TC CFAR Seminar

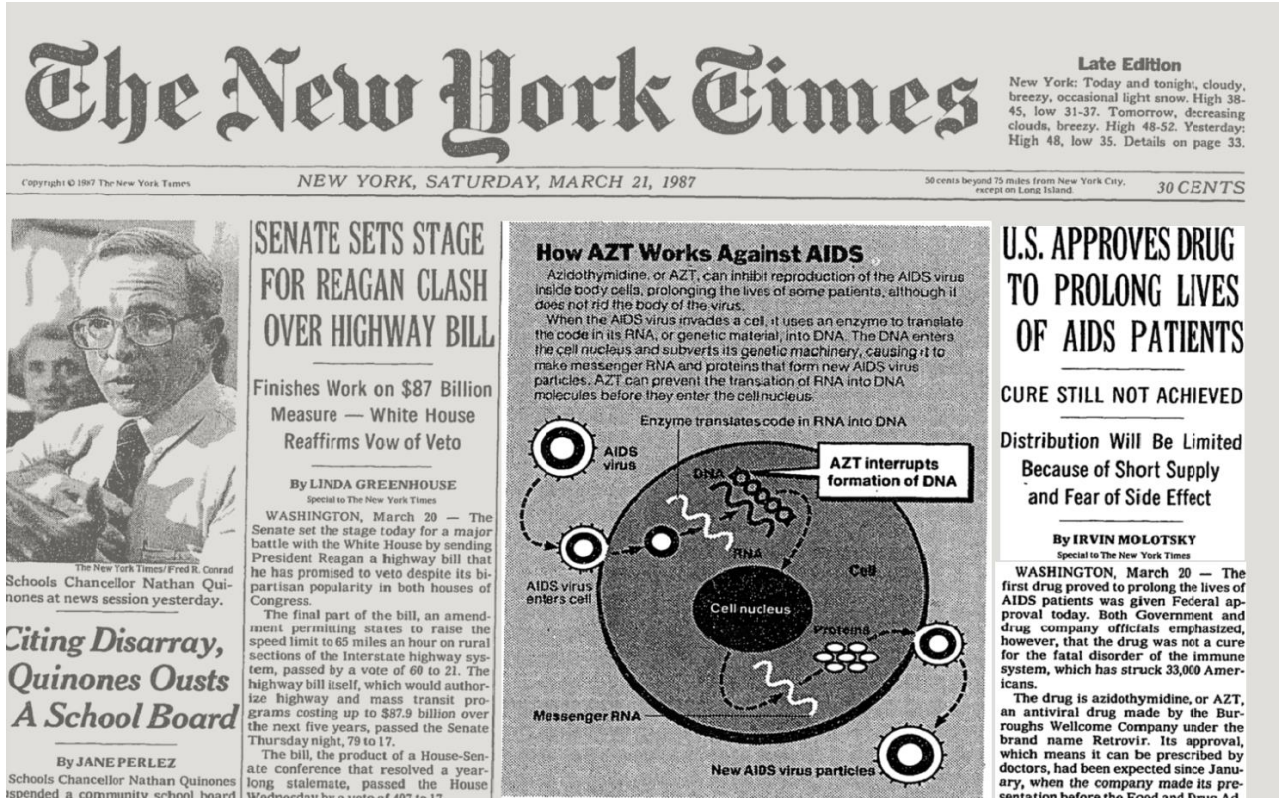
Technological Approaches to Improving Medication Adherence in People with HIV: Relational Agents and Electronic Adherence Monitoring

with Mark Dworkin, MD

Feb. 13, 2025
12:00PM CT

Oral Antiretroviral Therapy

- 1983 – the virus was identified
- 1985 began medical school – no treatment for human T-cell lymphotropic virus-type III/lymphadenopathy-associated virus (HTLV-III/LAV)
- 1987 AZT every four hours, high dosage, bone marrow suppression = anemia
- Other drugs followed (ddI, ddC), painful neuropathy
- 1995 recognition and beginning of adoption of “highly active antiretroviral therapy” -→ combination antiretroviral therapy – a revolutionary change that in 1996 began including a protease inhibitor in the regimen
- 1996 began working at the CDC, Division of HIV/AIDS as hospitalization and mortality began to decline from their high rates
- 2006 Atripla (efavirenz, emtricitabine, tenofovir) combined in one pill once daily!



The New York Times

Late Edition

New York: Today and tonight, cloudy, breezy, occasional light snow. High 38-45, low 31-37. Tomorrow, decreasing clouds, breezy. High 48-52. Yesterday: High 48, low 35. Details on page 33.

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NEW YORK, SATURDAY, MARCH 21, 1987

50 cents beyond 75 miles from New York City, except on Long Island. 30 CENTS

The New York Times/Fred R. Conrad

Schools Chancellor Nathan Quinones at news session yesterday.

Citing Disarray, Quinones Ousts A School Board

By JANE PERLEZ

Schools Chancellor Nathan Quinones suspended a community school board

SENATE SETS STAGE FOR REAGAN CLASH OVER HIGHWAY BILL

Finishes Work on $87 Billion Measure — White House Reaffirms Vow of Veto

By LINDA GREENHOUSE

Special to The New York Times

WASHINGTON, March 20 — The Senate set the stage today for a major battle with the White House by sending President Reagan a highway bill that he has promised to veto despite its bipartisan popularity in both houses of Congress.

The final part of the bill, an amendment permitting states to raise the speed limit to 65 miles an hour on rural sections of the Interstate highway system, passed by a vote of 60 to 21. The highway bill itself, which would authorize highway and mass transit programs costing up to $87.9 billion over the next five years, passed the Senate Thursday night, 79 to 17.

The bill, the product of a House-Senate conference that resolved a year-long stalemate, passed the House

How AZT Works Against AIDS

Azidothymidine, or AZT, can inhibit reproduction of the AIDS virus inside body cells, prolonging the lives of some patients, although it does not rid the body of the virus.

When the AIDS virus invades a cell, it uses an enzyme to translate the code in its RNA, or genetic material, into DNA. The DNA enters the cell nucleus and subverts its genetic machinery, causing it to make messenger RNA and proteins that form new AIDS virus particles. AZT can prevent the transation of RNA into DNA molecules before they enter the cell nucleus.

U.S. APPROVES DRUG TO PROLONG LIVES OF AIDS PATIENTS

CURE STILL NOT ACHIEVED

Distribution Will Be Limited Because of Short Supply and Fear of Side Effect

By IRVIN MOLOTSKY

Special to The New York Times

WASHINGTON, March 20 — The first drug proved to prolong the lives of AIDS patients was given Federal approval today. Both Government and drug company officials emphasized, however, that the drug was not a cure for the fatal disorder of the immune system, which has struck 33,000 Americans.

The drug is azidothymidine, or AZT, an antiviral drug made by the Burroughs Wellcome Company under the brand name Retrovir. Its approval, which means it can be prescribed by doctors, had been expected since January, when the company made its presentation before the Food and Drug Ad

Optimal Adherence to ART Can Reduce

- **Morbidity (personal health)**
- **Mortality (personal health)**
- **Viral resistance (personal and public health)**
- **Viral Transmission (public health)**

There Are Many Barriers to Adherence

- Forgetting
- Stigma
- Side effects
- Pill burden
- Low self-efficacy
- Low (health) literacy
- Distance
- Depression
- Housing instability
- Food insecurity
- And more

Avatar App Study

Scan to learn more about the My Personal Health Guide app!

My Personal Health Guide

- Theory-informed mobile phone app promoting ART adherence, viral suppression, and retention in care developed for young, Black men who have sex with men (YBMSM) living with HIV
- Customizable realistic relational agent (“avatar”) with plain-speaking, human voice that empathizes, motivates, and relates to user

Why did I include an Avatar in an intervention to promote adherence?

- **Oxford Dictionaries**

“An icon or figure representing a particular person in computer games, Internet forums, etc.”

An Avatar Can Serve As A Relational Agent

- **“Animated conversational agent designed to establish trust and therapeutic alliance with users over time”**
- **Less intimidating**
- **More accessible to patients with a wide range of computer, reading, and health literacy skills**
- **May establish a therapeutic alliance with patients through verbal and nonverbal behaviors such as**
  - **Empathy**
  - **Attentiveness**
  - **Social dialogue and even humor**

Response to a Relational Agent by Hospital Patients with Depressive Symptoms
Timothy W. Bickmore et al, Interact Comput 2010;22:289-98

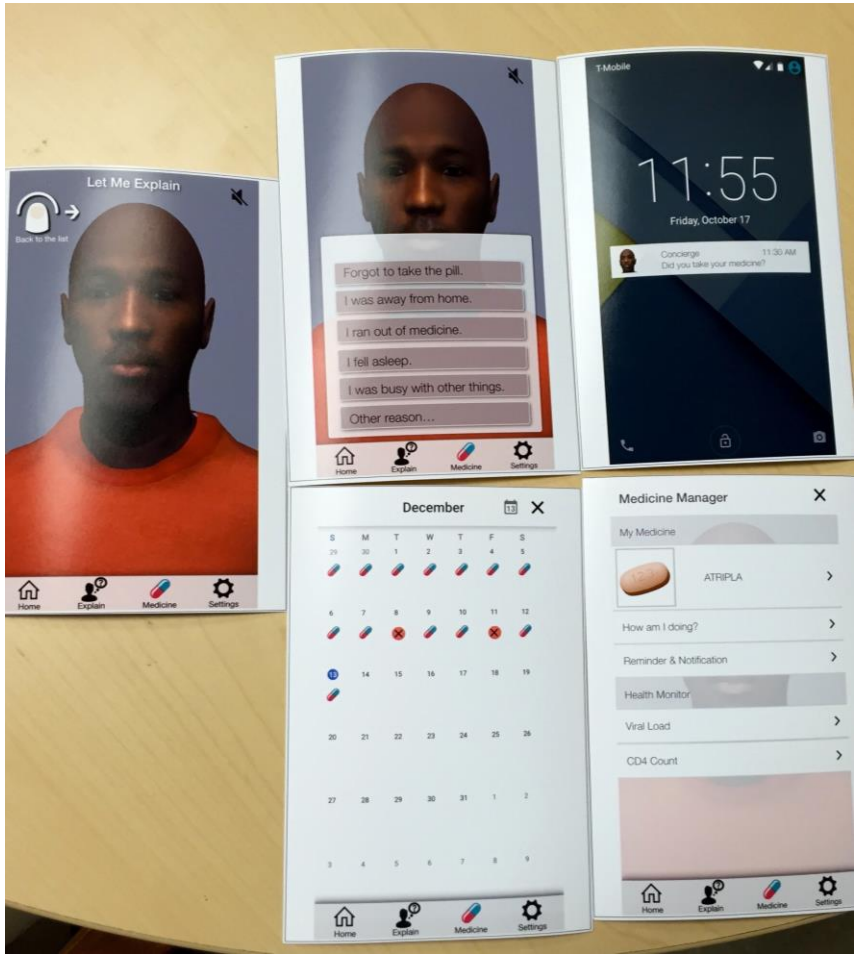
Avatars Have Been Used to Promote or Change Behavior

- **Program for modeling weight loss behaviors**
- **Hospital discharge instructions**
- **Post traumatic stress disorder, addictions, body image disturbance, binge eating disorder**
- **Condom use for MSM**

Application of the Information, Motivation, Behavioral Skills Model

Continuum Stage	Information	Motivation	Behavioral Skills	Behavior	Outcome Measure
Adherence	Avatar can explain not to wait for the next day to take a dose when missed in the morning	Avatar can encourage taking medication on time	Avatar explains a weekly pill box	Medication dose taken	>80% of medication taken by pill count and/or self-report

Informed by 5 iterative focus groups of YBMSM living with HIV in Chicago (NIH R21NR016420)



- **"I like this!" (all agreed)**
- **"Say I am afraid to get some help. You would know how to tap into this app and people think we are trying to play games. This is genius idea. Thank you!"**
- **Disliked medication icon**
  - **"No one who is HIV positive wants anything on their phone that screams out HIV positive."**

Preliminary App Efficacy Pilot in Young AAMSM

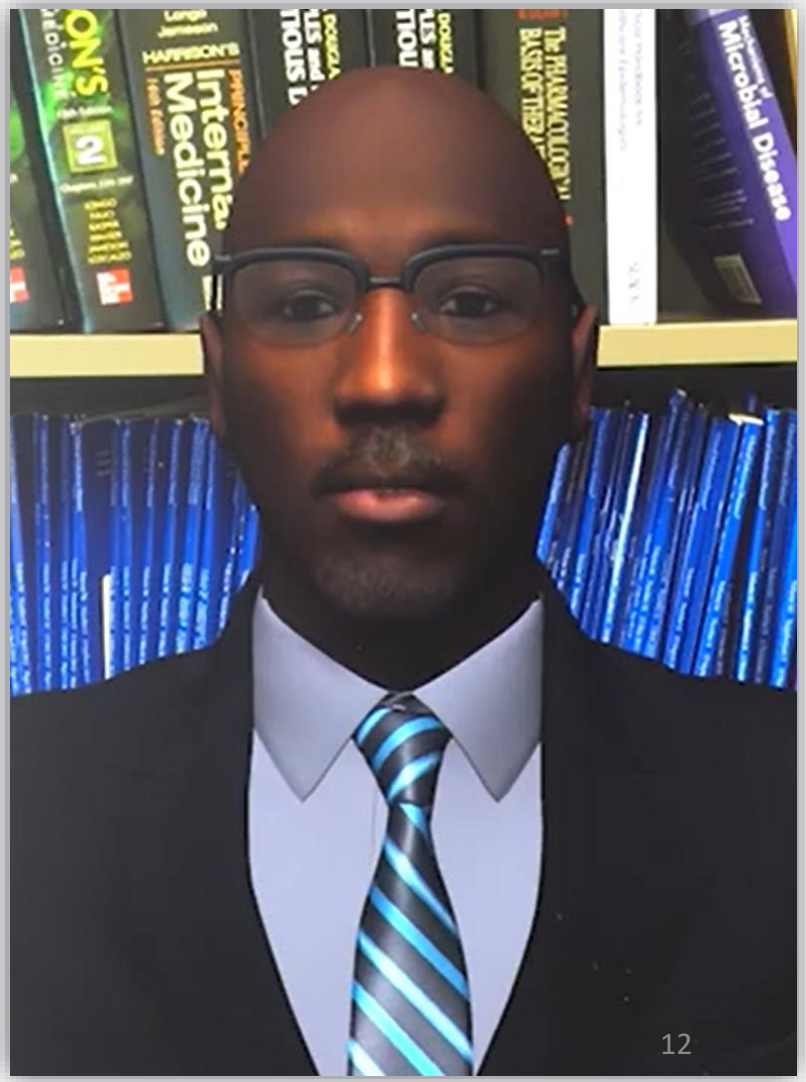
- **3-month follow-up**
- **No control group**
- **Pre and post pill count**
- **43 enrolled**
- **26 with 3-month follow-up and pill counts**
- **Pill count adherence > 80% improved from 62% at baseline to 88% at follow-up (p = .05)**

Acceptability, Feasibility, and Preliminary Efficacy of a Theory-Based Relational Embodied Conversational Agent Mobile Phone Intervention to Promote HIV Medication Adherence in Young HIV-Positive African American MSM.
Dworkin MS, Lee S, Chakraborty A, Monahan C, Hightow-Weidman L, Garofalo R, Qato DM, Liu L, Jimenez A.
AIDS Educ Prev. 2019 Feb;31(1):17-37. doi: 10.1521/aeap.2019.31.1.17.

Avatar App Study

My Personal Health Guide

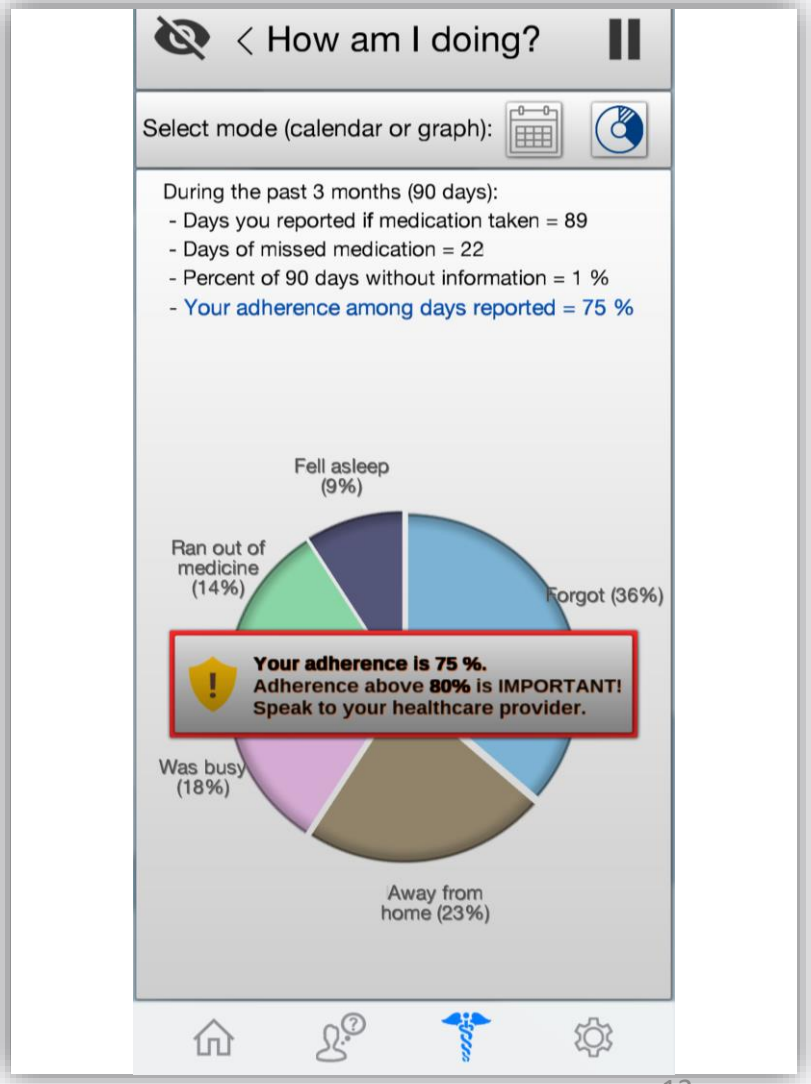
- Avatar asks and answers questions with branching logic
- Recordings of motivational messages from healthcare personnel and community peers living with HIV
- ‘Let Me Explain’ function has questions the avatar answers
- Reminder functions available for medication-taking, appointments, and blood draws
- Viral load and CD4 count graphs to monitor trends
- ‘Show My Medicine’ educates about HIV medications



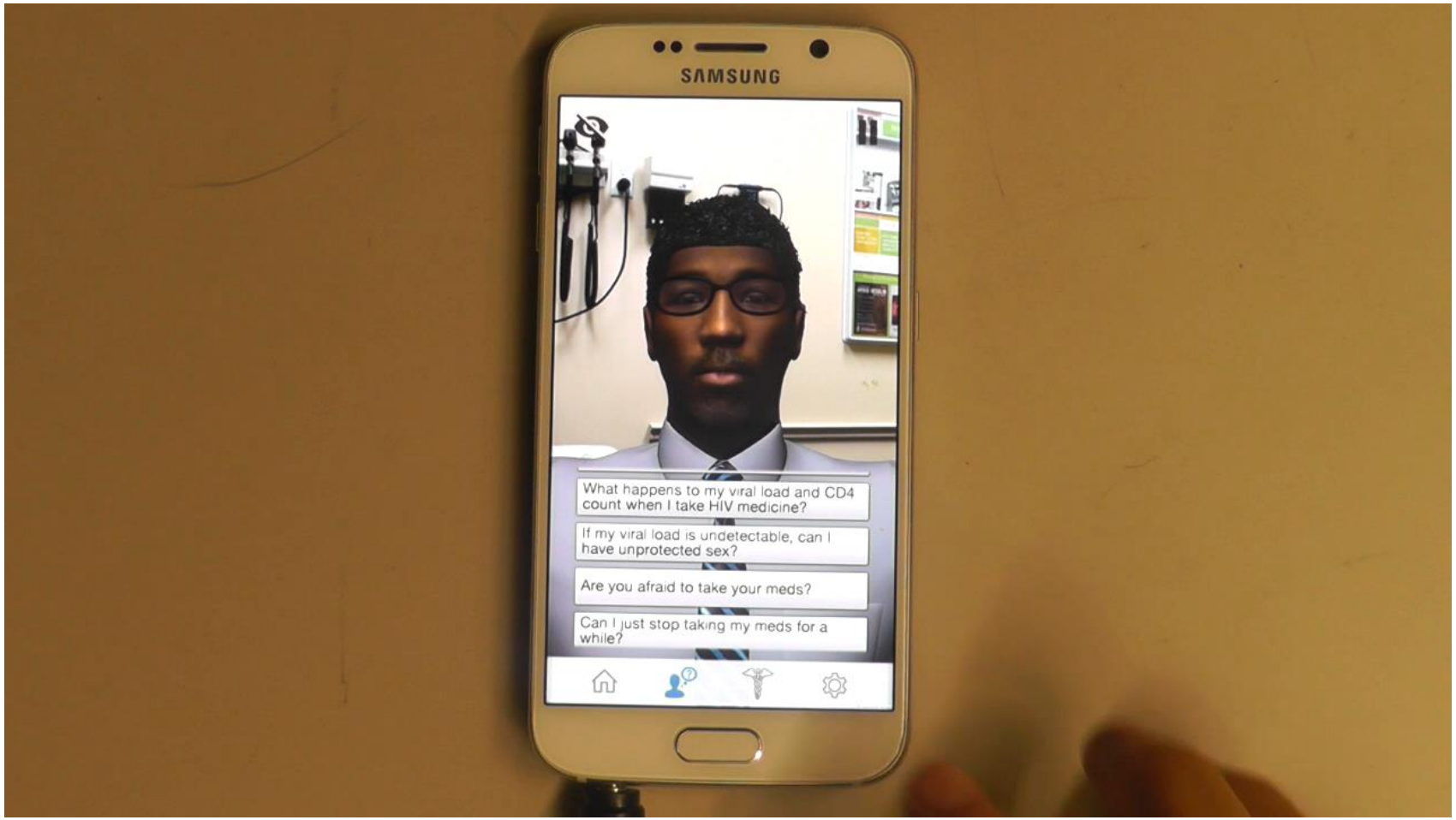
Avatar App Study

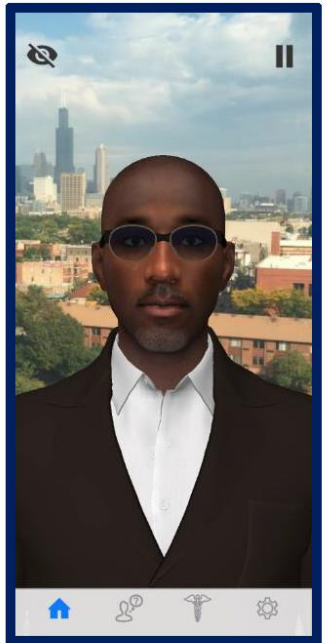
My Personal Health Guide

- ‘How am I doing taking my medicines?’ to monitor self-reported adherence
- Privacy features (pause/hide screen)
- Customization of app/avatar
- ‘The Dating Game’ (gamification) to reinforce learning of ‘Let Me Explain’ questions



1. Motivation –acknowledging fear about taking meds
2. Caution not to take a break from meds



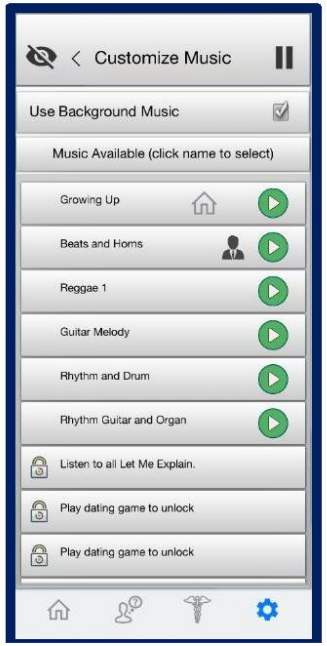


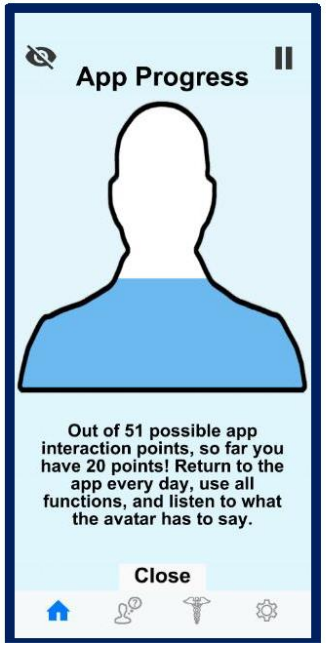
Customization example.

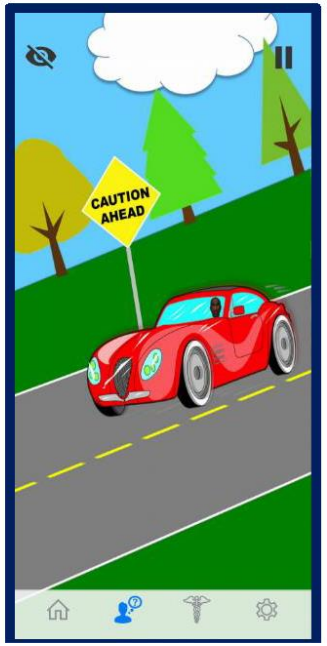
Customization example.

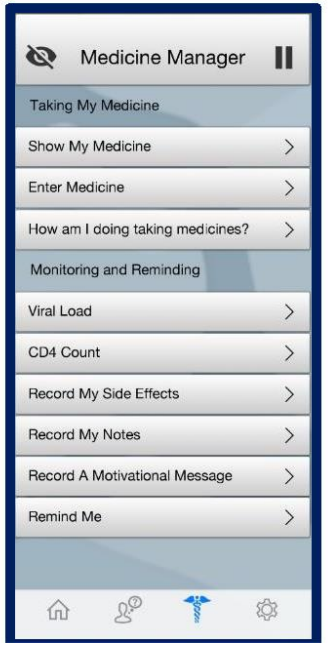
Female avatar. Let Me Explain Questions.

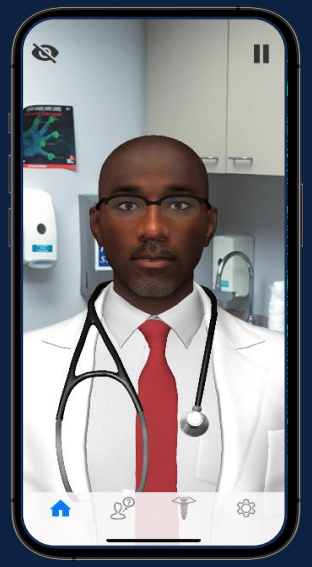
Customization screen.











Randomized Controlled Trial to Test Efficacy of My Personal Health Guide

R01MH116721, NCT04217174

- Two analyses: Determine the efficacy of the My Personal Health Guide app on ART adherence among YAAMSM at:
  - 1-month post-randomization (short-term efficacy)
  - 6-months post-randomization
- We hypothesized that those randomized to receive My Personal Health Guide would have greater ART adherence compared to controls at both 1-month and 6-month follow-up

Avatar App Study

Study Design

- Randomized controlled trial recruiting throughout the United States during February 2020 through September 2023 predominantly through social media to three enrolling sites: University of Illinois at Chicago, Emory University, and The University of Mississippi Medical Center
- Eligibility requirements:
  - 18-34 years old at recruitment
  - Self-reported as Black or African American, male sex at birth, and male gender
  - Self-reported having at least one male sexual partner in their lifetime
  - English speaking
  - Own a smartphone
  - Initiating or were already prescribed ART
  - Either self-reported non-optimal adherence in the last 30 days, self-reported having a detectable viral load in the past 4 weeks, or were referred by a healthcare professional as having non-optimal adherence

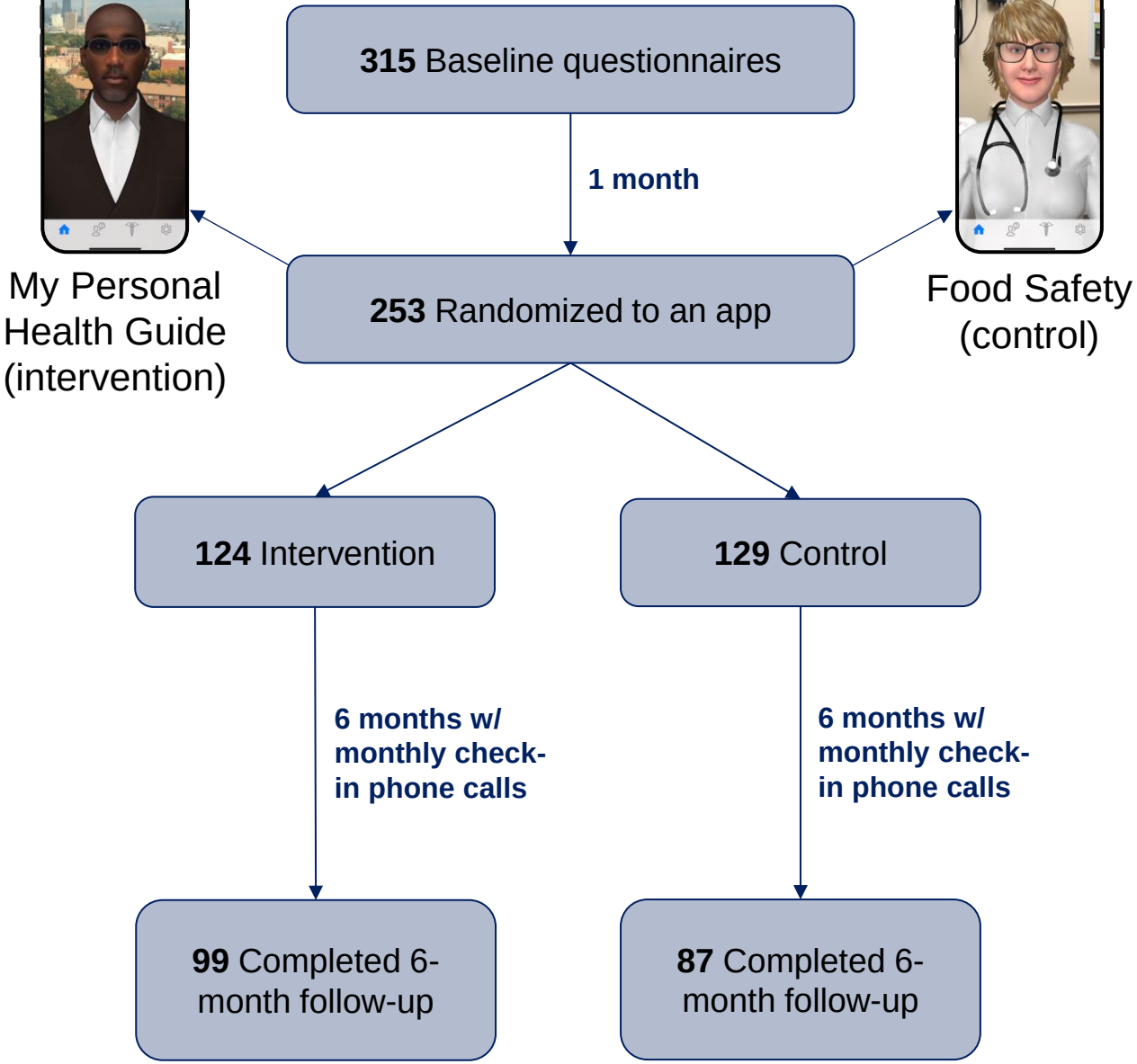
Avatar App Study

Study Design

- 315 participants completed a baseline questionnaire one month prior to app randomization
- 253 participants were randomized 1:1 to download either the My Personal Health Guide intervention app or an attention control app designed to deliver food safety education
- Participants were followed for 6 months with monthly check-in calls
- ART adherence for the past 30 days was assessed at baseline and monthly using Wilson's 3-item self-reported measure

My Personal Health Guide (intervention)

Food Safety (control)



Wilson IB, Lee Y, Michaud J, Fowler FJ Jr, Rogers WH. Validation of a New Three-Item Self-Report Measure for Medication Adherence. AIDS Behav. 2016 Nov;20(11):2700-2708. doi: 10.1007/s10461-016-1406-x.

Avatar App Study

Table 1. Selected baseline demographic characteristics of young AAMSM living with HIV by randomization group (N=253), 2020-2024

Characteristic	Intervention (n=124)	Control (n=129)	P-value
Enrollment site			
University of Illinois at Chicago	59 (47.6%)	72 (55.8%)	0.175[2]
Emory University	54 (43.5%)	52 (40.3%)	
University of Mississippi Medical Center	11 (8.9%)	5 (3.9%)	
Remote participation	98 (79.0%)	104 (80.6%)	0.874[2]
Age in years, mean (SD)	29.6 (3.45)	29.1 (3.98)	0.460[1]
Ethnicity, Hispanic	9 (7.3%)	9 (7.0%)	0.999[2]
Residence			
Midwest	34 (27.4%)	43 (33.3%)	0.416[2]
Northeast	12 (9.7%)	15 (11.6%)	
South	77 (62.1%)	68 (52.7%)	
West	1 (0.8%)	3 (2.3%)	
Education			
College	30 (24.2%)	38 (29.5%)	0.592[2]
Some college	51 (41.1%)	56 (43.4%)	
High school or GED	36 (29.0%)	29 (22.5%)	
Less than high school	7 (5.6%)	6 (4.7%)	
Employment			
Employed	75 (60.5%)	72 (55.8%)	0.450[2]
Student	10 (8.1%)	8 (6.2%)	
Unable to work or unemployed	36 (29.0%)	47 (36.4%)	

[1] t-test
[2] Chi-square test

Avatar App Study

Table 1. Selected baseline demographic characteristics of young AAMSM living with HIV by randomization group (N=253), 2020-2024

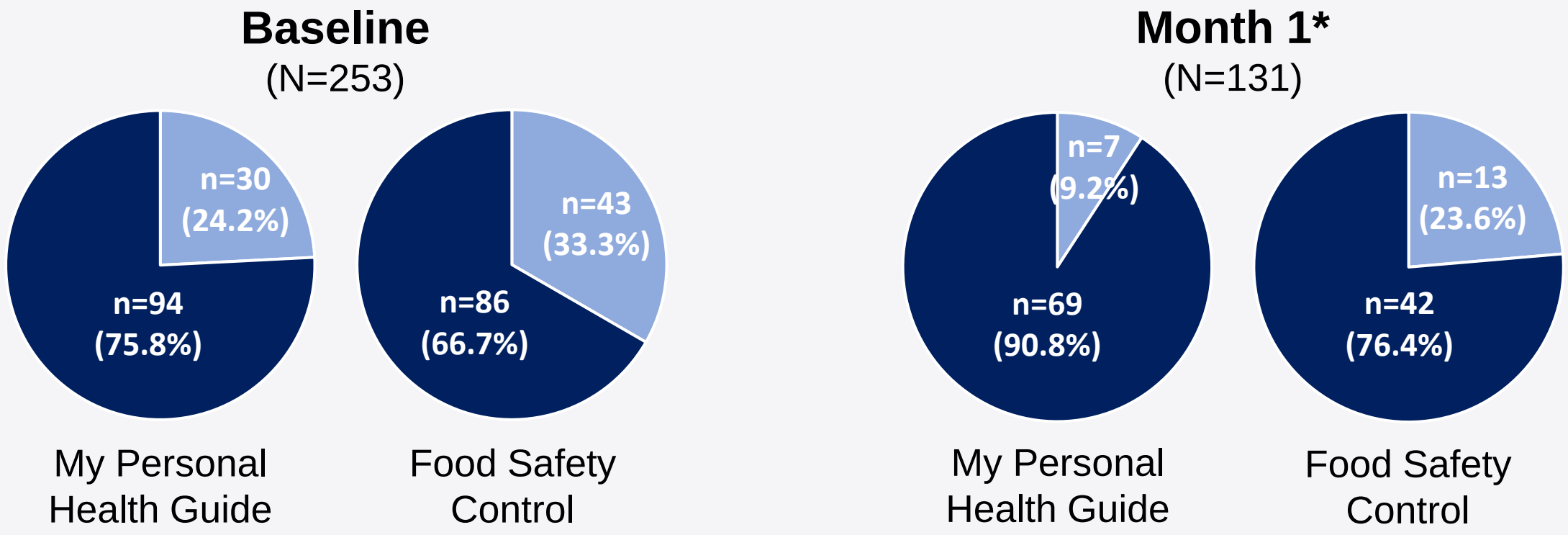
Characteristic	Intervention (n=124)	Control (n=129)	P-value
Marital status			
Legally married	4 (3.2%)	6 (4.7%)	
Domestic partnership or civil union	1 (0.8%)	0 (0%)	
Widowed	0 (0%)	1 (0.8%)	0.689[2]
Divorced	5 (4.0%)	3 (2.3%)	
Separated	2 (1.6%)	3 (2.3%)	
Never married	112 (90.3%)	116 (89.9%)	
Sexual Orientation			
Homosexual or gay	85 (68.5%)	95 (73.6%)	
Bisexual	27 (21.8%)	22 (17.1%)	0.809[2]
Heterosexual or straight	2 (1.6%)	2 (1.6%)	
Other	10 (8.1%)	10 (7.8%)	
Currently in a committed relationship with a male partner	25 (20.2%)	30 (23.3%)	0.648[2]
Housing insecurity in past 6 months	32 (25.8%)	29 (22.5%)	0.637[2]
Ever incarcerated	45 (36.3%)	32 (24.8%)	0.0646[2]
Health literacy (modified REALM-SF)			
Nonoptimal	47 (37.9%)	49 (38.0%)	0.999[2]
Optimal	77 (62.1%)	80 (62.0%)	

Abbreviations: REALM-SF, Rapid Estimate of Adult Literacy in Medicine–Short Form

[2] Chi-square test

Avatar App Study

Figure 1. Self-reported adherence to ART in the past 30 days at baseline and one month after randomization among those with adherence information at Month 1

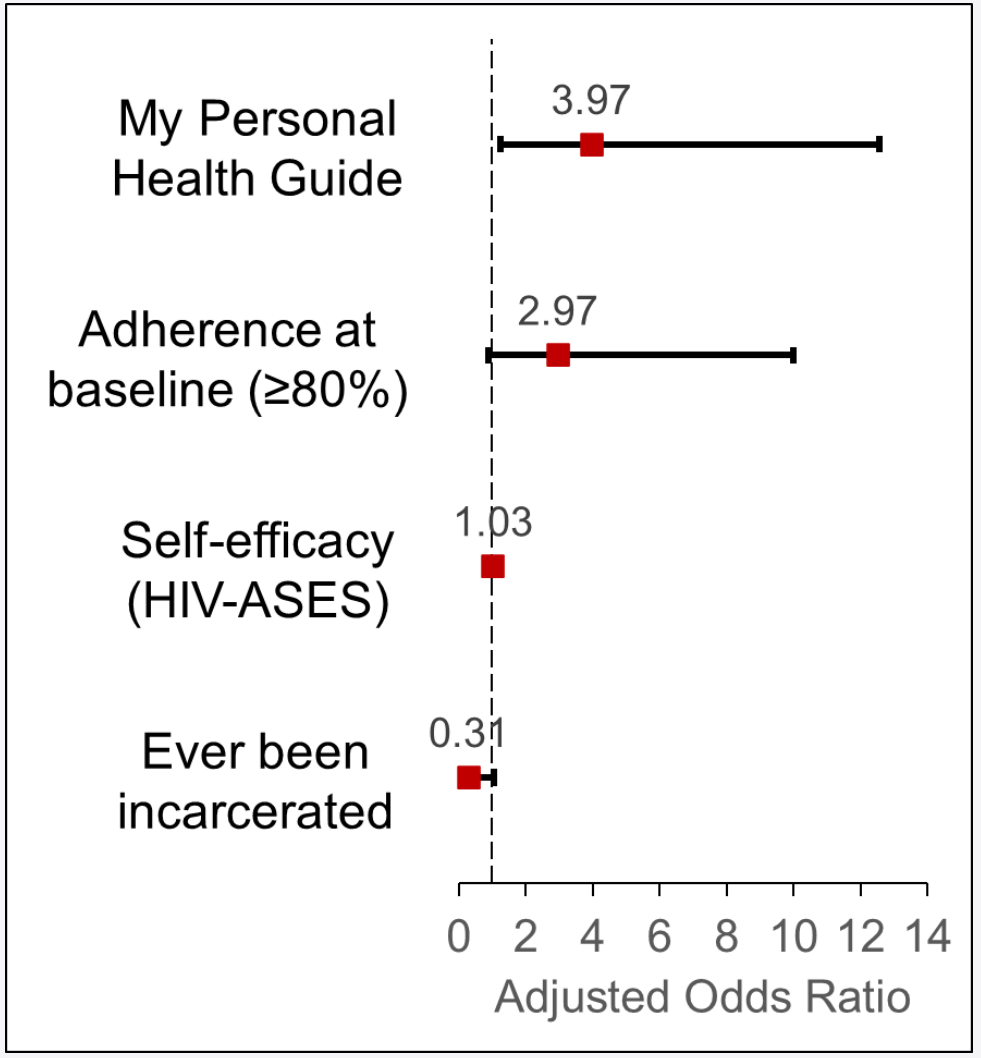


(Missing outcome data at Month 1: My Personal Health Guide 38.7%, Control 57.4%)

Avatar App Study

Figure 2. Multivariable logistic regression modeling the effect of the My Personal Health Guide app on having ≥80% self-reported adherence at Month 1 (N=131)

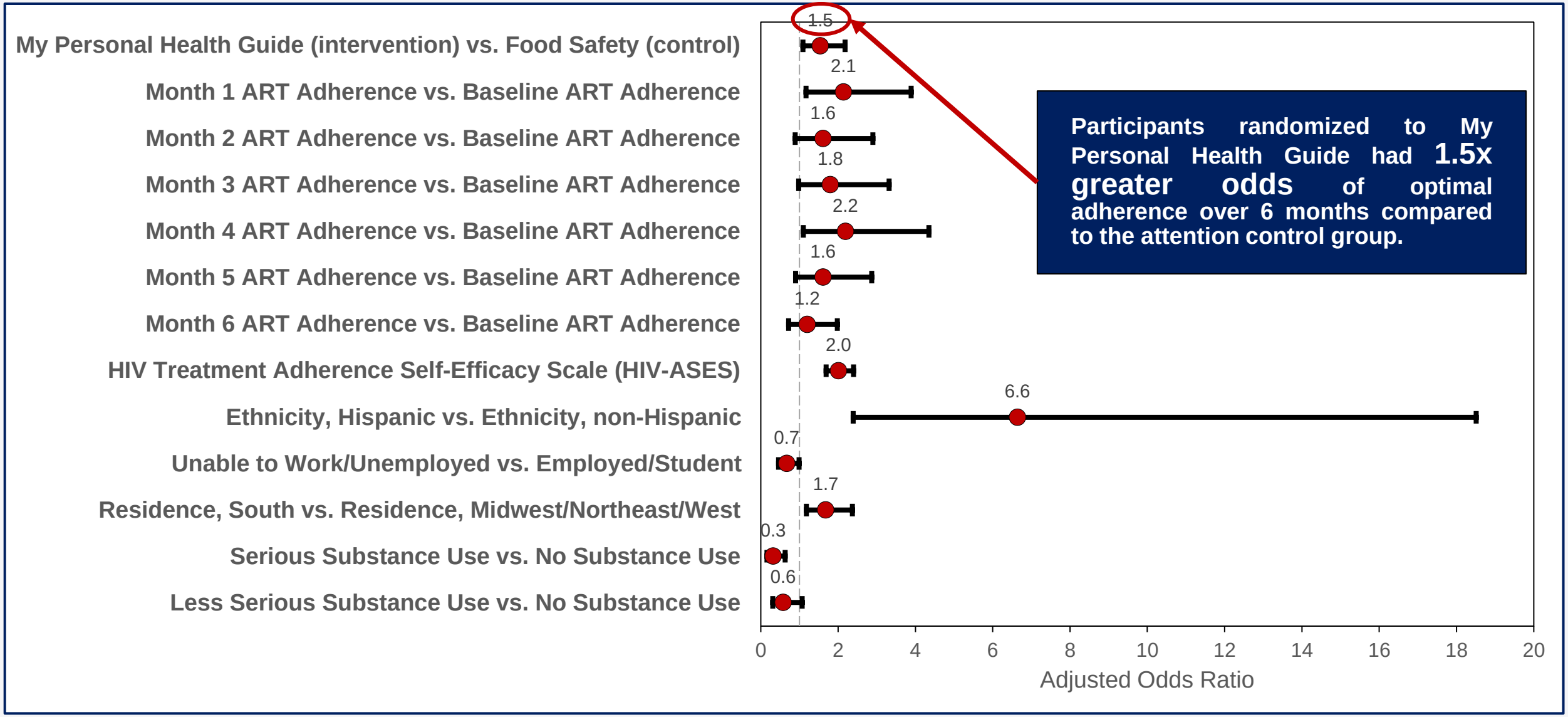
Participants randomized to My Personal Health Guide had nearly 4x greater odds of optimal adherence at 1-month post-randomization compared to the attention control group.



Avatar App Study

Figure 3. 6-Month Follow-up Analysis

GEE model for the association between My Personal Health Guide and ≥80% ART adherence over time among young AAMSM living with HIV (N=253), 2020-2024



Avatar App Study

Discussion

Efficacy

- This RCT is the first to demonstrate efficacy of a relational agent approach to improving ART adherence
- It provides evidence that this line of research is worth investing in further – refining the app to enhance efficacy and try in other populations

Study Limitations

- Self-reported ART adherence can overestimate individual medication taking behavior
- App use was voluntary, resulting in high variability in app usage throughout follow-up

Study Strengths

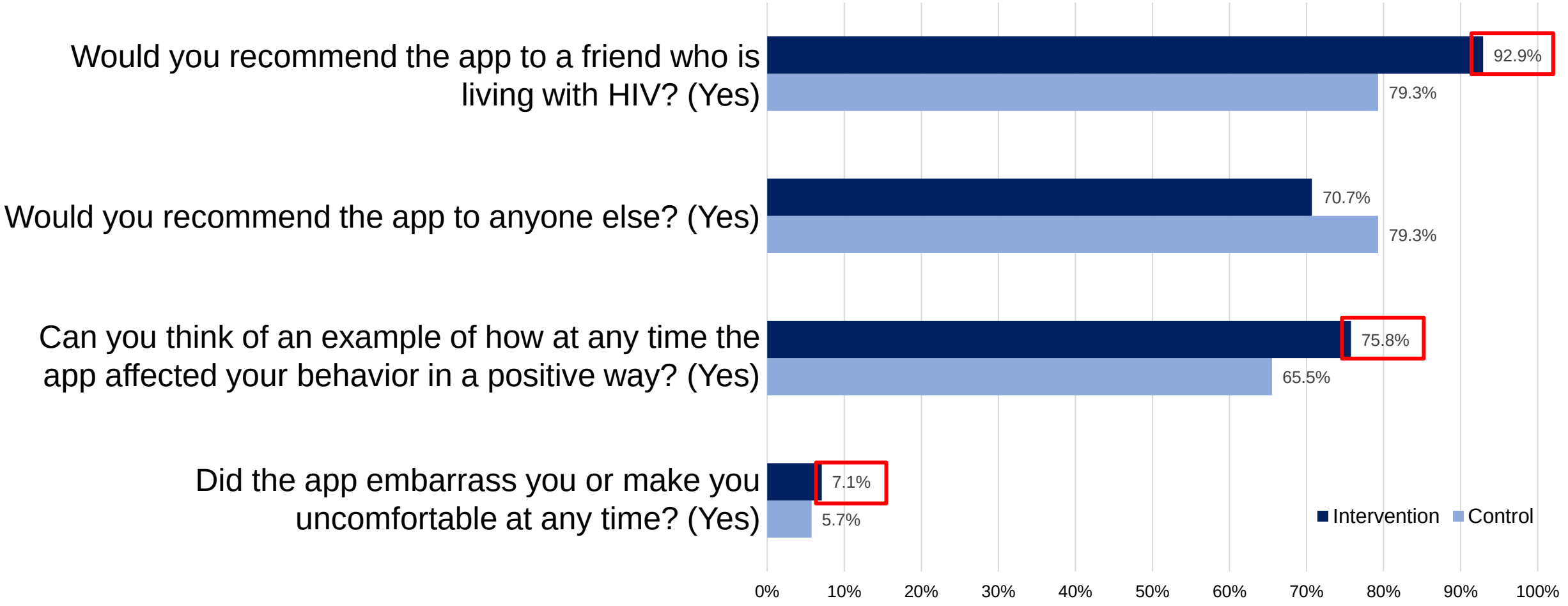
- The RCT has a diverse sample including a many experiencing housing insecurity, moderate/severe depression, and variability in health literacy and education
- There were many YBMSM living in the South (>50%)

Secondary Analysis

- Acceptability of the My Personal Health Guide app and usefulness of app functions

Avatar App Study

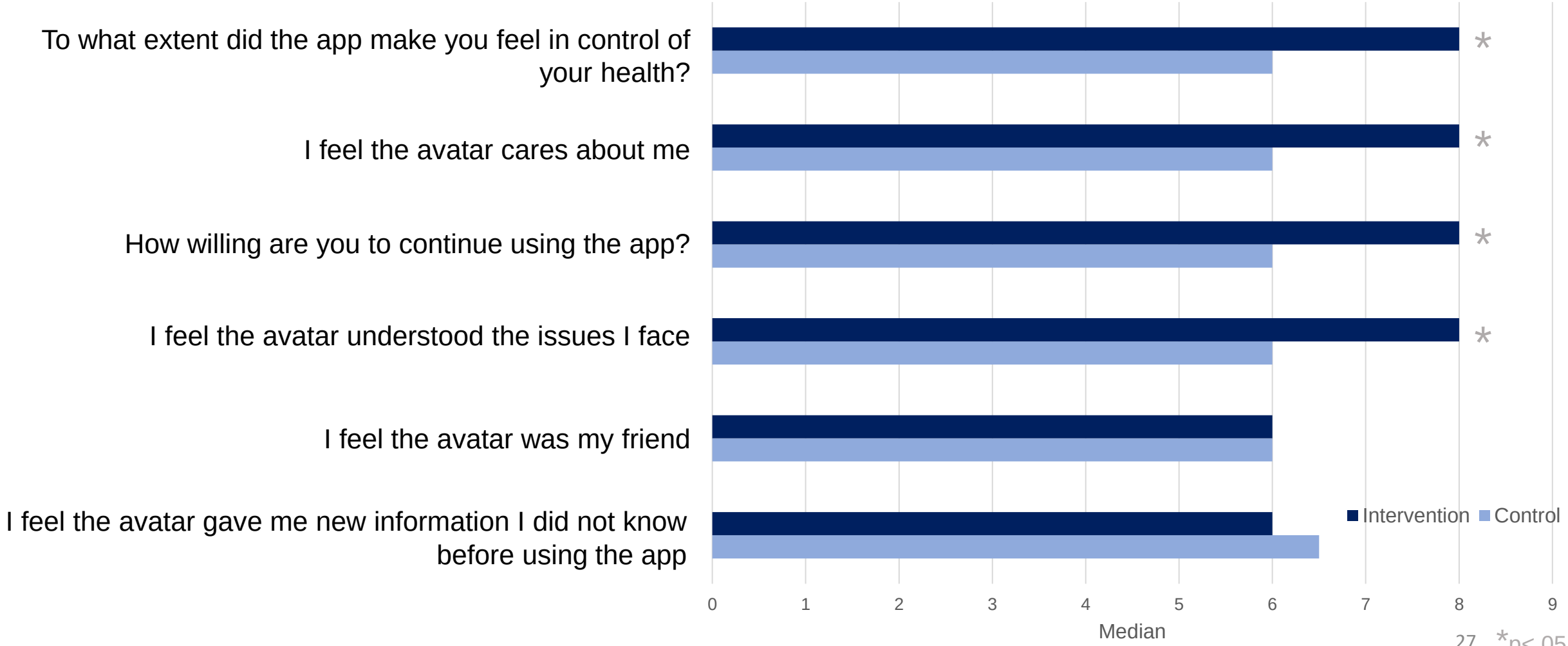
App acceptability by app randomization: Both apps had high acceptability!



Avatar App Study

Acceptability of relational aspects by app randomization

(1 = “not at all”, 10 = “very much”) Median scores

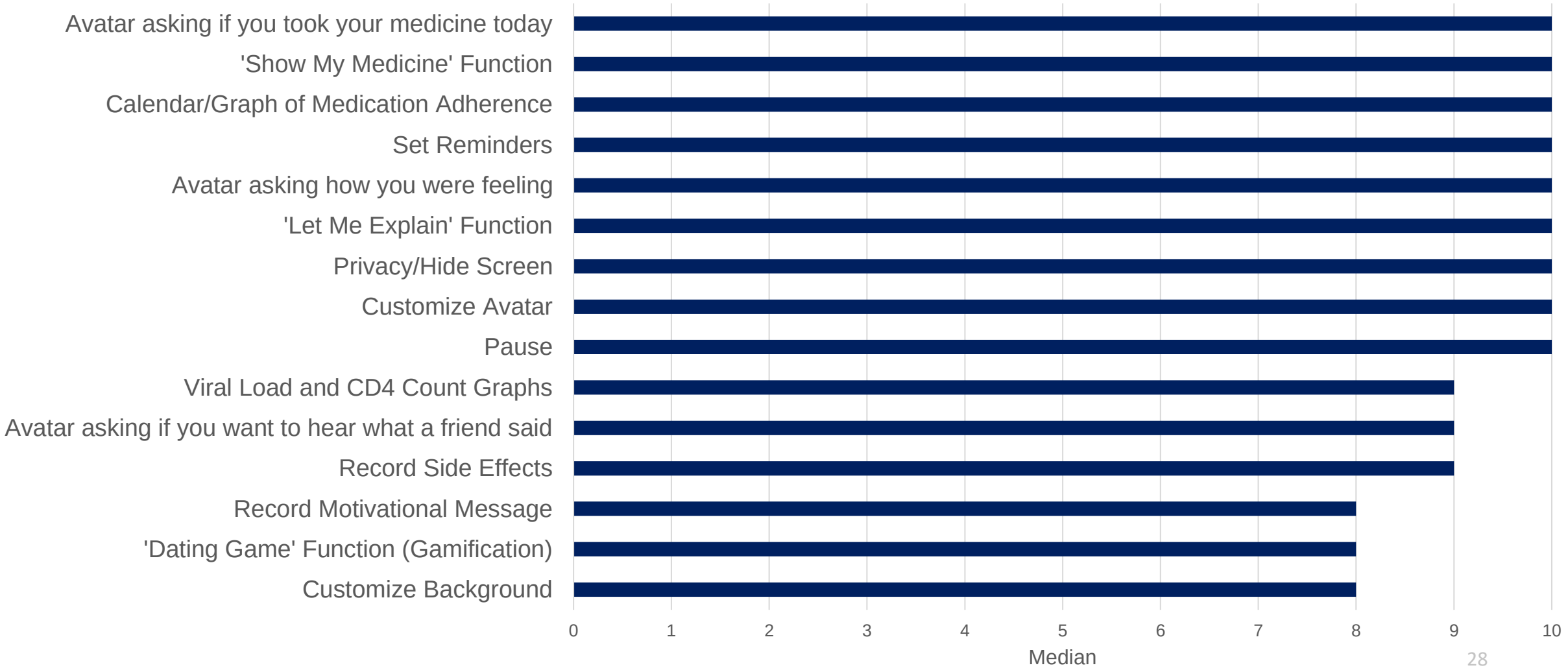


*p<.05

Avatar App Study

Usefulness of My Personal Health Guide functions

(1 = “not useful”, 10 = “very useful”)



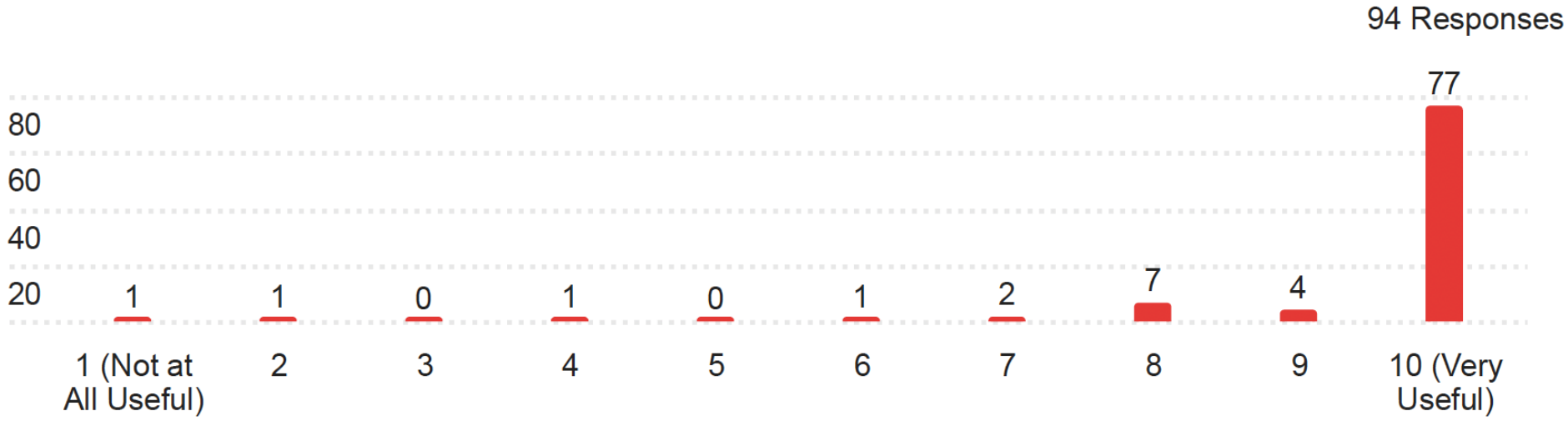
Translation to a Global Health Setting—India

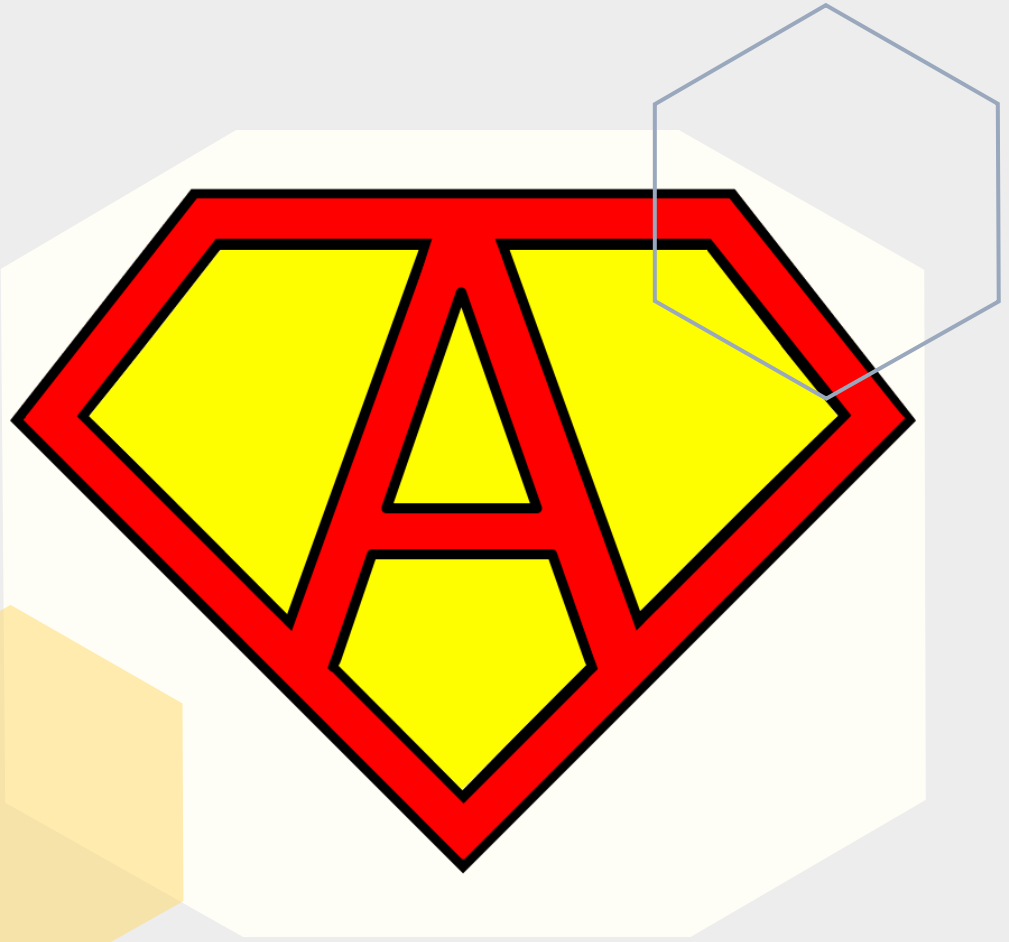
- My Personal Health Guide was translated into Telugu and adapted to the local population's needs and culture to create a demo app.
- Data collection has begun to assess feasibility and acceptability in Hyderabad MSM and women (especially female sex workers) living with HIV. 94 interviews completed to date. Goal = 400.

School of Public Health/
Division of Epidemiology and
Biostatistics/Avatar app

Preliminary data shows most participants in Hyderabad responded the app would be very useful

say: “Now I want to ask you about the entire mobile phone app. On a scale from 1 to 10 where 1 (point to 1) is not at all useful and 10 (point to 10) is very useful, please tell me how useful do you think this mobile phone app would be?





The A-TEAM Study

"Feasibility, acceptability, and pilot trial of a real-time electronic adherence monitoring intervention for antiretroviral therapy"

The Rationale for the A-TEAM Approach

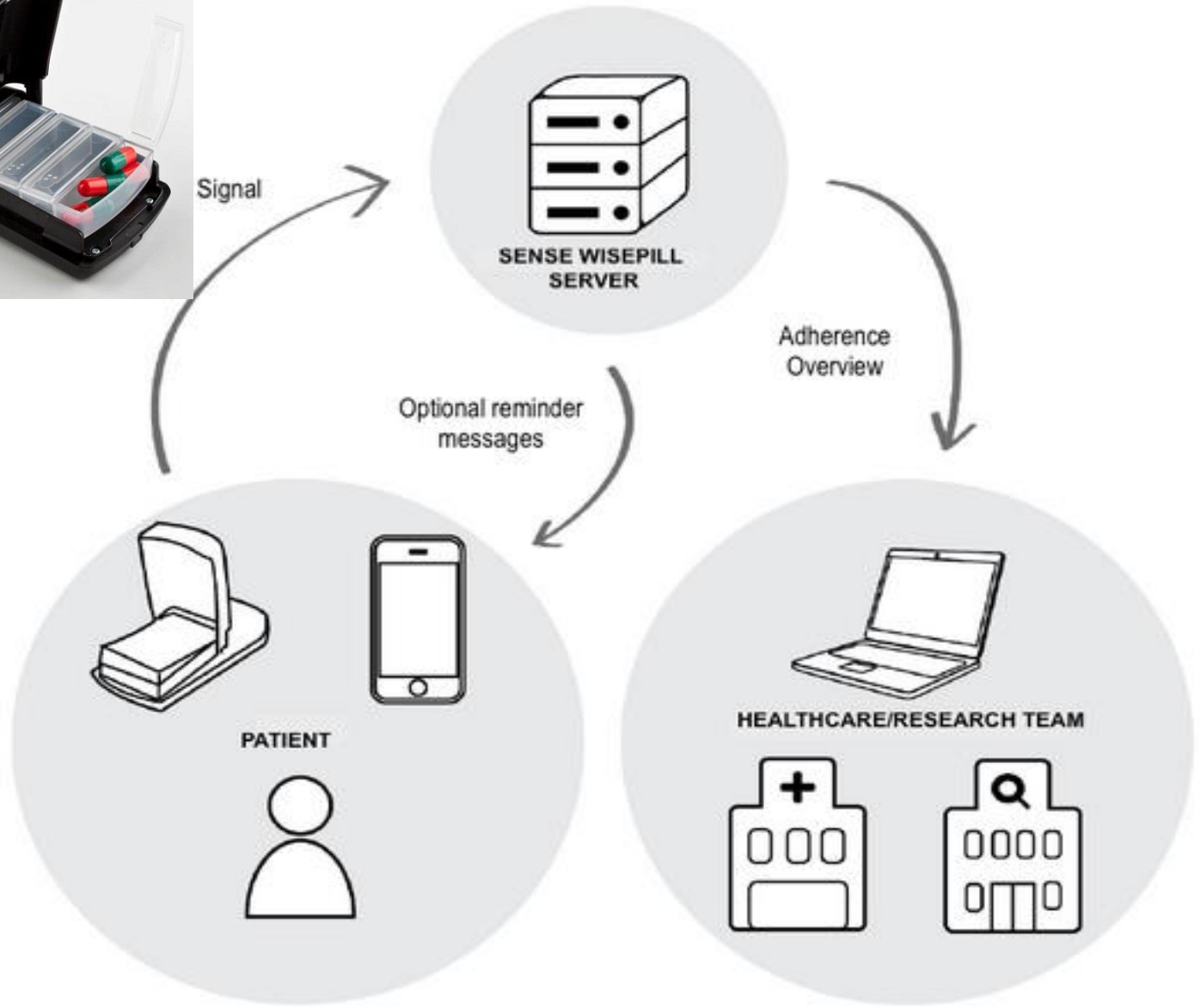
- Forgetting is one of the most common reasons for missing ART
- Some studies have demonstrated that interventions that include text messaging or reminder alerts may be effective at overcoming forgetting
- One of the facilitators of ART adherence is social support
- Social supporters may provide emotional support, informational support, and/or instrumental support (tangible services)

Real-time adherence detection has been employed as an ART adherence intervention

- Haberer et al, pilot RCT in rural Uganda of combination intervention that included social support for adherence lapses >48 hours, N=62
  - Adherence was 11% higher for the intervention compared to a control group
- Sabin et al, RCT in China of combination intervention that included personalized triggered real-time reminders when missed doses were detected, N=120
  - The intervention group was 2.4 times more likely than controls to achieve optimal (> 95%) adherence

Wisepill device

- Wisepill RT3000 Dispenser (some older RT2000)
- Uses mobile phone and Internet technologies for real-time medication management
- Dispenser sends an electronic medication event record to a central server



The Intervention Includes Reminders with Two Levels of Triaged Back Up Support

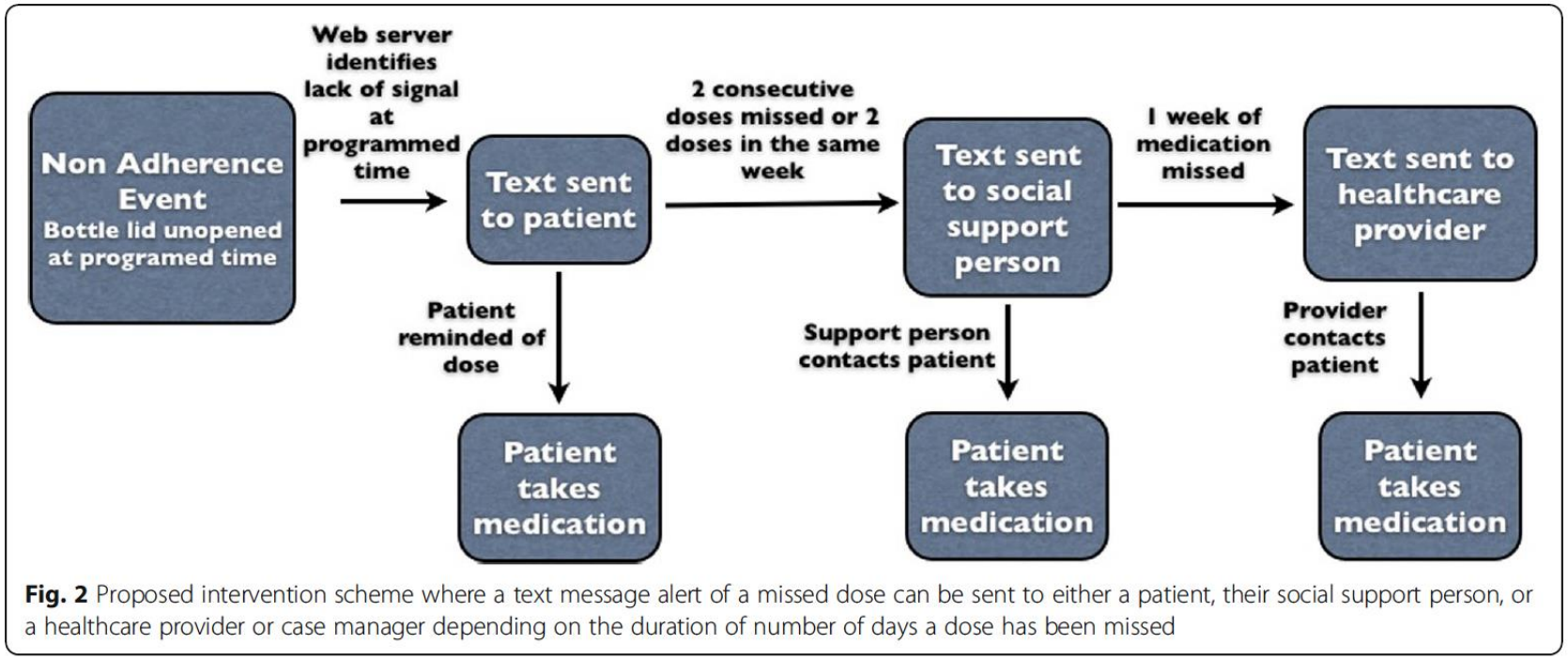


Fig. 2 Proposed intervention scheme where a text message alert of a missed dose can be sent to either a patient, their social support person, or a healthcare provider or case manager depending on the duration of number of days a dose has been missed

Formative Research in Chicago Among Young AAMSM Living with HIV

- Five focus groups and two individual interviews (N = 25) explored perceptions regarding the monitoring concept
  - Generally, the intervention was acceptable and useful
  - Concerns included possible disclosure of their status and possible friction with their social support
- Three months electronic monitoring of ART adherence (N=40)
  - Electronic monitoring was generally acceptable. 32 were interviewed after and 7 said the device attracted attention but no disclosure of HIV status occurred
- NIH R21NR017097

Current Work, NIH R34 MH132432

- We performed in-depth interviews in
  - 20 Black MSM living with HIV who have suboptimal adherence
  - 18 support persons and
  - 18 case managers to refine our proposed intervention approach
- Preliminary findings of the patients include
  - Accountability to a social support person was viewed as a potential motivator-making them work harder to avoid notifications of others
  - Participants saw the roles of the social support persons and the case manager as complementary in the intervention
  - "I think it's a great study because you have people supporting you. Some people may be depressed and not think life is worth living, so having someone reach out is a great idea."

Current Work, NIH R34 MH132432

- Preliminary findings of the social support persons include
  - Most liked that they would be better informed about the patient's adherence behavior but some were concerned if it would be considered intrusive or lead to tension
  - Many felt their advice would be effective because they had been supporting the person for years and their loved one had come to rely on them
  - There was variability about the effect on the relationship:

"I think it would make our relationship stronger."

"…the pill bottle is genius, but the calling people is concerning because *I* don't want to babysit you."

Current Work, NIH R34 MH132432

- Preliminary findings of the case managers include
  - Most liked that it would monitor adherence and open lines of communication to strengthen their relationship by showing care and concern
  - They noted that the success of intervention would depend on the strength of their pre-existing relationship
  - They expressed concern about a technological approach and long-term efficacy:

"If you've built that trust with your client, it will work out marvelously."

"There are issues with technology and keeping devices charged, especially for clients who are transient or have unstable living situations."

"What's to say they're going to keep this up after the study is over?"

A-TEAM Pilot Trial (soon to begin)

- We will be performing a 6-month pilot randomized controlled trial of the A-TEAM intervention among 54 BMSM living with HIV
- The primary objective of Phase 2 is to determine feasibility and acceptability of the A-TEAM approach. Preliminary efficacy on adherence and viral load suppression will be explored.

Thank You For Your Attention!

Avatar App Study

Acknowledgements

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- Sangyoon James Lee, PhD, Connecticut College
- Jeb Jones, PhD, Patrick Sullivan, DVM, PhD, E. Lisa Chung, MPH; Meaghan Woody, MPH, Emory University
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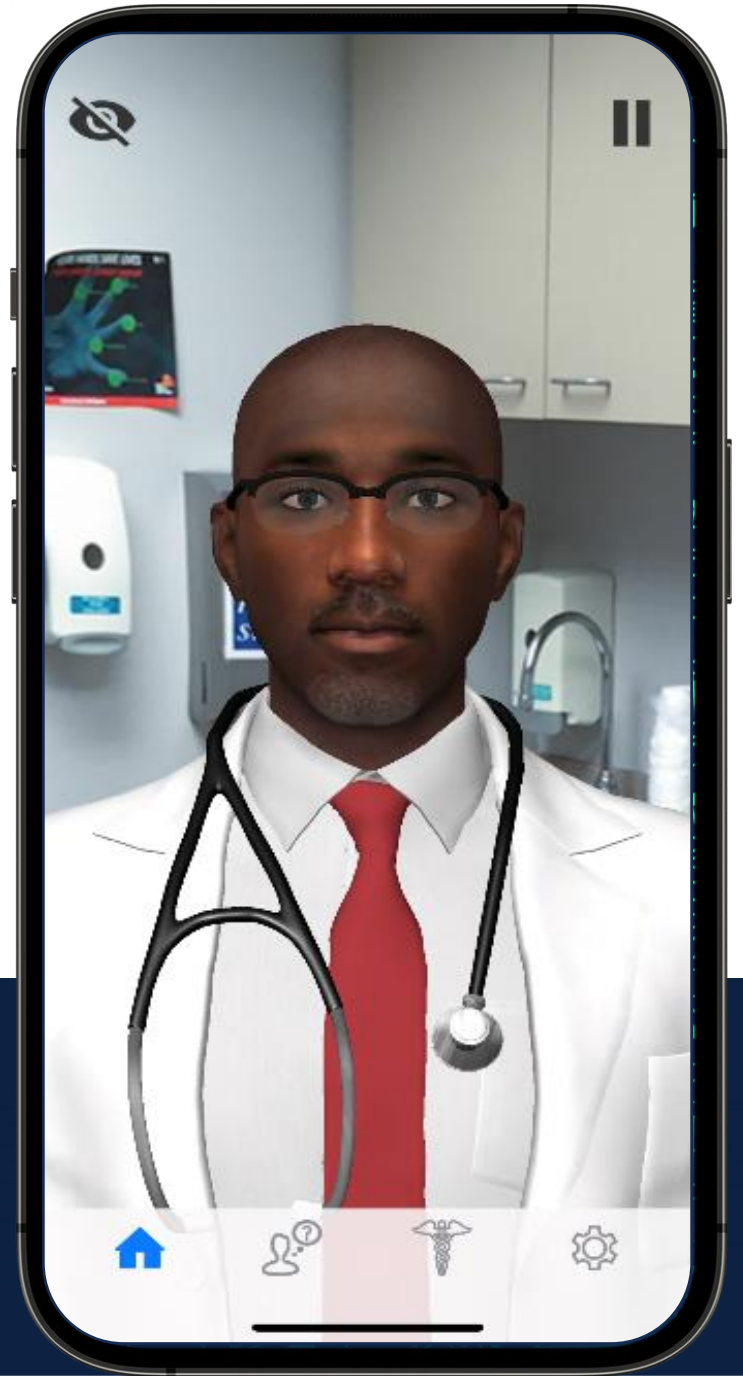

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