Major Article

# Methodologic considerations of household-level methicillin-resistant *Staphylococcus aureus* decolonization among persons living with HIV

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**Background:** People living with HIV (PLWH) have a higher prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization and likelihood of recurrent infection than the general population. Simultaneously treating MRSA-colonized household members may improve success with MRSA decolonization strategies. This article describes a pilot trial testing household-level MRSA decolonization and documents methodologic and pragmatic challenges of this approach.
**Methods:** We conducted a randomized controlled trial of individual versus individual-plus-household MRSA decolonization to reduce recurrent MRSA. PLWH with a history of MRSA who are patients of an urban HIV clinic received a standard MRSA decolonization regimen. MRSA colonization at 6 months was the primary outcome.
**Results:** One hundred sixty-six patients were referred for MRSA screening; 77 (46%) enrolled. Of those, 28 (36%) were colonized with MRSA and identified risk factors consistent with the published literature. Eighteen were randomized and 13 households completed the study.
**Conclusions:** This is the first study to report on a household-level MRSA decolonization among PLWH. Challenges included provider referral, HIV stigma, confidentiality concerns over enrolling households, and dynamic living situations. Although simultaneous household MRSA decolonization may reduce recolonization, recruitment and retention challenges specific to PLWH limit the ability to conduct household-level research. Efforts to minimize these barriers are needed to inform evidence-based practice.
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Methicillin resistant *Staphylococcus aureus* (MRSA) has emerged as a significant public health concern in community settings. MRSA can cause abscesses, boils, and systemic infections in persons colonized with the bacteria.[1] Community-associated MRSA disproportionately affects persons living with HIV (PLWH).[2] PLWH have a higher prevalence of MRSA colonization (8%-20% compared with 1.5%),[2-5] higher rates of MRSA-associated skin and soft tissue infections (SSTIs),[6-8] and an increased likelihood of recurrent infection than the general population.[9,10] Colonization with MRSA is associated with an increased risk of subsequent MRSA infection.[11,12]

Decolonization with a standard regimen is effective at preventing further infection in approximately 65% of patients[13-15]; however, the lasting effects of MRSA decolonization in the general population are minimal, with as many as 75% of patients treated showing evidence of recurrent MRSA colonization in long-term follow-up.[13]

Recurrence of MRSA colonization among individuals is associated with colonization of household members.[16] A whole-genome sequence comparison of 146 MRSA isolates in Chicago and Los Angeles found that households present an ongoing opportunity for transmission among people with SSTIs and family members may serve as a lasting reservoir of specific MRSA strains.[17] In the setting of HIV, preliminary studies found a shared MRSA strain type within 11.8% of couples served by an academic medical center HIV service.[18] Not only is concurrent colonization of household members associated with higher treatment failure rates,[19] but sexual partners may also play a role in transmission.[20,21] Skin-to-skin contact is a major source

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of transmission of community-associated MRSA.[22] A randomized trial evaluating MRSA decolonization in individuals found that a 1-week decolonization protocol had no effect on MRSA colonization after 6 months compared with a placebo.[15] Therefore, simultaneous treatment of MRSA-colonized household members and sexual partners may reduce long-term treatment failure.[17,20,23] Studies of the microbiome of cohabitating adults have demonstrated a shared microbial ecology.[24] As both a colonizing organism and one that survives for long periods of time on environmental surfaces, the household microbiome may clearly play a role in repeated colonization and/ or infection with MRSA.

Multiple studies in the past decade call for a household-level MRSA decolonization trial.[14,16,17,22,25-27] With increasing prevalence and burden of MRSA among PLWH, lasting decolonization in this population is all the more pressing.[28] This article describes the first pilot trial addressing the need for household-level MRSA decolonization and documents the methodologic and pragmatic challenges of this approach.

## MATERIAL AND METHODS

### Study design and sample

The Stop Community MRSA Colonization among Patients (SUSTAIN) study (ClinicalTrials.gov identifier: NCT02029872) was a prospective randomized controlled trial to test whether a MRSA decolonization intervention has greater influence if applied to all members of a patient's household and/or sexual partner network compared with the individual patient alone. This study was conducted within The Johns Hopkins University AIDS Service (JHUAS) Moore Clinic, a hospital-based outpatient practice that provides specialty care in Baltimore, Maryland. More than 50% of Moore Clinic patients reside in East Baltimore. At the time the study was conducted, the demographic characteristics of the patient population at this clinic paralleled the HIV epidemic in Maryland: 37% women; 81% African American; mean age of 39 years; and composed of the following self-reported HIV exposure categories: 33% heterosexual transmission, 18% men who have sex with men, 38% injection drug user, 4% both men who have sex with men and injection drug user, and 7% other/unknown. A previous study conducted in this setting found a MRSA colonization prevalence of 15.2% among 500 patients.[18]

Participants were recruited January 2014-March 2015, with follow-up visits completed during November 2015 and microbiologic outcomes completed during June 2016. Eligible index subjects were aged at least 21 years, receiving HIV care within the JHUAS Moore Clinic, had a history of MRSA colonization or SSTI, and had at least 1 household member or sexual partner willing to participate. Household members were defined as anyone physically living in the same home regardless of HIV status, age, or relationship. Sexual partner was defined as an individual in a self-defined sexual relationship for at least 6 months. Individuals were excluded if they had an allergy to any component of the decolonization protocol, were pregnant or breastfeeding, or were unable to provide written informed consent. Patients who were homeless or lived in group transitional and rehabilitative housing were also excluded due to inability to define the household members and challenges maintaining confidentiality.

Potential participants were recruited from the following sources: participants in a previous study by the principal investigator evaluating the prevalence of MRSA colonization who agreed to be contacted for future studies, flyers in the HIV outpatient clinic, targeted provider referral, and self-referral by interested patients. Recruitment of the household members and/or primary sexual partner occurred by referral from the enrolled index participant. If interested, household members were given the option to meet with the study team at their home or in the clinic to review the study

information and informed consent. Index participants were offered a $25 gift card at the completion of the MRSA decolonization regimen and also at the completion of the 6-month follow-up visit. Each household randomized to the intervention arm was offered a $50 gift card at the completion of the MRSA decolonization regimen and the 6-month follow-up visit. The SUSTAIN study was approved by The Johns Hopkins Medicine Institutional Review Board.

### Risk factor evaluation

A baseline 48-item questionnaire that was used by the principal investigator in prior studies to assess a participant's risk for acquisition of MRSA was administered at enrollment.[18,29,30] An abbreviated 39-item version of the questionnaire was completed at 3 months and 6 months after study enrollment. The interviewers were study team members who were trained in administration of the questionnaire and participated in pilot testing the instrument. Interviews were conducted face-to-face in a private setting. The clinic population is routinely screened for substance use, sexual history, and sexually transmitted infections at each clinic visit and study participants were informed about the confidentiality of their responses. The time frame for any sexual activity or drug use was the 12 months before the interview. Medical records were reviewed by the study team for HIV-related lab results, medications, and comorbidities. Information from medical records was used if discrepancies occurred with self-reported information.

Precautions, including a separate consent form and questionnaire for household members, were used to ensure no disclosure of HIV status among household members. Household members could select enrollment through a one-on-one session or as a household group. Once enrolled all questionnaires were completed in a private location of the participant's choosing, either in their home or at the clinic. For children younger than age 13 years, a parent completed the risk factor questionnaire with the child.

### Intervention

A total of 4 swabs for men and 5 for women were collected, plus an additional swab for anyone with a wound. Anterior nares, throat, perineum, rectal, and vaginal swabs were obtained using BactiSwab II (Becton, Dickinson and Company, Franklin Lakes, NJ) dual-headed culturettes and evaluated using standard culture methods. For children younger than age 18 years, only the nares, throat, and rectum were screened. All screening of children younger than age 13 years were conducted with a parent present. Household screenings were completed at the home if requested and swabs were collected privately in the bathroom. The intervention did not include environmental testing nor any study-recommended cleaning procedures for the household environment.

Participants who screened positive for MRSA in any site were randomized to either individual or individual-plus-household MRSA decolonization and followed for 6 months to determine whether there was a difference in treatment success between the individual and individual-plus-household arms. According to the Infectious Diseases Society of America clinical practice guideline,[23] the standardized decolonization regimen for the nose and groin included a 7-day course of nasal mupirocin calcium 2% ointment applied inside the nose twice daily, plus a 4% chlorhexidine gluconate soap used in the shower/bath every day for 7 days. For individuals colonized in the throat we added chlorhexidine gluconate oral rinse 0.12% used in a gargle and spit fashion twice daily for 7 days.[19,25] A standardized educational session on use, accompanying the Centers for Disease Control and Prevention frequently asked questions handout, and an instructional medication sheet were also provided. Participants were contacted daily during the treatment period to record data on self-reported treatment adherence and side effects. Upon completion of the decolonization regimen, individuals were
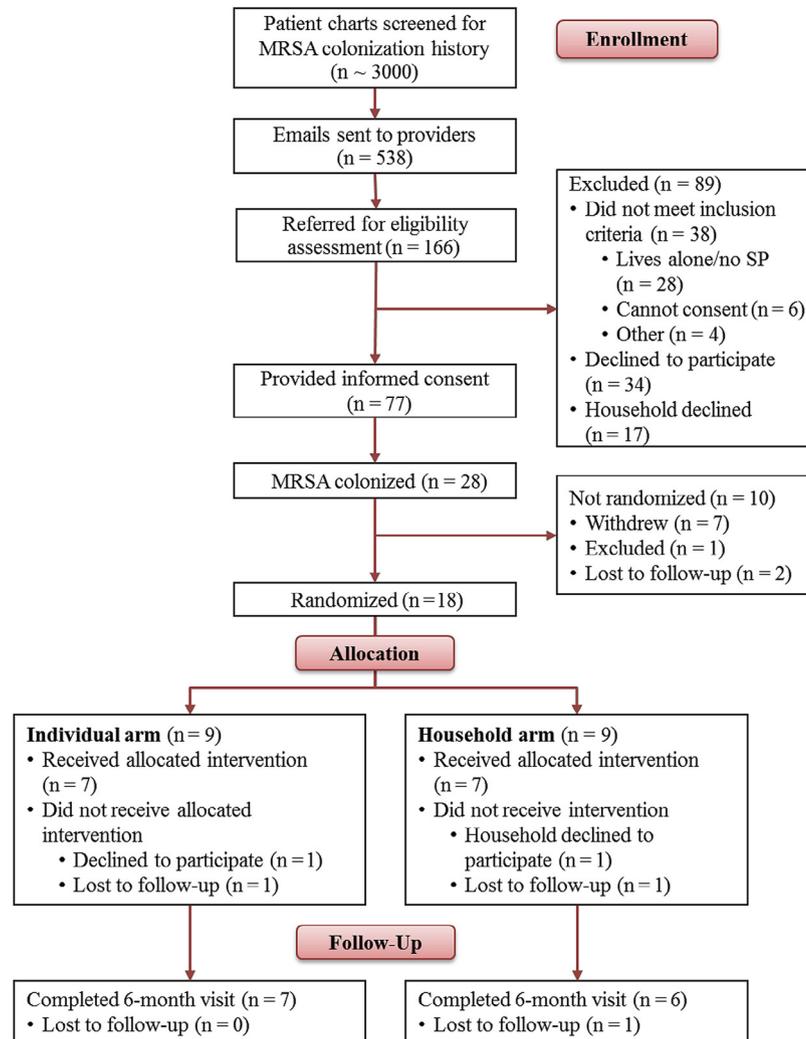
**Fig 1.** Consolidated standards of reporting trials diagram. *MRSA*, methicillin-resistant *Staphylococcus aureus*; *SP*, sexual partner.

rescreened for MRSA between 7 and 10 days and if positive, treatment was repeated until no MRSA was detected.

*Data analysis*

Differences between patients who were randomized and those who were not were tested with $\chi^2$ and *t* tests. Similarly, differences between those who did and did not screen positive for MRSA were tested. The sample size to test the primary outcome, difference between the 2 arms in proportion of index participants colonized with MRSA 6 months after enrollment, could not be statistically tested due to small sample size. The outcome results are presented descriptively.

**RESULTS**

A consolidated standards of reporting trials diagram (Fig 1) depicts study recruitment and retention. Approximately 3,000 electronic medical records were reviewed for eligibility. Five hundred thirty-eight clinic patients with a history of MRSA colonization were identified based on an infection control flag in the electronic medical record and individual e-mail messages were sent to providers in the JHUAS to request referral of their patients to the study. One-hundred sixty-six of these patients (31%) were referred to the study team, and of these 77 consented and were screened for MRSA

colonization. Among these participants, 28 were found to be colonized with MRSA and 18 met all inclusion criteria and were randomized for participation in the study.

Participants screened for MRSA were mostly black or African American (83.1%) with an average age of 50.7 years (Table 1). The highest education level was most commonly a high school diploma or high school equivalency diploma (40.3%) or no high school degree (39.0). Only 10.4% were working, whereas 76.6% received social security or disability benefits as a primary source of income. This was an HIV-experienced sample, with an average of 20.2 years since HIV diagnosis, and a mean CD4 T-cell count of 603. Nearly all (96.1%) were prescribed antiretroviral therapy and 79.2% of participants had an undetectable HIV viral load. Most participants had a household size of 2. Fourteen household members and/or sex partners enrolled in the study from 13 different households. There were no differences in baseline characteristics between those randomized and not randomized.

Compared with the 49 participants who were not colonized with MRSA at the time of the baseline visit, the 28 index participants with MRSA colonization were significantly more likely to have been hospitalized during the past 12 months (42.9% vs 20.4%; *P* = .036), have an abscess during the past 12 months (53.6% vs 30.6%; *P* = .047), and report using intravenous drugs during the past 12 months (17.9% vs 0%; *P* = .023) (Table 2).

**Table 1**
Baseline characteristics of participants

| | Total | | | P value (randomized compared with not randomized index participants) |
|---|---|---|---|---|
| | All index participants (n = 77) | Randomized index participants (n = 18) | Household/sex partner participants (n = 14) | |
| Age, y | 50.7 ± 10 | 51.1 ± 8.8 | 43.5 ± 13-69 | |
| Sex | | | | .27[‡] |
| Female | 38 (49.4) | 12 (66.7) | 8 (57.1) | |
| Male | 38 (49.4) | 6 (33.3) | 6 (42.9) | |
| Transgender | 1 (1.2) | 0 (0) | 0 (0) | |
| Race | | | | .27[‡] |
| Black | 64 (83.1) | 13 (72.2) | 14 (100) | |
| White | 9 (11.7) | 3 (16.7) | 0 (0) | |
| Other | 4 (5.2) | 2 (11.1) | 0 (0) | |
| Education level | | | | .10[‡] |
| No high school | 30 (39.0) | 5 (27.8) | 7 (50.0) | |
| High school/equivalent | 31 (40.3) | 6 (33.3) | 7 (50.0) | |
| Some college/vocational school | 14 (18.2) | 7 (38.9) | 0 (0) | |
| College graduate | 2 (2.6) | 0 (0) | 0 (0) | |
| Primary source of income | | | | .65[‡] |
| Social Security/disability | 59 (76.6) | 15 (83.3) | 6 (46.1)[*] | |
| Work full/part time | 8 (10.4) | 0 (0) | 2 (15.4)[*] | |
| Other | 10 (13.0) | 3 (16.7) | 5 (38.5)[*] | |
| Annual income | | | | .27[‡] |
| <$25,000 | 69 (89.6) | 16 (88.9) | 10 (83.3)[†] | |
| $25,001-$50,000 | 7 (9.1) | 1 (5.6) | 1 (8.3)[†] | |
| $50,001-$75,000 | 0 (0) | 0 (0) | 1 (8.3)[†] | |
| >$75,000 | 1 (1.3) | 1 (5.6) | 0 (0)[†] | |
| Years diagnosed with HIV (index participants only) | 20.2 ± 7.5 | 19.3 ± 8.5 | – | .52[§] |
| CD4 (index participants only) | 603 ± 389 | 682 ± 345 | – | .34[§] |
| HIV viral load, detectable (> 20) (index participants only) | 16 (20.8) | 4 (22.2) | – | .55[‡] |

NOTE. Values are presented as mean ± standard deviation or n (%).
[*]n = 13; 1 participant declined to answer.
[†]n = 12; 1 participant declined to answer and 1 was not asked (household income not included on child questionnaire).
[‡]Based on Fisher exact test.
[§]Based on *t* test.

Among the 18 randomized index participants, the throat was the most common site of colonization (55.6%). Participants were also found to be colonized in the nares (33.3%), perineum (27.8%), rectum (27.8%), and vagina (22.2%). One index participant had a skin infection with MRSA. Six of 14 (42.9%) enrolled household members were colonized with MRSA at baseline. Pulsed-field gel electrophoresis revealed a shared MRSA type between 33.3% of households that had more than 1 member colonized with MRSA at baseline. USA300 was the most common isolate identified, accounting for 56% (25 out of 45) of body sites at baseline.

Follow-up data at 6 months were collected on 13 participants and their households (7 individuals only and 6 individuals plus household); 5 were lost to follow-up. The number of participants with MRSA colonization at 3 months or 6 months was similar between the individual only (n = 2 at both time points) and the individual-plus-household (n = 2 at 3 months and n = 3 at 6 months) arms in this small sample. Among 5 participants recolonized at 6 months, only 2 (40%) were colonized with the same pulsed-field gel electrophoresis type as at baseline.

Multiple barriers to recruitment and retention were identified. Among those referred to the study, 17% lived alone and identified no active sexual partner. Acceptability of participating in a household-level study was low among both index participants and their household members (Table 3). More than 20% of index participants who spoke with the study team declined to participate, and 17 interested patients were excluded because their household members did not want to participate. Once determined eligible and MRSA-colonized, 10 out of 28 (35.7%) withdrew because they were no longer interested, no longer living with someone, or lost to follow-up. Among those who did remain in the study, demand for the intervention was high; the mean self-reported adherence rate was

87.7% and 100% achieved decolonization of all sites after completing the decolonization protocol.

## DISCUSSION

The SUSTAIN study screened medical records for patients with prior known MRSA colonization and found that 538 of the clinic's 3,000 patients had an infection control flag for MRSA. This overall MRSA prevalence of 17.9% is consistent with prior point prevalence studies in the East Baltimore population[18] and other HIV-infected samples.[31] This indicates that medical record screening could be a potential way to identify patients at high risk for current MRSA colonization and SSTIs. However, the challenges associated with strict privacy and institutional regulations limit the ability of researchers and clinicians to directly approach these known high-risk patients without a direct provider referral. As shown in Figure 1, in a busy infectious disease clinical practice, such requirements can significantly limit referral.

Among those screened, we found a high prevalence of MRSA (36.4%) using the criteria of previous known MRSA infection or colonization. However, despite being a high-risk group, not all were colonized. Given the institutional policy requiring 3 consecutive negative MRSA screenings to remove the infection control flag from a patient's record, this is not surprising. Risk factors for MRSA colonization among this population were consistent with the literature: low income,[18,31] recent hospitalization,[9,20] incarceration,[2,9,21] visiting a public gym,[8] current or recent skin abscess,[18] and illicit drug use.[8,18] Our sample had fairly well-controlled HIV; CD4 count and HIV viral load did not differ between participants who were and were not colonized with MRSA. Vieira et al[31] also found that HIV-related clinical factors are less important than social factors in

**Table 2**
Methicillin-resistant *Staphylococcus aureus* (MRSA) risk factors

| | Total | | |
|---|---|---|---|
| | MRSA+ participants (n = 28) | MRSA– participants (n = 49) | P value |
| Education level | | | .29[‡] |
| No high school | 10 (35.7) | 20 (40.8) | |
| High school/equivalent | 9 (32.1) | 22 (44.9) | |
| Some college/vocational school | 8 (28.6) | 6 (12.2) | |
| College graduate | 1 (3.6) | 1 (2.0) | |
| Primary source of income | | | .26[‡] |
| Social Security/disability | 25 (89.3) | 34 (69.4) | |
| Work full/part-time | 0 (0) | 8 (16.3) | |
| Other | 3 (10.7) | 7 (14.3) | |
| Arrested/incarcerated, past 12 mo | 3 (7.1) | 2 (4) | .46[‡] |
| CD4 | 626.89 ± 372.26 | 590.7 ± 401.5 | .70[§] |
| HIV viral load, detectable (> 20) | 7 (25.0) | 9 (18.4) | .49[¶] |
| Hospitalized, past 12 mo | 12 (42.9) | 10 (20.4) | **.036**[¶] |
| Prescribed antibiotics, past 12 mo | 13 (46.4) | 20 (40.8) | .63[¶] |
| Routinely visited a gym, past 12 mo | 5 (17.9) | 4 (8.2) | .27[‡] |
| Abscess | | | |
| Baseline | 10 (35.7) | 9 (18.4) | .09[¶] |
| Past 12 mo | 15 (53.6) | 15 (30.6) | **.047**[¶] |
| Sexually active, past 12 mo | 15 (53.6) | 35 (71.4) | .11[¶] |
| Condom use, self-report | | | .53[‡] |
| Never | 4 (26.7%)[*] | 7 (20.0)[†] | |
| 25% of the time | 0 (0)[*] | 5 (14.3)[†] | |
| 50% of the time | 3 (20)[*] | 5 (14.3)[†] | |
| 100% of the time | 8 (53.3)[*] | 18 (51.4)[†] | |
| Number of sex partners, past year | 1.93 ± 2.46[*] | 1.37 ± 0.84[†] | .23[§] |
| In a monogamous relationship | 14 (93.3)[*] | 25 (71.4)[†] | .14[‡] |
| Substance use, past 12 mo | 6 (21.4) | 7 (14.3) | .42[¶] |
| Injection drug use | 5 (17.9) | 0 (0) | **.023**[¶] |
| Total household size | 3.79 ± 5.24 | 2.96 ± 1.77 | .32[§] |

NOTE. Values are presented as n (%) or mean ± standard deviation. Bold values are statistically significant (*P* < .05).
[*]n = 15 (subset of MRSA+ participants who reported sexual activity during the past 12 months).
[†]n = 35 (subset of MRSA– participants who reported sexual activity during the past 12 months).
[‡]Based on Fisher exact test.
[§]Based on *t* test.
[¶]Based on $\chi^2$ test.

**Table 3**
Feasibility of household-level methicillin-resistant *Staphylococcus aureus* (MRSA) decolonization

| | |
|---|---|
| Acceptability | • 20% of eligible patients were not interested<br>• 18% of eligible households declined to participate when contacted by the index participant<br>• 35.7% of confirmed MRSA+ participants withdrew after the initial screening once their randomization status was known |
| Demand | Among those who initiated decolonization regimen:<br>• 87.7% adherence to treatment<br>• 100% were decolonized |
| Implementation | • 6-mo follow-up data collected on 13 participants<br>• No difference in MRSA colonization at 6 mo between individual and individual-plus-household arms |

predicting MRSA colonization among PLWH. Despite theoretical evidence to support household-level MRSA decolonization, we found no differences in MRSA colonization at 6 months between the individual-only and individual-plus-household in this small sample. Colonization of the home environment may explain some of the persistent MRSA exposure among study participants; future interventions should also include environmental decolonization, including household pets.[32,33] A recent analysis of household contamination among persons known to have MRSA found that transmission was more likely to occur if a person required direct care assistance or if family members shared towels. The authors evaluated MRSA colonization among common environmental surfaces and found environmental contamination in 79% of these households,[34] clearly demonstrating the importance of environmental decontamination in household-level interventions.

*Limitations*

*Recruitment and retention*

The SUSTAIN study proposed enrolling 100 PLWH and their household members to test household-level MRSA decolonization, but recruited only 77 participants in 15 months. This led to 18 eligible randomized index participants and 14 household members completing the study protocol. Several barriers to recruitment of participants and their household members were identified, including narrow eligibility criteria, poor provider referral rate, low participant interest and acceptability, HIV stigma and confidentiality, and dynamic household situations. These challenges represent the complexities of recruiting PLWH and their households into clinical trials.

The demographic characteristics of the target population limited the number of eligible participants for a household-level intervention. The JHUAS provides HIV care to patients with low socioeconomic status and complex psychosocial circumstances. One-fifth of patients who spoke with the study team were not eligible because they lived alone with no regular sexual partner. Many potential participants were not eligible because they were homeless or lived in transitional, rehabilitation, or group housing. Although these are obviously settings that increase risk of community-level MRSA transmission and colonization, the study was not designed to enroll large communal settings and to offer decolonization and follow-up for such sites.

Existing literature on recruitment and retention of participants in clinical trials suggests that effective recruitment involves eliminating participant-related barriers related to time and place of study visits.[35,36] Retention in clinical trials is also associated with flexible appointments and compensation for transportation, parking, and childcare.[37,38] Based on this information, the SUSTAIN study provided home visits to maximize recruitment and retention of household participants. In our study population, home visits minimized participant burden and allowed several households to participate in the study that otherwise would not have been able to do so. For PLWH, home visits may also allow for improved confidentiality and should be considered in studies involving household members or partners. Nevertheless, it is important to disclose the unintended consequences of home visits to participants, including mandatory reporting of child and dependent elder abuse or neglect. Further, we experienced substantial challenges from eligible participants who opted not to participate over concerns related to disclosure of their status to household members. It was anticipated that offering to screen family members in either the home or the research clinic would result in greater participation, but the fear of disclosure of HIV diagnosis seemed to be more concerning to some eligible participants than the location of the study visit.

Relationships between families and sexual partners change. We encountered this unpredictable household-level circumstance that affected recruitment or retention with nearly every enrolled participant. The instability of housing and/or influence of incarceration, relocation, and/or transition of household members in and out of the household was common. This suggests that household-level decolonization of MRSA may be challenging in the real world and limited at best to households with some level of stability. In future household-level research, study teams must anticipate the real-world complexities of family and partner relationships. Establishing communication with all household members rather than the index

participant alone helped this study maintain follow-up with participants regardless of changes within the household.

*Way forward*

Our study provides practical methodologic and study design considerations for future household-level interventions. As patients with antimicrobial-resistant organisms continue to be discharged to the community, households become an increasingly important opportunity for intervention. Based on the findings identified in this study, the authors recommend that future household-level intervention studies include considerations of recruitment methods that optimize household participation. Clearly in this protocol, the potential for HIV disclosure was an important consideration for index subjects, yet concerns over other diseases or conditions, including antimicrobial-resistant infections is also possible. Investigators must give careful consideration to processes that limit disclosure of personal health information either directly or inadvertently within a household. Our protocol team worked closely with our investigational review board to enhance human subject protections as described in the methods section related to separation of consent and questionnaires to avoid such disclosures.

Practically, household-level interventions also carry some degree of personal risk to the study personnel visiting households. All home visits required 2 study personnel. We used app-based car services (eg, Uber or Lyft) to offer transportation to and from the site to facilitate tracking and accountability along with reducing risk associated with use of personal vehicles. Upon arrival and departure, the safety protocol required personnel to send a text message to the study coordinator. All participants were informed as part of the informed consent process of mandatory reporting laws for child and elder abuse as well as domestic violence. Chaperoned procedures for screening were described above. Finally, all household members were offered to have all procedures conducted in a clinic setting, should they not wish to have a team visit their home.

## CONCLUSIONS

This is the first study to report the barriers to recruitment of PLWH and their households. In household-level intervention studies, recruitment challenges should be anticipated and addressed in the design of protocols and sample size calculation. Flexibility is critical to accommodating multiple members of a household. Efforts to maintain confidentiality around HIV status with households must be emphasized to maximize recruitment of this population.

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