working alliance with the RA, and navigating the system itself. Overall most participants agreed that the RA could be a valuable supplement to in-person therapy but were less certain about using the Sophie system as self-guided depression therapy. Participants found the RA to be a useful resource for support and developing skills to manage comorbid depression and symptom burden from medical illness.

E.2.a. Sophie as a Response to Mental Healthcare Access Barriers: Participants identified advantages to the RA compared to in-person therapy alone in addressing barriers to care. One advantage identified was access and availability. More specifically, participants preferred the option of working with "Sophie" in the comfort of their own homes with constant and flexible access, and no financial investment required. They spoke of hesitance to connect with in-person behavioral health providers due to feelings that talk therapy "just isn't me." Often when patients did express desire to utilize these services, they faced difficulty when trying to schedule appointments. For these patients, Sophie was a valuable resource: "…feels like I'm having therapy with a tablet." Some also shared that the RA could help overcome some of the barriers that limit access such as decreased motivation and increased pain. "If my pain is unbearable, I could talk to Sophie instead of running to the ER."

Most participants also felt that working with the RA removed a great deal of the judgment and stigma involved with seeking behavioral health treatment or support for chronic pain because of the virtual platform. One participant stated, "I didn't hold back because she was virtual," while another said "A computer is not a person that's going to judge you, it's more private." Further testimony indicates that Sophie was seen as someone who would not patronize patients, who would always be able to repeat material, and who would not grow tired of patients' needs, as opposed to patients' existing social and behavioral health supports.

A final aspect of the program's ability to address barriers to care involves health literacy. Participants mentioned that Sophie was easier to understand than an in-person therapist and appreciated that the material could be repeated. They overwhelmingly felt that the system provided clear explanations and straightforward language, and was easy to follow. One participant recommended that the script be translated to Spanish.

E.2.b. Response to Character Attributes: The second theme that emerged was Sophie's acceptability, namely the participants' response to her character and her ability to form a working alliance with participants. There was a positive response to the RA's ability to connect with the participants, as many described feeling able to tell her how they were feeling. The RA's empathic tone, optimistic and nonjudgmental attitude, and most importantly, personalized use of their names contributed to the establishment of trust. "I trust Sophie even though I just met her today because she made me feel like she wanted to help," said one participant. Others were particularly impressed by the system's ability to track mood and symptom burden over time, describing Sophie's ability to "remember" as another facet of the working alliance. The RA was also an empowering support for many of the participants. Coping strategies and encouragement provided by Sophie gave participants concrete ways of helping themselves, and one mentioned that the RA "makes me feel more normal…this makes it sound like other people experience the same thing.

In terms of voice, response was not as positive. One interviewee said, "I found her slightly off-putting," due to pronunciation and speech issues. Other agreed, finding the voice to be "monotonous" and "robotic". There were differing opinions on the non-verbal aspects of the RA. Interviewees felt that the avatar's appearance was generally relatable, though it could be more so if it were customizable. One female participant noted that "it was helpful that she was female," while another said, "the fact that she's a woman of color is relatable. A third mentioned the avatar's age, noting that she would not have taken the program as seriously if Sophie were younger. Some participants made note of the minimal range in facial expressions and asymmetry of eyebrow movements while others felt the facial expressions were realistic. Similarly, some participants described her hand gestures as "a little weird," though others appreciated that "she's not a statue," claiming the gestures and expressions contributed to feeling more comfortable with the RA.

E.2.c. System Usability - CBT Curriculum Content: The third theme arising from user testimony is the usability of the system itself in its content and navigation. With regard to content, most participants felt the system was informative and provided techniques that encouraged setting goals and taking action. "I feel happy and reassured I actually am being proactive," commented one participant. "I can actually take control back," noted another, one of several who emphasized the opportunities to make their own choices throughout the program. Users also felt that the content was thorough, honest, and relatable to their own experiences as patients. They appreciated that their progress with the system was measurable. They generally preferred relaxation techniques, reframing negative thoughts, and pacing over the thought record activity that was described as "confusing" and "unhelpful." Some participants felt the modules were too long and "people might lose interest," and one participant described the first module (Intro to CBT) as "boring" but denied that the RA character herself is boring. The RA's limited response options were noted, and participants indicated that they would prefer talking to the RA using their own words rather than preset answers options. With the preset options, reported one user, "sometimes you're a little boxed in."

E.2.d. System Usability - Navigating the Sophie System: With regard to navigation, there were mixed opinions among users. Some participants noticed the timing and the layout of answer options were out of sync in modules 1 and 2; others reported modules 2 and 3 did not work; still others reported technical errors in modules 5 and 6 that required restarting the program. However, there were several participants who did not notice any technical glitches in the first few modules. There were also mixed opinions on the graphics. Some liked the bright colors and felt the text boxes were readable, while others thought the text and charts could be bigger. Most thought the watermark on the images was distracting and some were displeased with the graphics being cut off on the right side at times. Many participants agreed that, while the graphics were conducive to the CBT content, there was too much time allotted to read graphics: "Sophie shouldn't leave time for patients to read the graphics if she's going to read them anyway."

E.2.e. Suggestions for Next Steps: Suggestions for further development include having access to the RA via an app. It was suggested that this would make the RA more accessible to use more often, which would assist users in retaining more information. Also, several participants had trouble with the general functioning of the program and with the keyboard feature due to complications from their medical conditions. One participant suggested having a stylus to assist in ease of use. Another participant suggested selling to the program to behavioral health providers to use in conjunction with in-person therapy. Some recommended starting use in the hospital, both so any tech glitches could be fixed or explained, and also so that patients could continue behavioral health therapy even when unable to make it to an outpatient provider due to hospitalization. Others recommended that the RA system be directly connected to providers. For example, one participant suggested having the RA connect to a case worker who could monitor data and send it to a PCP or psychiatrist, and another suggested sending a summary report to providers with the patient's answers and trends.

Overall the RA's unique human-like aspects made the virtual platform more relevant than any online CBT. "Even though the system isn't like a face-to-face interaction with a provider, it's like Sophie's sitting right here with me," noted one user. However human-like the RA may be, the majority of participants agree that Sophie could be a good supplement to in-person therapy, but not yet worthy to serve as a substitute. Many felt the system reinforced working with a therapist but wouldn't replace the in-person provider: "you need the human part of it."

F.   Conclusion: Using a relational agent system programmed to deliver self-administered cognitive behavioral therapy for depressive symptoms for patients with advanced chronic disease and comorbid depression is feasible and acceptable. Further research is warranted to determine the clinical efficacy of the Sophie Relational Agent system for improving depression and adherence to depression treatment.

G.   Implications and Significance: In addition, this innovative tool holds the promise to overcome access barriers to mental healthcare that contribute to prevailing health disparities in mental health and address important problems with adherence to mental health treatment such as stigma associated with mental illness and difficulties with transportation or child care.

H. References

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Fig1. Patient using relational agent in hospital. Fig 2. Sophie relational agent for CBT.

I. List of Publications and Products:

Mitchell SE, Krizman K, Cawley M, Bhaloo J, Welch M, Bennett M. Jack BW. Feasibility Testing for Relational Agents System Designed to Deliver CBT for Comorbid Depression in Patients with Advanced Chronic Medical Conditions (manuscript in progress)

Table 2. Feasibility, Acceptability, and Usability of the relational agent SOPHIE

Acceptability	
WAI Bond*	
There is a sense of discomfort in the relationship	2.00 ± 1.52
There is a good understanding between the subject and SOPHIE	5.33 ± 1.80
There is a mutual liking between subject and SOPHIE	4.95 ± 1.86
The subject is aware that SOPHIE is genuinely concerned for his/her welfare	5.38 ± 2.01
The subject and SOPHIE respect each other	5.24 ± 2.17
The subject feels that SOPHIE is not totally honest	2.33 ± 1.80
The subject feels confident in SOPHIE's ability to help client	5.29 ± 1.82
The subject feels that SOPHIE appreciates him/her as a person	5.14 ± 2.24
There is mutual trust between subject and SOPHIE	5.33 ± 2.00
Both the subject and SOPHIE see their relationship as important to the subject	5.05 ± 1.83
The subject fears that if he/she says or does the wrong thing, SOPHIE will stop working with him/her	2.48 ± 1.99
The subject feels that SOPHIE respects and cares about subject	4.90 ± 2.32
WAI total score	149.95 ± 35.5
Feasibility	
How much do you trust Sophie (1=very much; 7=not at all)	1.76 ± 1.14
Would you have rather talked to a healthcare provider than Sophie (1=definitely prefer my provider; 7=definitely prefer Sophie)	4.05 ± 1.75
How easy was it to talk to Sophie (1=easy; 7=difficult)	1.76 ± 1.22
Based on this module, would you like to talk with Sophie again (1=definitely yes; 7=definitely no)	2.10 ± 1.64
Would you seek healthcare information from Sophie, n (%)	
Yes	15 (71.43)
No	6 (28.57)
Usability	
How did you feel about the time for each module for Sophie (1=too short; 7=too long)	4.05 ± 1.16
How well did Sophie listen to you	
Fair	1 (4.76)
Good	5 (23.81)
Great	12 (57.14)
Okay	3 (14.29)
Did you feel the amount of time spent with Sophie was…	
Good	7 (35.00)
Great	10 (50.00)
Okay	3 (15.00)

*WAI: Working Alliance Inventory, based on Likert scale, where 1=never to 7=always