Regular Reminders via Text Message Increase Adherence to Medication Regimen, Significantly Reduce Risk of Organ Rejection in Pediatric Liver Transplant Patients

**Snapshot**

**Summary**
Working in partnership with CareSpeak Communications, Mount Sinai Hospital sends regular reminders to pediatric liver transplant patients and/or their caregivers via two-way text message, reminding them to take their medications, with follow up alerts sent to the caregivers of those who do not respond within a predetermined time range. Physicians can also proactively monitor performance and then send motivational messages to encourage continued adherence, or identify and intervene with nonadherent patients before the risk of rejection increases significantly. The program increased adherence to medication regimens and significantly reduced the risk of organ rejection. In addition, patients who continued to use the CareSpeak system 1 year after termination of the study had significantly fewer rejection episodes in comparison with patients who discontinued use of the system 1 year after the study.

**Evidence Rating** *(What is this?)*
Moderate: The evidence consists of pre- and post-implementation comparisons of the standard deviation in mean serum medication levels and the number of at-risk patients and rejection episodes.

**Developing Organizations**
CareSpeak Communications; Mount Sinai Hospital
Mount Sinai Hospital is located in New York, NY; CareSpeak Communications is located in East Brunswick, NJ.

**Date First Implemented**
2007 November

**Patient Population**
Age > Adolescent (13-18 years); Child (6-12 years); Vulnerable Populations > Children; Age > Infant (1-23 months); Preschooler (2-5 years)

**What They Did**

**Problem Addressed**
Many pediatric liver transplant recipients do not adhere consistently to their medication regimens, increasing the risk that the body will reject the new organ and potentially leading to severe morbidities, the need for another transplant, and/or death. Traditional methods of encouraging adherence have not been effective in this population, and little attention has been paid to using cell phones and text messages—integral parts of everyday life for adolescents—to boost adherence.

- **Failure to adhere to prescribed regimen:** Up to 40 percent of pediatric liver transplant recipients do not adhere to their medication regimens, even though following such regimens is critical to long-term health. One of the most common reasons for nonadherence is forgetfulness caused both by impaired liver function before the transplant and as a side effect of immunosuppressant medications that need to be taken after transplantation, which often have a negative effect on cognitive function. Young patients may stop taking their medications because they or their families face financial issues, they rebel against authority (as teenagers and young adults often do), they tire of taking so many medications every day, and/or they feel they are invincible and thus no longer need them.

- **Negative health consequences, vicious cycle of nonadherence:** Nonadherence can lead to poor health outcomes, including serious complications such as acute or chronic rejection of the organ, end-stage liver disease, and/or death. Continued nonadherence often leads to acute cellular rejection, treatment for which typically requires an expensive hospitalization (lasting a week or more), increased doses of immunosuppressants, and the addition of new immunosuppressant drugs. Requiring the patient to take more drugs may, in turn, lead to greater risk of nonadherence, as patients already struggling with taking their medicines then have to juggle more of them. In addition, taking more immunosuppressants increases the risk of negative side effects, including high blood pressure, growth delay, infections, and malignancies. Patients unable to recover from a rejection episode often need a second transplant (at a cost of roughly $500,000), although guidelines may prevent providing new organs (which are in short supply) to patients who have proven incapable of following the required medication regimen.

- **Limited impact of current methods, unrealized potential of cell phones:** Like other organizations dealing with pediatric transplant patients, Mount Sinai Hospital historically had limited success in changing the behavior of those who did not adhere to their medication regimens. For example, use of electronic chip monitors (that record how often a pill bottle is open) proved to be ineffective, as did calling patients into the office more often. In addition, little attention has historically been paid to the potential of cell phones and text messaging—integral parts of everyday life for most adolescents, young adults, and parents—to increase adherence.

**Description of the Innovative Activity**

Working in partnership with CareSpeak Communications, Mount Sinai Hospital sends regular reminders to pediatric liver transplant patients (ranging in age from 1 to 27) and/or their caregivers via two-way text messages, reminding them to take their medications, with follow up alerts sent to the caregivers of those who do not respond within a predetermined time range. Physicians can also proactively monitor performance...
and then send motivational messages to encourage continued adherence, or identify and intervene with nonadherent patients before the risk of rejection increases significantly. Key elements of the program include the following:

- **Initial sign up, setting of alert preferences:** Patients or caregivers who have a cell phone and active cell phone service can participate in the program. Interested patients/caregivers sign a consent form and then register online for the system (developed by CareSpeak Communications), creating a user name and password for security. For the initial study, Mount Sinai had a coordinator assist patients/caregivers in signing up, which generally takes just a few minutes. As part of this process, participants enter the patient's name and cell phone number, the caregiver(s) name/nickname and cell phone number, medication name(s) and frequency (e.g., typically at least twice a day), and the exact times they prefer the alerts to arrive (thus catering to the unique needs of the patient, such as an adolescent who prefers to sleep late and take his or her first dose at 10 a.m.). Although the appropriate dose could be included in the alert, this information is omitted for liver transplant patients, because dosages change frequently based on the patient's condition and laboratory test results.

- **Regular text messages, with prompt to reply:** Messages automatically come to the person responsible for medication intake (usually the patient, except for young patients where the parent or another caregiver gives the medication) at the designated time. The simple messages read as follows: "Take [name of medication] at [designated time]. To confirm intake, press REPLY, type CARE 1, and press SEND."

- **Follow up messages to caregivers:** If a reply to the first message is not received within an individually set time frame (typically 15 minutes to 1 hour), up to two designated caregivers receive a second message notifying them of the lack of response and encouraging them to contact the patient immediately.

- **Ongoing physician monitoring, motivational messaging to encourage adherence:** The system allows physicians to view information for an individual patient at any time and periodically generates and sends reports on adherence rates for all patients to the physician. The goal is to allow the physician to encourage continued adherence in patients following their prescribed regimen, and to intervene proactively with those who appear to not be doing so by verifying nonadherence (e.g., the patient may be taking medications appropriately but not responding to the messages) and addressing any barriers (e.g., bringing in a therapist if the adolescent is acting out or contacting a social worker if the family faces financial issues or some other crisis). Rather than waiting until the next office visit (visits typically occur every 2 months) to identify and intervene with those not adhering to their regimen, physicians can call those patients and/or send a customized text message urging them to call immediately. The physician can also send motivational messages to those patients doing a reasonably good job (e.g., 70 or 80 percent adherence), with an emphasis on the need to keep it up and do even better, or send a warning message if a patient appears to be overmedicating (as indicated by too many confirmation messages being sent). Clinicians can also send "blast messages" to all participants at once. For example, in the event of a medication safety alert, the clinician can immediately send a message to all patients on that medication telling them to "please stop using [medication name] immediately and call [phone number] ASAP."
**Did It Work?**

**Results**

The program increased adherence to medication regimens and significantly reduced the risk of organ rejection.

- **Increased adherence to medication regimen:** The standard deviation of mean serum tacrolimus levels (a measure of the amount of tacrolimus—a common immunosuppressant taken by all study participants—in the blood) fell significantly, from 3.46 micrograms per liter in the year before the study to 1.37 micrograms per liter during the year-long study. Lower standard deviations are associated with higher levels of adherence, as they suggest more consistent amounts of medication in the blood. Results were consistent regardless of the number of medications being taken or who (the caregiver or patient) took responsibility for medication intake.⁶

- **Fewer at-risk patients:** Among the 41 study participants, the number with a standard deviation above the threshold level of 2.5 micrograms per liter (which puts the patient at increased risk of a rejection episode) fell from 24 before program implementation to 6 afterward.⁶

- **Fewer rejection episodes:** Among participants, the number of episodes of acute cellular rejection fell from 12 in the year before implementation to 2 during the study.⁶ In addition, 1-year followup after termination of the study revealed that patients who continued to use the CareSpeak system had less rejection in the year after the study.

*Evidence Rating (What is this?)*
Moderate: The evidence consists of pre- and post-implementation comparisons of the standard deviation in mean serum medication levels and the number of at-risk patients and rejection episodes.

How They Did It

Context of the Innovation

Founded in 1852, Mount Sinai Hospital is a 1,171-bed tertiary facility that handles more than 325,000 inpatient days, over 400,000 outpatient visits, and nearly 80,000 emergency department visits each year. The hospital draws most of its patients from New York City and the surrounding area, although a sizable number of patients travel to the hospital for care from throughout the United States and around the world. The hospital, affiliated with the Mount Sinai School of Medicine, performed its first liver transplant in 1988, with approximately 500 liver transplants having been performed on pediatric patients since that time (an average of more than 20 per year). Most receive their new organ before the age of 3, although the procedure can be performed on newborns (within a few weeks of birth) or on older pediatric patients.

CareSpeak Communications uses everyday wireless technologies to encourage adherence and get patients more involved in their own care. The company focuses on products and services that are effective, easy to use (fitting into existing lifestyles and workflows), and affordable for the end user, including patients, caregivers, and health care professionals. The vast majority of these services involve text messaging, which is inexpensive and can be supported by virtually any cell phone and carrier. In addition to supporting text messages for pediatric liver transplant patients, CareSpeak has a similar program for diabetes patients and is currently developing and/or testing applications for hypertension, asthma, and congestive heart failure.

The impetus for the Mount Sinai program came when Dr. Tamir Miloh, Assistant Professor in Pediatrics and Transplant in the Recanati Miller Transplant Institute at Mount Sinai, met Serge Loncar, Founding President and CEO of CareSpeak Communications at a conference; after hearing about CareSpeak’s products, Dr. Miloh immediately recognized its potential for improving adherence among pediatric liver transplant patients.

Planning and Development Process

Key steps in the planning and development process included the following:

- **Developing application:** Dr. Miloh and Mr. Loncar met several times to discuss patient, caregiver, and provider needs with respect to encouraging medication adherence in this population. CareSpeak designed the system based on these needs, building on an existing Web-based platform to create a customized patient interface and to otherwise meet hospital and patient/caregiver needs.

- **Developing consent form, policies:** The two organizations worked together to develop a consent form and other program-related policies, such as eligibility requirements. Program leaders decided to limit the initial study to those who already had a cell phone and service.

- **Initial testing:** As noted, the initial year-long study compared the amount of medication...
in the bloodstream and the number of rejection episodes in the year before the study to the same metrics during the study. Program developers chose to use the standard deviation of serum medication levels as an indicator of compliance, because regular compliance leads to low variation, while sporadic compliance creates high levels of variability. Most patients who completed the year-long study requested that they continue to receive the alerts on an ongoing basis; both Mount Sinai and CareSpeak agreed to continue providing the service to these patients.

- **Planning for additional testing:** Plans for additional, expanded tests of this approach are under way, including evaluating the impact of newly developed features that alert physicians (via reports and text messages) when a patient consistently does not reply to the alerts. Program developers are currently applying for funding to cover the costs of a national multicenter study of this program.

**Resources Used and Skills Needed**

- **Staffing:** The program requires no new staff within the provider office in which it is implemented; at Mount Sinai, an existing coordinator assisted participants with the initial signup and log in, which took only a few minutes per patient. (Patients can also sign up on their own if they wish.) Ongoing monitoring of reports and other alerts takes just a few minutes of physician time each week.

- **Costs:** The service costs between $5 and $30 per month per patient to cover both fixed development costs and variable costs for sending the messages. Actual costs will depend on the number of messages sent each day and the number of patients receiving the alerts. Because fixed costs related to system development comprise the majority of program expenses, per-patient costs decline significantly as the number of participants increases.

**Funding Sources**
CareSpeak Communications
CareSpeak covered the initial costs of system development and offered reimbursement to study participants for any program-related text-message charges imposed by cell phone service providers; relatively few participants requested reimbursement.

**Tools and Other Resources**

**Adoption Considerations**

**Getting Started with This Innovation**

- **Address potential financial barriers:** More than 40 percent of participants in the initial study dropped out before the end of the year, with the inability to pay for cell phone service being the single biggest reason for ending participation. To address this issue, consider providing prepaid cell phones with text-messaging capabilities to
patients.

**Sustaining This Innovation**

- **Consider use of incentives, other behavioral motivators:** Adolescents may respond to positive and negative incentives that reward adherence and/or penalize those who consistently do not take their medications. They may also respond to periodical motivational text messages that reinforce appropriate behavior and/or encourage improvement.

**Additional Considerations and Lessons**

- **Consider expansion to other chronic diseases:** This program has the potential to improve adherence for pediatric patients with any chronic disease that requires following a regular medication schedule, including asthma and diabetes. The program may also have applicability to adult populations, such as those who require regular medications to control hypertension, congestive heart failure, coronary artery disease, and other chronic conditions. The approach can be expanded to encourage adherence to needed testing/screening as well. For example, the diabetes program reminds patients to measure their blood glucose level and then allows them to input the results into the phone, which automatically transmits the information into an online medical record. (Future applications may allow the glucometer to directly interface with the phone, eliminating the need for user input.) Once completed, the congestive heart failure program will remind the patient to measure and input his or her blood pressure, pulse rate, and weight, and then will alert the physician if the patient is at risk.

- **Consider adding other types of alerts:** The program can be expanded to incorporate other types of messages and alerts. For example, as noted, the system can notify patients, caregivers, and/or physicians if a patient appears to be overmedicating or can send out safety warnings to all patients taking a particular medication.

**Use By Other Organizations**

- CareSpeak Communications is working in collaboration with a 20-physician medical group in New York on developing a similar program for patients with asthma; company leaders are currently in discussions with several other organizations that have expressed interest in this type of program.

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4 Lurie S, Shemesh E, Sheiner PA, et al. Non-adherence in pediatric liver transplant


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