A Pilot Study of mDOT for Immunosuppressant Adherence in Solid Organ Transplant Recipients

Version 1.0

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SYNOPSIS

Study Aims:

Primary Objective: To compare medication adherence of solid organ transplant recipients, specifically liver and kidney transplants, using the mobile DOT (mDOT) application (i.e., intervention) to those who did not use the mDOT application (i.e., control). We will compare medication adherence between intervention and control arms using the Medication Level Variability Index (MLVI), a validated measure of adherence derived from the standard deviation of measured drug levels (22-23).

Secondary objectives:

- Clinical endpoints including rejection and hospitalization
- Patient reported adherence on immunosuppressant therapy instrument (ITAS)
- Patient-reported QoL outcomes as measured by PedsQL and SF-36
- Patient-reported self-efficacy using the Riekert Self-efficacy scale
- Patient-reported usability using the PSSUQ (treatment arm only)
- To examine the patterns of medication adherence in transplant recipients in both groups to better understand baseline medication adherence
- To understand the feasibility and acceptability of implementing such a system into the clinical workflow and patient follow-up care management

Design and Outcomes:

In this multi-center study, patients >/= 13 years of age who receive a liver or kidney transplant at Johns Hopkins Hospital, University of Virginia Medical Center or University of Miami Medical Center will be recruited to participate in this randomized control trial (RCT).

There will be 2 arms participants may be randomly assigned to: intervention and control arms. Participants in the intervention arm will receive the mDOT application, and participants in the control arm will not. Both arms will still receive standard of care post-transplant.

We will use block randomization to assign participants to the intervention or the control group using random block sizes ranging from 2 to 8. Block randomization will improve the probability of balanced groups over the course of the study as well as during shorter time horizons. A research data analyst, blind to the group allocations, will generate a list of sequential group assignments using this method. The list will be used to create sequentially numbered, sealed envelopes that will be used to allocate consenting participants to the control or intervention arms of our study. Each patient will have a 50% chance to be in the intervention arm of the study.

Interventions and Duration:
Participants will be enrolled in the study for 12 months. All subjects will complete study assessments and have immunosuppressant levels and clinical outcomes followed for 12 months. This subjects randomized to the intervention group will use the app for the first 3 months following enrollment. Subjects randomized to the control group will not use the app and will follow routine standard of care.

No study visits are required of research participants after enrollment, but they will complete surveys and an interview over the phone.

Procedure	Baseline	3 months	6 months	9 months	12 months
Baseline clinical/demographic/lab info/baseline survey	X				
Immunosuppression levels and laboratory values collected from medical record	X	X	X	X	X
Interval health information collected		X	X	X	X
Patient-reported outcomes*	X	X			X
Phone Interview					X

*these include ITAS, PedsQL <18 years at enrollment or SF-36 if >18 years at enrollment, Reikert self-efficacy scale, PSSUQ (treatment arm only and only at 3 months)

Sample Size and Population:
Participant enrollment will continue until we have reached 25 participants in each arm by age (13-21 years and 22 years and older) for a total of 100 participants. We will follow all study participants for 12 months.

1. STUDY OBJECTIVES

1.1 Primary Objective

To compare medication adherence of solid organ transplant recipients, specifically liver and kidney transplants, using the mobile DOT (mDOT) application (i.e., intervention) to those who did not use the mDOT application (i.e., control). We will compare medication adherence between intervention and control arms using the Medication Level Variability Index (MLVI), a validated measure of adherence derived from the standard deviation of measured drug levels (22-23).

1.2 Secondary Objectives

- Clinical endpoints including rejection and hospitalization
- Patient reported adherence on immunosuppressant therapy instrument (ITAS)
- Patient-reported QoL outcomes as measured by PedsQL and SF-36
- Patient-reported self-efficacy using the Riekert Self-efficacy scale
- Patient-reported usability using the PSSUQ (treatment arm only)
- To examine the patterns of medication adherence in transplant recipients in both groups to better understand baseline medication adherence
- To understand the feasibility and acceptability of implementing such a system into the clinical workflow and patient follow-up care management

2. BACKGROUND AND RATIONALE

In adolescent and adult solid organ transplant recipients, poor adherence to immunosuppressant medications carries the risk of graft rejection, short- and long-term post-transplant complications, and increased healthcare costs (1-8). In transplant recipients, adherence to immunosuppressive drugs, as well as general medical indications is imperative to overall outcomes (9). The rate of non-adherence to immunosuppressive medications in transplant patients varies vastly, with reports ranging from 15-40% in adults and much higher at 50-70% among adolescents (9-14). Additionally, medication adherence is a key concern in the transition from adolescent to adult-centered transplant care, and transition planning should be prioritized in these transplant patients (15-18). Because of lacking objective and accurate non-adherence measurements, both to immunosuppressive drugs and medical indications, the true implications and prevalence of non-adherence is not yet well understood (19-21). Therefore, we believe that mobile health (mHealth) technology has the potential to allow clinicians and researchers to more comprehensively address and understand non-adherence in adolescent and adult transplant recipients.

emocha Mobile Health Inc. has developed an application that enables users to track dose-by-dose medication adherence through asynchronous, video directly observed therapy (DOT). This helps patients take their medication as prescribed and gives providers the assurance that their patients are supported and successful in treatment. DOT is the practice of watching a patient take every dose of medicine in-person, and has typically only been done in extreme cases because it can be both costly and burdensome: DOT is the standard of care for Tuberculosis treatment and has proven high-adherence rates. Through mHealth technology, DOT can be used more broadly and without added burden; emocha's technology allows this through enabling patients to use their mobile application

to view their regimen, record themselves taking every dose of their medication, report side effects or symptoms, visualize their treatment progress, and access educational content. This information is encrypted and transmitted to a HIPAA-secure web portal for providers to review. The aim of this study is to conduct a randomized control trial to compare medication adherence between patients who use the mHealth system against controls who do not.

emocha has formally evaluated their mDOT platform across several disease states: tuberculosis, Hepatitis C virus, and opioid use disorder. The U.S. Centers for Disease Control and Prevention (CDC) recognizes emocha's video modality as an acceptable form of DOT, according to their latest guidelines (24). To date, emocha has partnered with Johns Hopkins and three Maryland health department tuberculosis programs to assess quantitative, qualitative, and cost outcomes associated with emocha video DOT implementation. Among all participants – with more than 1,400 videos submitted thus far – mean patient adherence was 94 percent (median adherence 96 percent, interquartile range 93 to 100 percent). Similar adherence rates were proven in independent studies using emocha performed by Harris County, TX and the Puerto Rico Department of Health. Additionally, emocha is conducting a trial on the feasibility of video DOT for patients undergoing the initiation phase of buprenorphine treatment through office-based opioid treatment programs, as well as conducting ongoing research on Hepatitis C medication adherence among injection drug users.

3. STUDY DESIGN

The purpose of this study is to understand how the use of an mHealth application, mDOT, changes medication adherence behaviors among liver or kidney transplant recipients. For the purpose of this research, the mobile app is a device of non-significant risk and exempt from the IDE requirement. emocha Mobile Health is the device manufacturer.

In this multi-center study, patients >/= 13 years of age who receive a liver or kidney transplant at Johns Hopkins Hospital, University of Virginia Medical Center or University of Miami Medical Center will be recruited to participate in this randomized control trial (RCT). There will be 2 arms participants may be randomly assigned to: intervention and control arms. Participants in the intervention arm will receive the mDOT application, and participants in the control arm will not. Both arms will still receive standard of care post-transplant.

Participants are followed for their compliance with standard of care recommendations. No additional care or procedures will be administered to study participants. Given the uncertainty in whether this mHealth intervention will improve rates of immunosuppression medication adherence in liver and kidney transplant recipients, a non-treatment group is necessary in order to identify whether an advantage exists.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1 Inclusion Criteria

Participants must meet all of the following inclusion criteria to participate in this study:

- ≥ 13 years old
- Own a smartphone and are willing to receive information through it
- Received a liver or kidney transplant at a participating study site during or prior to the study period.

4.2 Exclusion Criteria

All candidates meeting any of the following exclusion criteria at baseline will be excluded from study participation:

- Patients with cognitive impairments will not be eligible for enrollment due to inability to provide informed consent.
- Inability or unwillingness of individual or legal guardian/representative to give consent.

4.3 Study Enrollment Procedures

Participants will be approached by the following methods:
For subjects ages 13-21 years old: either while they are an inpatient post-transplant or at any follow-up outpatient clinic visit by a study member to participate in this study.
For subjects >21 years old: either while they are an inpatient post-transplant or at their first post-op outpatient clinic visit by a study team member to participate in this study.

For all subjects:
When feasible to conduct in-person consenting, written consent will be obtained explaining the purpose of the study, their part in it, and that they can withdraw from the study at any time. As much time as necessary will be allowed for obtaining consent. Assent will be obtained from participants age 13-17 years, along with parental consent.

Additionally, we will make provisions for phone consent and enrollment if needed due to potential COVID-19 restrictions so that enrollment may proceed according to plan. If unable to conduct in-person consenting and enrollment process, patients will be contacted by phone and the study team will conduct the appropriate oral consent/assent procedures and conduct the procedures listed below remotely.

We will use block randomization to assign participants to the intervention or the control group using random block sizes ranging from 2 to 8. Block randomization will improve the probability of balanced groups over the course of the study as well as during shorter time horizons. A research data analyst, blind to the group allocations, will generate a list of sequential group assignments using this method. The list will be used to create sequentially numbered, sealed envelopes that will be used to allocate consenting participants to the control or intervention arms of our study. Each patient will have a 50% chance to be in the intervention arm of the study.

Participant enrollment will continue until we have reached 25 participants in each arm by age (13-21 years and 22 years and older) for a total of 100 participants and we will follow study participants for 12 months. No study visits are required of research participants after enrollment, but they will complete surveys and an interview over the phone.

5. STUDY PROCEDURES

5.1 Schedule of Evaluations

Procedure	Baseline	3 months	6 months	9 months	12 months
Informed Consent	X				
Randomization	X				
Baseline clinical/demographic/lab info/baseline survey	X				
Immunosuppression levels and laboratory values collected from medical record	X	X	X	X	X
Interval health information collected		X	X	X	X
Patient-reported outcomes*	X	X			X
Phone Interview					X

*these include ITAS, PedsQL <18 years at enrollment or SF-36 if >18 years at enrollment, Reikert self-efficacy scale, PSSUQ (treatment arm only and only at 3 months)

5.2 Description of Evaluations

5.2.1 Enrollment, Baseline, and Randomization

Consenting Procedure:

For all subjects:

When feasible to conduct in-person consenting, written consent will be obtained explaining the purpose of the study, their part in it, and that they can withdraw from the study at any time. As much time as necessary will be allowed for obtaining consent. Assent will be obtained from participants age 13-17 years, along with parental consent.

Additionally, we will make provisions for phone consent and enrollment if needed due to potential COVID-19 restrictions so that enrollment may proceed according to plan. If unable to conduct in-person consenting and enrollment process, patients will be contacted by phone and the study team will conduct the appropriate oral consent/assent procedures and conduct the procedures listed below remotely.

Enrollment and Baseline Assessments:

Once consent and, when applicable, assent is obtained, participants will complete a baseline survey containing questions about basic demographic, health, and smartphone usage information. After completing the baseline survey, subjects will be randomized into either the control or intervention arm. Study personnel will assist participants assigned to the mHealth intervention (mDOT) with downloading the mDOT application and explain its functioning. Patients will be strongly discouraged from discussing which treatment they are receiving with their clinical team.

In regard to using the mDOT app, a designated study team member will enter the medications prescribed and times to take the medications into the app for each participant in the intervention arm. As a second check, another member of the study team will ensure that medications entered into the app are consistent with what is in the patient's EHR to reduce the risk of transcription error. The app will then remind participants when it is time to take their medication, and what to take. Participants will then take a video of themselves taking the prescribed immunosuppression medications. A designated study team member will then review the uploaded videos and either accept or reject them in regard to adherence. Participants can view their progress, adherence, and what days they are expected to take their medications in a calendar-like view.

Randomization:

We will use block randomization to assign participants to the intervention or the control group using random block sizes ranging from 2 to 8. Block randomization will improve the probability of balanced groups over the course of the study as well as during shorter time horizons. A research data analyst, blind to the group allocations, will generate a list of sequential group assignments using this method. The list will be used to create sequentially numbered, sealed envelopes that will be used to allocate consenting participants to the control or intervention arms of our study. Each patient will have a 50% chance to be in the intervention arm of the study.

5.2.2 Blinding

Research team members responsible for enrollment and reviewing emocha app submissions will not be masked to who is in the intervention or control arm. Patients will be aware of which arm they are randomized to as well. In this sense, the study will not be blinded to patients. Furthermore, patients/families will be strongly discouraged from discussing with their clinical team to which treatment arm they are enrolled. Data extraction (labs, drug levels) will be performed by study personnel that are blinded to the treatment arm. Individuals performing data analysis will receive de-identified data that does not explicitly describe which group is intervention and which is control, but simply the code without a key. Only the PI at each site and necessary personnel performing data extraction will have the key for the code to minimize bias in data analysis.

5.2.3 Follow-up Visits

After enrollment in the study, we will measure medication adherence in both arms at 3 month intervals for 12 months. MLVI, the standard deviation of recorded drug levels, will be calculated for each subject. Medication adherence will be ascertained through electronic health record (EHR) review of immunosuppression levels (i.e. tacrolimus, sirolimus, cyclosporine, prednisone, mycophenolate). Organ transplant recipients get labs post-transplant drawn frequently. Included in these lab draws are immunosuppression levels. A significant change in trough levels (i.e. undetectable or supra therapeutic) signal an issue of adherence to the prescribed regimen (i.e. missing doses, taking extra doses, etc.). We will track lab values using EHR, and record these in the secure REDCap database.

Participants in both arms will complete the immunosuppressant therapy instrument (ITAS), a validated tool to measure medication adherence at baseline for those subjects who have been on immunosuppressant therapy for at least 3 months at time of enrollment, at 12 weeks post enrollment for all subjects, and at 12 months post enrollment. Scores on the ITAS scale range from 0 (very poor adherence) to 12 (perfect adherence), and scores will be compared between the control and intervention arms (25). Participants will complete age appropriate QOLs at matching intervals to the ITAS. Follow-up questionnaires will be completed by phone with a designated study team member. Indicate treatment and followup visit assessments for each visit. List all measurements and procedures in bulleted format.

6. RISKS AND BENEFITS

6.1 Risks

The only risk to participants in using this mHealth application is the loss of confidentiality, which will be kept to a minimum. This application will comply with HIPAA regulations on how to handle PHI, including but not limited to secure encryption of data, access controls, and industry-standard best practices. All information gathered will be de-identified and only linked through a study-specific identification number.

All study data except identifying information will be entered into a central access database (REDCap). These data will be accessible by only authorized study personnel

from the secure study database. User level authentication will be required to gain access to the REDCap account. A separate access database will be created which has patient identifiable information along with a unique identifier. All specific assessments will have labels (individual study ID number) affixed to them and the results will remain strictly confidential. Risks to confidentiality will be minimized by separating identifiers from the results of the questionnaires.

6.2 Benefits

Participants may or may not benefit directly from participation in this study. Participation in the study could help providers, transplant centers, and liver transplant recipients in the future from the information gathered in this study.

6.3 Renumeration

Subject will receive $100 after completion of participation.

6.4 Costs

There is no cost to patients for participating in this study.

7. SAFETY ASSESSMENTS

This is a minimal risk study. However, there is a slight risk of loss of confidentiality. To minimize this risk, hard copies of all study materials, including consent forms, will be stored in locked cabinets that are only accessible to the study team. Electronic copies of all study materials will be kept on a secure, password-protected server that is only accessible to the study team. All study data except participants' identifying information will be entered into a central access database. These data will be accessible by only authorized study personnel from the secure study database. User level authentication will be required to gain access to the central database. A separate access database will be created which has patient identifiable information along with a unique identifier. All specific assessments will have labels (individual study ID number) affixed to them and the results will remain strictly confidential. Risks to participants' confidentiality will be minimized by separating identifiers from the results of the survey responses.

8. INTERVENTION DISCONTINUATION

Participants may withdraw from the study at any time without penalty. This would not preclude participants from obtaining regular medical care or follow-up care related to their transplant. If participants choose to withdraw, the study team will use the data collected prior to withdrawal and mark the remaining data as censored.

Upon study completion or if study participation ends prematurely, those who were randomized to mDOT app will return to their usual standard of care. Those who were randomized to standard of care will continue in that manner.

9. STATISTICAL CONSIDERATIONS

Primary outcome variables:

12-week immunosuppression medication adherence:

We will measure medication adherence in both arms at 12 weeks. The Medication Level Variability Index (MLVI) will be used to analyze immunosuppression lab

values to determine adherence with a relative risk noted for standard deviation >2.

Secondary outcome variables:
Hospitalization days
Biopsy-proven rejection
Clinician-assigned rejection

We will recruit 100 liver and kidney transplant recipients (50/arm), and compare recipients who received the mHealth intervention to controls that did not receive it. The Medication Level Variability Index (MLVI) will be used to analyze immunosuppression lab values to determine adherence with a relative risk noted for standard deviation >2. Descriptive statistics will be performed to compare frequencies of secondary outcomes (e.g., hospitalization, rejection, etc). Patient reported outcomes will be scored as appropriate and differences compared between treatment arms. Additionally, we will perform subgroup analyses for younger transplant recipients (age at transplant <40), older transplant recipients, men, and women.

In addition to understanding the efficacy of this technology in a transplant patient population, we will also evaluate the feasibility of implementing such a system into clinical workflow. We will examine time spent by reviewers each week using mDOT, most ideal time post-transplant to consent and educate participants on using the application, and streamlining the workflow involved in the application. In order to ensure acceptability among the patients who will be using the app, we will survey all participants in the intervention arm at the end of the study period on their overall satisfaction in using the app. This survey will be administered with the ITAS scale over the phone. In addition, we will also examine consent rate and use of the mDOT app by participants over time to understand acceptability of using the application.

Feasibility will also be measured through phone interviews with all study participants at 12 months. We will contact all patients who consented to be in the study to participate in the phone interviews. The interviews will be semi-structured, with a set of pre-written questions as the guide. All interviews will be audio recorded. Transcription of the interviews will be conducted by Production Transcripts, Inc.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

All study data except identifying information will be entered into a central access database (REDCap). These data will be accessible by only authorized study personnel from the secure study database. User level authentication will be required to gain access to the REDCap account. A separate access database will be created which has patient identifiable information along with a unique identifier. All specific assessments will have labels (individual study ID number) affixed to them and the results will remain strictly confidential. Risks to confidentiality will be minimized by separating identifiers from the results of the questionnaires.

10.2 Coordinating Center Functions and Multi-site Study Plan

10.2.1 Responsibilities

A Clinical Coordinating Center (CCC) will be responsible for overall recruitment and retention, data management, monitoring and communication among the enrolling sites, and the general oversight of the conduct of this human subject research project. The CCC for this trial is the Epidemiology Research Group in Organ Transplantation, located at 2000 E. Monument Street, Baltimore, MD 21202.

10.2.2 IRB Document Management

There is a plan in place for reviewing site approval documents. An sIRB coordinator oversees the process of reviewing site approval documents and consent forms prior to sIRB review. The coordinator collaborates with the JHM IRB and conducts web calls with each enrolling site to promptly and adequately pre-review site documents prior to site-specific JHM IRB submissions. The sIRB specialists confirm that each participating site has on file an FWA with OHRP. Throughout the study, the sIRB specialists and CCC site managers will assure that all centers have the most current version of the protocol, which will be stored in the electronic trial management file (eTMF). Site managers will communicate protocol amendments to enrolling site PIs and lead study coordinators via receipt-confirmed email and telephone contact follow-up.

10.2.3 Screening and Enrollment Tracking

Recruitment and retention at the sites will be supported by a centrally managed electronic data collection (EDC) system in REDCap where data will be entered on every screening and enrollment, including inclusion and exclusion criteria met, and demographics needed for reporting. Enrollment reports will be generated monthly and reported annually as part of the renewal process.

10.2.4 Data Safety and Monitoring Plan

This is a minimal risk study. However, there is a slight risk of loss of confidentiality. To minimize this risk, hard copies of all study materials, including consent forms, will be stored in locked cabinets that are only accessible to the study team. Electronic copies of all study materials will be kept on a secure, password-protected server that is only accessible to the study team. All study data except participants' identifying information will be entered into a central access database. These data will be accessible by only authorized study personnel from the secure study database. User level authentication will be required to gain access to the central database. A separate access database will be created which has patient identifiable information along with a unique identifier. All specific assessments will have labels (individual study ID number) affixed to them and the results will remain strictly confidential. Risks to participants' confidentiality will be minimized by separating identifiers from the results of the survey responses.

Although this study is deemed minimal risk, any unanticipated problems or study deviations will first be reported to the site investigator, study principal investigator and then the sIRB.

Events meeting the sIRB prompt reporting guidelines will be reported to the lead site IRB within 72 hours and will be reported to the relying IRBs per their guidelines.

10.2.5 Identifying Enrolling Sites

The lead study team will be responsible for notifying JHM IRB of sites added using the template below. Final approval will be withheld until the JHM IRB and the OHSR have all required documentation on file. The protocol will be amended, as a change in research if additional sites are added to the project. Johns Hopkins will be an enrolling site. If any problems arise with enrolling sites, IRB specialists will communicate with the site contact person named in the application, if necessary.

Site Identification Template	Site name and address
	PI name and contact (phone and email)
	Confirmation that the research can be conducted at that site, has an IRB, and that the IRB has completed its approval of the research
	Site FWA number
	An executed agreement to rely on the JHM IRB

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   Email: txm760@med.miami.edu

10.3 Data Management and Monitoring

10.3.1 Source Documents

Source documents for this study will include the subjects' medical records and study record documents. If the investigators maintain separate research records, both the medical record and the research records will be considered the source documents for the purposes of auditing the study. The local site investigator will retain a copy of source documents. The local site investigator will permit monitoring and auditing of these data, and will allow the sponsor, IRB and regulatory authorities access to the original source documents. The local site investigator is responsible for ensuring that the data collected are complete, accurate, and recorded in a timely manner. Source documentation (the point of initial recording of information) should support the data collected and entered into the study database/case report form and must be signed and dated by the person recording and/or reviewing the data. All data submitted should be reviewed by the site investigator and signed as required with written or electronic signature, as appropriate. Data entered into the study database will be collected directly from subjects during study visits or will be abstracted from subjects' medical records.

10.3.2 Data Management Plan

Study data will be collected at the study site(s) and entered into the study database. Data entry is to be completed on an ongoing basis during the study.

10.3.3 Data Capture Methods

Clinical data will be entered into a secure REDCap database. The data system includes password protection and internal quality checks to identify data that appear inconsistent, incomplete, or inaccurate.

10.3.4 Participant Confidentiality, Security and Storage

Coded identifiers, password-protected data files, and locked file cabinets kept in a secure building will be used to protect against breaches of confidentiality.
emocha Mobile Health's plan is to store the data for a minimum of 7 years according to HIPAA requirements, and provide Johns Hopkins with accessibility to the raw data submitted by participants in the intervention arm through the mDOT app and its audit logs. emocha only accesses the data on a need-to-know basis, in order to support any issues that may come up. All data access is logged and accessible to study administrators. All emocha applications comply with HIPAA regulations on how to handle protected health information, including but not limited to secure encryption of data, access controls, and industry-standard best practices. A robust role-based permission system limits system access to only authorized, authenticated users to ensure the need-to-know basis of PHI. All PHI is encrypted both in-flight and at-rest, and all access to, or modification of, patient data and system configuration is logged. The server infrastructure is secured from both physical and remote access.

In-flight encryption refers to the encryption of all data while being transmitted. Data is sent over a secure HTTPS connection secured by a 2048-bit SSL certificate. The SSL configuration is audited regularly, ensuring that system configuration is as up-to-date as possible. All connections between the database and application servers are

made over SSL/TLS, using the same 2048-bit certificate. At-rest encryption means that all PHI in the database and disk is always stored encrypted. This includes any record of a user, anything in the error log or audit log tables, and any patient data. The encryption scheme uses the Advanced Encryption Standard (AES) algorithm of at least 256 bits, with the ability to revoke and issue new keys as needed. Data being sent from mobile devices is encrypted on the device as soon as it has been collected. Data is then transmitted to the server over a secure HTTPS channel and deleted from the device as soon as receipt of the transmission is confirmed. Encryption/decryption keys are housed on a separate server and only accessible through a highly-restrictive API, which is not directly reachable from the database server. Keys are only stored in memory on the application server and never in permanent files written to a disk. Effectively, the database cannot decrypt its own data; even in the event of the server being compromised and a malicious party acquiring an export of the data, PHI will remain secure.

Any viewing or modification of the system or patient data is logged in a persistent and unmodified database. Audit trail records include but are not limited to the action being taken, the date and time, and, in the case of modifications, both the old and new values. These logs are available to be searched with numerous sorting and filtering options on the administrative interface. In addition, nothing is ever deleted in the system; data is "soft-deleted" via marking with a flag that will hide the record during normal operations, but leave it easily recoverable if needed.

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