

## Final Progress Report

### HIV/HCV Support Team to Improve Medication Safety and Engagement in Care

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Organization: Johns Hopkins University School of Medicine

Project Period: 09/30/2015 – 08/31/2021

Federal Project Officer: Eileen Hogan, MPA

This project was whether

a hospital-based nurse and pharmacist Kuman LmmunodeficiencyYrus/  
Kepatitis C iMus (HIV/HCV) Vupporteam (HST) could reduce inpatient medication errors and improv H  
engagement in outpatient HIV care for persons living with HIV (PLWH).

Scope: Adults hospitalized at Whe Johns Hopkins Hospital, 2017-2019.

, only three involved incomplete HIV  
regimen errors historically a common and highly consequential error type. Among 109 PLWH not virally  
suppressed on admission, 24 of 57 (42%) control and 23 of 52 (44%) intervention hospitalizations were followed  
by viral suppression within 6 months ( $p=0.49$ ).

Our results reflect a national shift to simpler, safer HIV regimens

discontinued plans for an online HST toolkit and  
for a cost-effectiveness analysis.

However, the study's electronic medical record (EMR) alert for PLWH was 100% sensitive (82%-100%) with a  
PPV of 83% (81%-85%). The EMR alert that facilitated our interventional study is novel and was successful, and  
we have submitted results of an analysis of its accuracy as well as a description of lessons learned in the process  
of creating it. The project team has also implemented and started to evaluate a similar alert for HCV.p64pr 3 T>BD20.25



Many ART agents interact with other drugs. The most important example is the pharmacologic booster ritonavir, which was part of >50% of regimens during hospitalizations during 2000-2010 (Ann Pharmacother 2008). Ritonavir inhibits cytochrome p450 and other hepatic pathways and consequently has complex and often dangerous interactions with glucocorticoids, opioids, calcium channel blockers, statins, antiarrhythmics, and other agents.

Incomplete regimen errors are common and have dangerous consequences. Unique to HIV. Incomplete regimens may occur in over half of instances (Clin Infect Dis 2012). PLWH often cannot name their ART medications and doses (JAIDS 2001). Low health literacy and polypharmacy are compounding problems for many PLWH (AIDS Care).

## Engagement in Outpatient HIV Care

As of 2011, the large proportion (two thirds) of US PLWH who were not using ART represented a health system crisis given ART's transformative potential and low risk. ART cannot be prescribed and safely monitored without regular engagement (follow-up) in outpatient HIV care. Helping PLWH "link" to care (make a first HIV provider visit) and then remain engaged are major obstacles to increasing ART use. The continuum of HIV care (Figure 1) from initial infection to suppression with ART has

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LQFUHPHQW may be devoted as required. A hospital with <250 hospitalizations of PLWH may use a small  
increment e.g. 25% . RN-level inpatient nurses are available in every acute care hospital in the US. Clinical  
pharmacists who could be trained in HIV and HCV medications are also commonly available. There are limited  
data on the cost and cost-effectiveness of linkage and re engagement strategies. New patient222

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'LVHVVHV FRQVXOWDWHYHDPWHKage  
Pertains only to PLWH who have never had an outpatient HIV appointment and  
is defined as keeping an HIV outpatient appointment within 30 days of discharge. Re engagement pertains only to  
previously linked-to-care PLWH who have not kept an outpatient HIV appointment within a year prior to admission  
and is defined as keeping an HIV outpatient appointment (previous or new provider) within 30 days.

All hospitalized PLWH were briefly evaluated by the HST nurse. Per current hospitalization rates, the  
expectation was that there would be an average of 2.5 new patients per workday including weekend admissions  
being met on Monday. All PLWH on ART received medication reviews throughout their hospitalization. All unlinked-  
to-care PLWH (including new hospital diagnoses) and all PLWH out of care for over a year would receive linkage/  
re engagement activities7Tc 0.122E4iu as ko5w (498 Tf 0 Tc 0 Tw <000ever)Tj -0.06oCV;w ( e)Tj -0. 0 Tw 5644j -0.019

Table 3. Linkage/Re engagement Activities

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Patient Learning

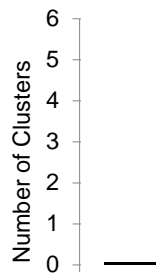
Active Learning: Teach Back Method

Family/Caregivers: encourage participation; respect WKS/DW patients keep HIV confidential

Starting Point: assess baseline HIV knowledge, assess fears (e.g. conspiracies, Rx side effects)

Facilitators and Barriers:

## Study Setting, Design, and Duration





## Analytic Plan

Hypothesis 1A: The HST will reduce HIV and HCV medication errors by at least 75%.

The primary analysis compared the proportion of hospitalizations with any HIV medication error present on the second day of HST availability. Weekends and holidays are unavailable days.

Table 5. Power Calculations ( . IRU DOO FDOFXODWL Rosters Pp Wd GRQH ZLWK WKI

(www The curriculum included didactic modules, similar to the R Used for central line infections

E H X V H G L Q V W H D G for the project [Am J Epidemiol 2003]). Additional clinical data derived from the published literature; see Table 6.

Model outcomes:

As indicated in Table 6, the project team projected key outcomes, including clinical events and costs. We first simulated short-term, 6 month outcomes including ART toxicity, resistance, and viral rebound validating the model by ensuring that results match observed trial data. Next, we projected long-term outcomes.

The costs associated with the clinical events, in particular transmission to partners, may partially or fully offset the cost of the HST program, making it an excellent value from the healthcare system perspective.

Table 6. Selected Data Parameters and Outcomes for CEPAC Model-based Analysis of HST Program

Data from the HST study		
Parameter	Short-term outcomes	Long-term outcomes
Medication error	ART toxicity	Switch to next line of ART (more costly, greater pill burden, risk of reduced ART adherence), “exhaust” one available ART regimen Morbidity, mortality, costs related to toxicity
	ART resistance	Switch to next line of ART, next line may be less efficacious, more costly
	Increase in HIV RNA	Increase transmission to partners, CD4 decline, morbidity, mortality, costs
No linkage to care	HIV disease progression	HIV transmission to partners due to unsuppressed HIV RNA
No re engagement	HIV disease progression	HIV transmission to partners due to unsuppressed HIV RNA
Additional key parameters from published literature		
Viral suppression rates for six successive lines of HIV regimens; CD4 gain on ART; CD4 decline off ART		
Opportunistic infection and mortality rates (by CD4 and ART use)		
HIV transmission to partners (a function of HIV RNA level)		
HIV care costs (inpatient care, outpatient care, medications, laboratory studies)		
Hospital-level factors: HIV prevalence among inpatients, training costs and salaries for HST personnel		

Key sensitivity analyses:

The project team conducted univariate and multivariate sensitivity analyses on model parameters to identify the factors with the greatest influence on the clinical and economic value of the HST program. We described thresholds of effectiveness and cost needed to render the HST program cost-effective. We also conducted probabilistic sensitivity analyses, conducting very large numbers of simulations in which we vary multiple parameters through specified distributions simultaneously to determine the proportion of clinical and cost scenarios in which the HST program remains cost-effective.

Potential Limitations Considered at Study Conception

Hiring a motivated HST nurse with inpatient experience would be important. Based on inpatient nurse salaries, adequate money has been budgeted to provide a competitive offer to an early /mid-career nurse. Alternative strategies include higher salary and flexibility with schedule. If a less-experienced nurse is hired, the amount of time shadowing on the HIV/AIDS unit could be increased.

Some physicians may see patients in hospital units with different control and intervention status H.VThe direction of effect of contamination would be difficult to anticipate. For example, having had a patient receive HST medication review, a provider may become more knowledgeable about the meds and more thorough in his/her own review. Alternatively, he or she may shrug off the work expecting the HST to fill in. The study is adequately powered to withstand some contamination.

However, the degree of any contamination effect may be small as most providers would only occasionally admit PLWH or persons on HCV Rx ( R Q H R U a W - 7 6 th period). Nurses and case managers have highly unit-based roles, so little or no contamination in this setting was expected. Contamination in ascertaining outcomes may happen when patients are transferred within the hospital (e.g. from medicine to surgery). The HST was expected to see patients transferred in and to continue seeing patients who were t

OHDVW RQFH ZLWKLQ following discharge as the new primary outcome, to be assessed for patients whose baseline HIV RNA OHYHOV ZHURSLHV P/

The rationale for this change was that VLQTH original planning in 2014, two paradigms in HIV management have changed. First, it has become clear that essentially all PLWH should receive antiretrovirals as soon as reasonably possible after their HIV diagnosis with a goal of achieving and maintaining perpetual HIV viral suppression. Second, once viral suppression has been achieved and maintained for 6 W12 months, HIV provider visits can be scheduled yearly or even less frequently as long as laboratory studies confirm ongoing viral suppression, appropriate immune response, and no signs of toxicity. Additionally, from a practical standpoint, hospitalized PLWH often do not remember or may not disclose their most recent HIV provider visit date to a study coordinator. In contrast, HIV viral load results are available broadly across several health systems that utilize the same electronic health record software.

The first meaningful finding from the overall study is that we only captured a total of 992 hospitalizations of PLWH. In 2014, based on best-available data, we had hypothesized a total of 1,400 PLWH hospitalizations on study services in a 2-year period. We believe the decrease was due to at least two factors.

First, hospitalizations among PLWH have been swiftly declining. These declines have been tracked in several studies including a study co-authored by the PI using a large North American HIV consortium (J Infect Dis 2020) and are also evident in looking at administrative data from the Johns Hopkins Hospital. Improvements in HIV viral suppression and consequent immune recovery are the driving reasons for declining hospitalizations.

The second reason this study's total sample was lower than hypothesized was a failure to capture most hospitalizations on inpatient psychiatry services. Around the start of the intervention, these services changed their status within the electronic medical record, and our electronic alert system therefore did not scan these services when trying to identify hospitalized P/WH. Because a handful of



The second, "Mentor Approach for Promoting Patient Self-Care " randomized 400 inpatients who were not engaged in outpatient care to control educational sessions about safer sex and needle sharing vs. mentoring by volunteer peers with both inpatient visits and post-discharge follow-up phone calls. Thirty-nine percent of control patients compared 40% of intervention patients (relative risk 1.15 95% confidence interval 0.94 1.40) (Clin Infect Dis 2016) Taken together these three studies indicate that intensive, HIV-specific case management starting from the inpatient setting may not be a fruitful area for additional investment by hospitals and HIV providers.

The decrease we noted in the proportion of PLWH with uncontrolled HIV RNA on hospital admission may reflect success from an ongoing national focus to help PLWH initiate and maintain antiretroviral therapy at all times and from the far simpler (typically one-pill-once-a-day) regimens that carry little potential for side effects compared Z L W K regimens of just 50 years ago. Overall, this represents success in one of the most important areas for quality improvement in the care of PWLH. While recognizing this success, it is also important for national efforts to continue focusing on people who remain unengaged in HIV care. These individuals may represent an even harder-to-reach population with all themore need for innovative approaches.

One such approach, and a possible avenue for future work, is promoting rapid (re)start of antiretroviral therapy. In the outpatient setting, starting antiretroviral therapy from the day of (or as soon as possible after) HIV diagnosis has been shown to have a



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positive HIV antibody result. We used manual chart reviews and an EMR database search to determine the  
sensitivity and the positive predictive value (PPV) of the overall alert and of its individual criteria.

Over the planned 24-month intervention period, the alert functioned as intended, notifying both  
our intervention team and our data abstraction team about admissions of PLWH. Manual review of an  
approximately 3% sample of annual hospitalizations to adult services (1634 hospitalizations) identified 18  
hospitalizations of PLWH, all of which were captured by the alert (sensitivity 100%, 95% CI: 82%-100%). Over the  
24 months, the alert triggered for 1191 total hospitalizations. Of these, 992 were hospitalizations of PLWH (84%).

The following two criteria are then used to determine if identified patients have already been treated:

- A negative Hepatitis C Quantitative RNA PCR after an initial positive
- Any history of oral direct acting antiviral Hepatitis C medications

Based on experience with the HIV alert, the project team planned

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Finally, the EMR alert that facilitated our interventional study is novel and was successful. The results of the analysis of its accuracy, as well as a description of lessons learned in the process of creating