Final Outcomes and Analysis: Transplant Medication Adherence

Target clinicians participating in CME significantly improve rates of counseling patients on adherence and increase readiness to individualize immunosuppressive therapy post transplant.

Patients continue to survive longer after liver transplantation, so the focus on patients' outcome measures has shifted to appropriate immunosuppressive treatment and improved quality of life. To improve routine clinical management, CME Outfitters conducted an outcomes study to assess the major issues related to immunosuppressive medication (ISM) adherence: Do clinicians counsel on and communicate about quality of life to optimize maintenance ISM? Do clinicians understand patient behaviors and patient-related barriers vis-à-vis ISM adherence? Do clinicians select ISM to help patients maintain adherence?

Clinicians specializing in transplant surgery, general surgery, gastroenterology, and nephrology who participated in a live symposium at the 2013 American Transplant Congress or a two-part, on-demand, enduring Webcast were evaluated for knowledge, attitude, skill at individualizing therapy, and practice changes relating improving adherence to life-saving ISM therapy.

Findings

Better knowledge and attitude

Because of their participation in this activity, clinicians changed their attitude toward selecting an ISM agent or formulation: based on their experience, the choice of immunosuppressive regimen influenced graft survival at five years, according to 70.9% of clinicians (n = 55) responding to a live-meeting, iPad-mediated, ARS survey question designed to encourage reflection on past practice (competence).

Indicating clinicians' greater attention to this matter after the meeting, a much higher 92.3% in the long-term outcomes survey (n = 28) stated that ISM selection does affect five-year graft survival; only 15.4% of these outcomes respondents registered any reservations about choosing between the starkly contrasting responses of "yes" and "no" that the regimen matters to graft survival (e.g., one mentioned "kidney toxicity").

Medication adherence can be impacted by many factors. In a pre-survey (n = 66) during the live symposium, 21% of respondents chose medication side effects, 36% chose complexity of dose, 18% cited lack of social support, and 24% chose poor memory. Considering the performance measure to "discuss adherence to immunosuppressive medication at all visits," these participants' awareness of treatment-selection should improve results with regard to adherence … because non-adherent patients would be encouraged to discuss why they are not adhering to

Outcomes Methods

Format

Independent symposium at the 2013 American Transplant Congress, with two-part, on-demand, enduring material Webcasts.

Practice Patterns (Outcomes Measures)

- Consider all available immunosuppressive therapies as part of the individualized treatment plan for transplant patients
- Initiate a discussion regarding adherence to immunosuppressive medication—at all visits—for patients who have undergone transplantation surgery

Demographic Inclusion Criteria

Degrees: Physicians, physician assistants, and nurse practitioners

Specialties: Transplant surgery, general surgery, gastroenterology, nephrology

Participation Dates: Credit requests by April 30, 2014, eligible for outcomes survey pool.

Data Collection

Live note-taking via iPad technology

- Individual participants could write notes on slides and receive an email message with their own notes on the corresponding slides.
- Interspersed polling questions among slides helped participants remain ready to take notes as they learned and set follow-up goals.

Pre- and post-testing and surveying

Live Symposium via ARS/iPad: Pre-activity knowledge, practice, and reflection data gathered from participants via an iPad-based audience-response (ARS) system. In-content ARS post-test participant question. Post-activity online post-test and post-activity survey on practice commitments for credit-requesters.

Enduring (2 Modules): Pre-activity and in-content knowledge, practice, and reflection data gathered via online registration process and in-content Web-based survey questions. Post-activity knowledge posttest and practice commitment survey for each of 2 modules.

Outcomes testing and surveying

Case vignette, reflection, and practice survey using staggered timing (average 8-month post-participation date across formats). Statistical significance determined with Fisher's exact test of 2x2 contingency tables.

treatment, giving participants the opportunity to adjust treatment as needed to improve adherence and support graft success. These outcomes data on changed attitudes show that education about selecting the best immunosuppressive regimen for a patient's medical needs and lifestyle—perhaps a once daily formulation that encourages adherence and reduces side effects such as gastrointestinal (GI) discomfort—was appropriate for these participants, as we showed in the pre-activity needs assessment.

Participants thought their patients had improved ISM adherence by the time we issued the outcomes survey: at presurvey, only 38.2% of live-meeting and Module 1 enduring webcast participants (n = 202) thought that at least 9 of every 10 patients were adherent. This changed over the months leading up to the outcomes survey: over one third *more* (46.2%) clinicians thought 9 of every 10 patients were adherent (n = 29).

Content on ISM adherence followed up on the above-mentioned, live presurvey poll, supporting clinicians' reflections on patient adherence patterns: post-transplant non-adherence occurs in 5% – 45% of patients, and that top reasons for non-adherence were "lack of social support" and simply being "forgetful." Looking at a random sample of pretest and posttest data (combined from live and enduring webcast groups), clinicians learned that patients were not "misunderstanding the impact of missed doses," not showing "lack of concern about being adherent that could be due to depression or denial," and not simply "deciding to ignore" adherence to ISM (pretest, 12.0% correct [n = 133]; posttest, 66.7% correct [n = 111]. Once clinicians learned that "forgetfulness" was the most common reason for non-adherence to immunosuppressive medication and that "lack of social support" affected adherence, they seemed to renew their efforts at educating patients, carrying out the activity's performance measure of discussing adherence at all visits, and helping patients with individualized treatment-selection and technological reminders (including text messages and social media; one participant wrote on the iPad-enabled interactive slide, "Technology to the rescue!").

Application of improved knowledge and attitude to treatment-selection

Partnering with patients includes listening to quality-of-life issues caused by side effects, and the improved attitudes documented above indicate that participants are now more willing to consider changing treatment regimens for individual patients, and not that they were not complying with medical advice.

Case: "Robin S." is a 23-year-old white woman with history of biliary atresia and orthotopic liver transplantation at age 1. Robin had maintained good lifelong adherence to ISM, using multiple alarm clocks, but had been experiencing gastro-intestinal issues with her immunosuppressive agent, mycophenolic mofetil (MMF), that could have led her to reduce her adherence to medication.

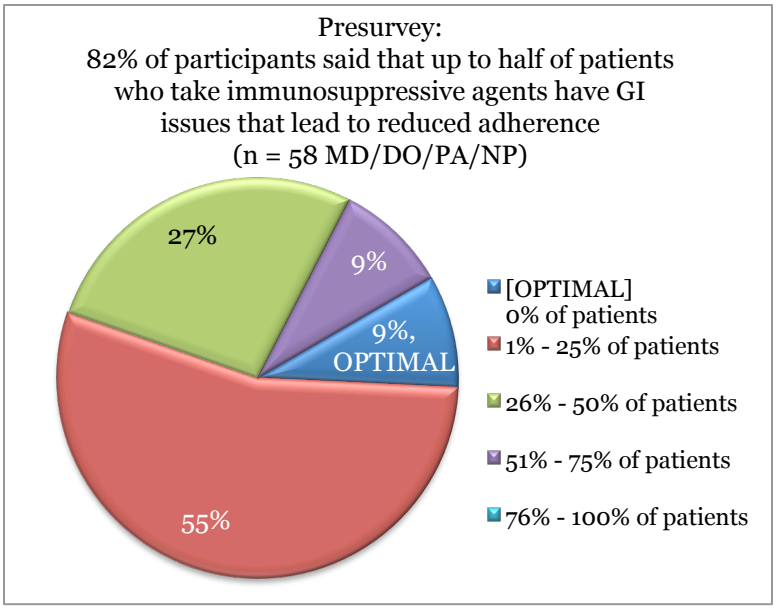
We asked participants to rank four choices (switch to another immunosuppressant, change to an enteric-coated formulation, add a proton-pump inhibitor, add a bismuth-containing agent) as their next step in managing Robin's GI issues and potential non-adherence; they also had the opportunity to mark as inappropriate or omit any choice they believed was not appropriate.

To help their patient, "Robin," remain adherent to ISM as before, more participants (n = 26) than controls (n = 29) would switch to another immunosuppressive agent or formulation, whereas more controls than participants would add a proton-pump inhibitor or bismuth to help with Robin's GI side effects. Suggesting reliance on longer-standing clinical use of MMF, the 27.5%-difference between participants' and controls' *readiness to switch agents was far greater* than the 10.0%-difference between participants' and controls' readiness to change formulations. These findings indicate that participants were ready to "consider all available immunosuppressive therapies as part of the treatment plan," another activity performance measure. Control-group clinicians remained focused on side effects, as expected, with approximately the same, but opposite/negative, percent difference in treating MMF side effects as participants were ready to switch to different ISM agents that could help avoid those side effects.

Participants' choices in the "Robin" case vignette are consistent with a random sample of posttest answers from the second module of the enduring webcast, where many more participants learned the presented findings by Veroux and colleagues that "switching to a once-daily formulation of the immunosuppressant" influenced a significant improvement in *Gastrointestinal Symptom Rating Scale*

(*GSRS*) scores in patients with history of kidney transplant (participants showed a large knowledge gain from 27.3% in the pretest [n = 58] to 100.0% in the posttest [n = 58]).

This issue of GI symptoms is relevant to clinicians: we issued participants a presurvey question in the second module of the enduring webcast asking what percentage of their transplant patients have GI complaints that lead them to reduce or stop taking their ISM, and 81.8% answered that GI complaints reduced adherence in up to half of their patients (n = 58; see Figure, right). Another 9.1% answered that *over half of their patients* were experiencing GI issues sufficient to cause non-adherence to ISM. Just 9.1% of these participants estimated that no patients were reducing adherence because of GI issues, and this is proof of a continuing gap in selecting treatment and/or counseling on adherence for clinicians treating patients taking ISMs.



Improved performance at outcomes

The strong knowledge, attitudinal, and treatment-competence (Level 3 and 4) data above are consistent with outcomes performance (Level 5) data gathered with regard to ISM adherence in the three months before the outcomes survey (see below). Baseline, self-assessed data were gathered for each enduring webcast, according to its learning objective and related performance measure: 1) considering all available immunosuppressive therapies, and 2) discussing adherence to ISM with patients with a history of transplant at all visits.

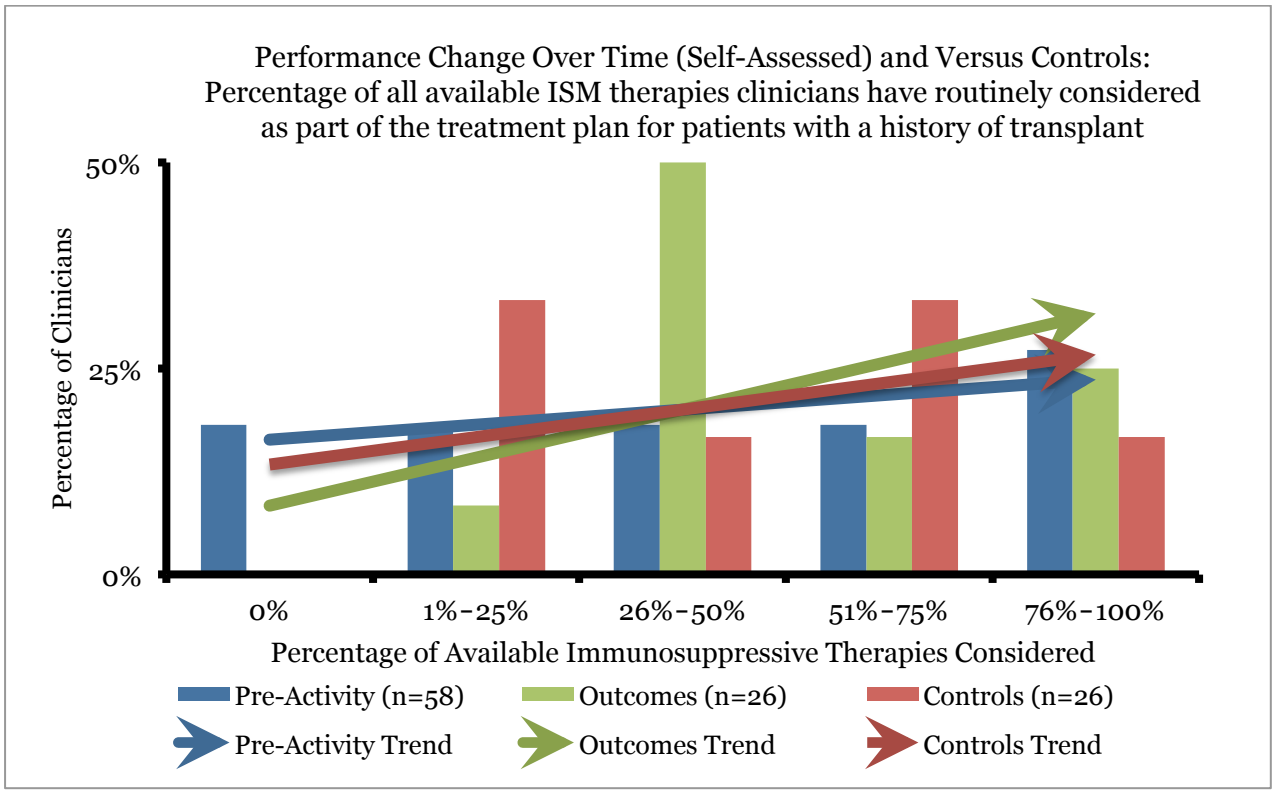
Individualizing plans using all available immunosuppressive therapies

In addition to competence data showing that participants are more *ready* than controls to switch agents or to once-daily formulations to help individual patients remain adherent, a higher percentage of participants than of controls overall stated that they *actually were* considering all available ISM therapies over the months since receiving education. Outcomes in the figure below show that 25.0% of participants (n = 26) were considering all available therapies for the highest proportion of their patients (76% – 100%), which was 50.0% higher than the percentage of controls (or 8.3 percentage-points higher; control n = 26). Moreover, education had led to improvement in which 33.3% of controls, but a more optimal 8.3% of participants, were considering all therapies in only few (a quarter or less of) their patients.

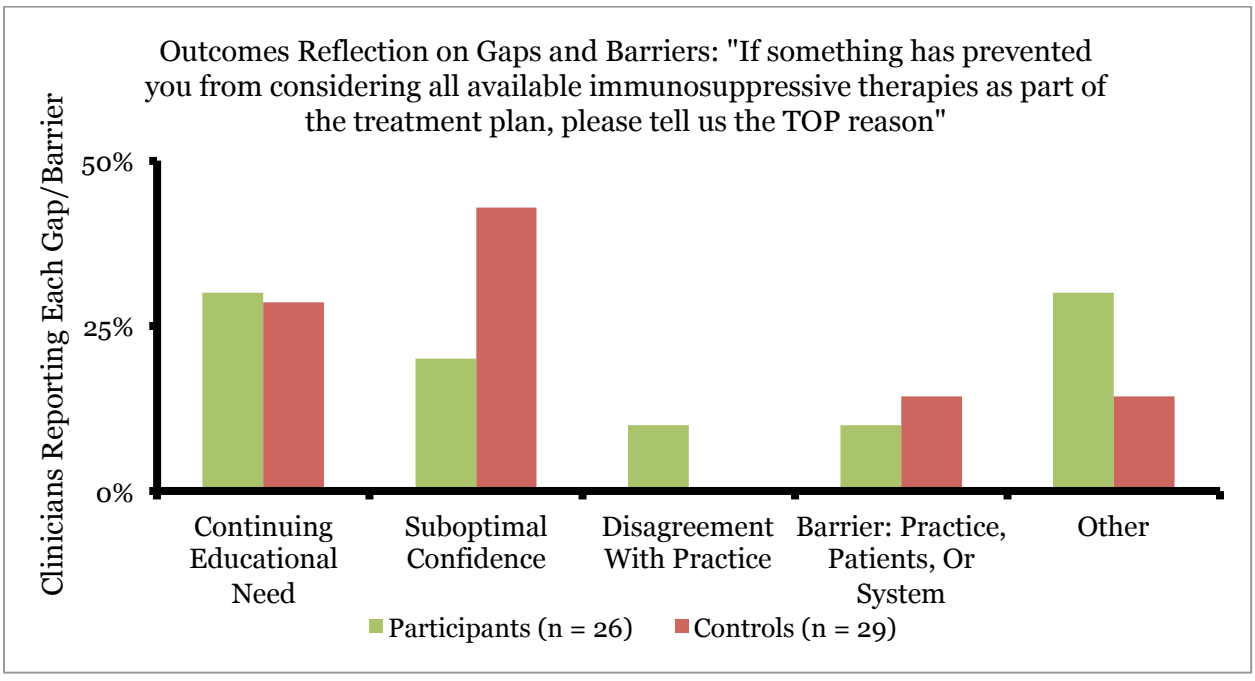
Data show performance change due to participation, as well. Outcomes show that nearly half (41.7%, n = 26) of responding participants had been routinely considering all available immunosuppressive therapies as part of the treatment plan for *over half of their patients* with a history of transplant. Again looking at the figure below, it is easy to see outcomes data in which 91.7% of participants had been considering all ISMs for over one quarter of these patients (n = 26), an improvement over presurvey data in which only 63.7% of clinicians had been doing this before participating (n = 58). This indicates that participants opting into the enduring webcast had identified their need for education (their performance was lower than for controls at the time) and they durably raised their long-term performance after participating.

In summary, participants more than made up the difference between their own baseline and controls' performance rates, showing higher rates in considering all ISM therapies after receiving education on ISM treatment-selection than controls showed in the same period. Reinforcing education on the clinical

evidence needed to aid a clinician's consideration of all available therapies would help ongoing individualization of therapy.



Participants provided reasons for not increasing their performance even further (see Figure, below), and either a need for additional education or a lack of confidence in considering all available ISM therapies continue to be ongoing concerns, showing that participants still recognize their need for education.

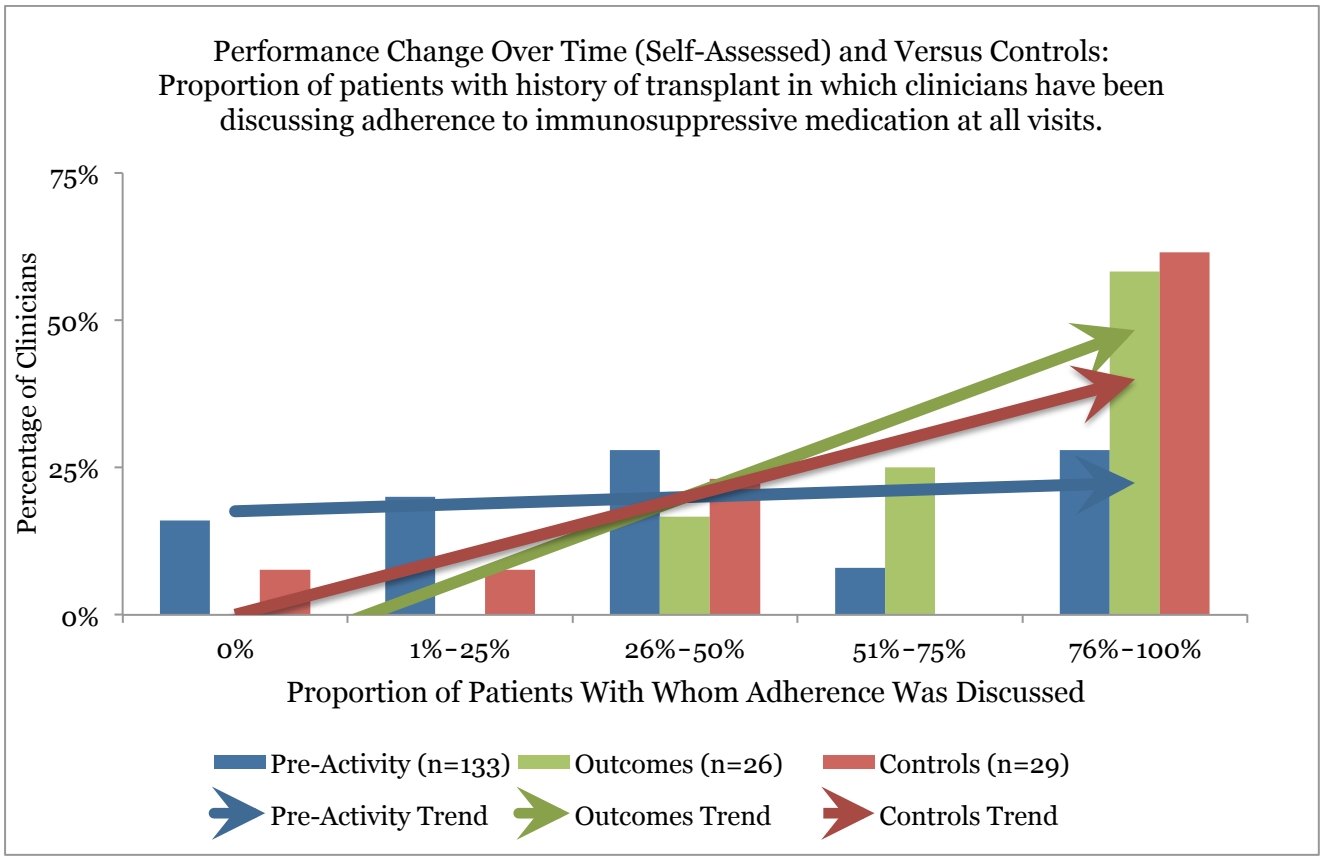


Participants' comments on considering all available ISM therapies included these: 1) "Once one starts on a particular course of immunosuppression, there has to be very good reason to switch; if it [the reason] exists then should be done and then the patient monitored especially closely"; and 2) "Transplant stable, no need to change." These thoughts need to be addressed by the faculty of future educational initiatives, as they moderate the competence and performance outcomes data shown above.

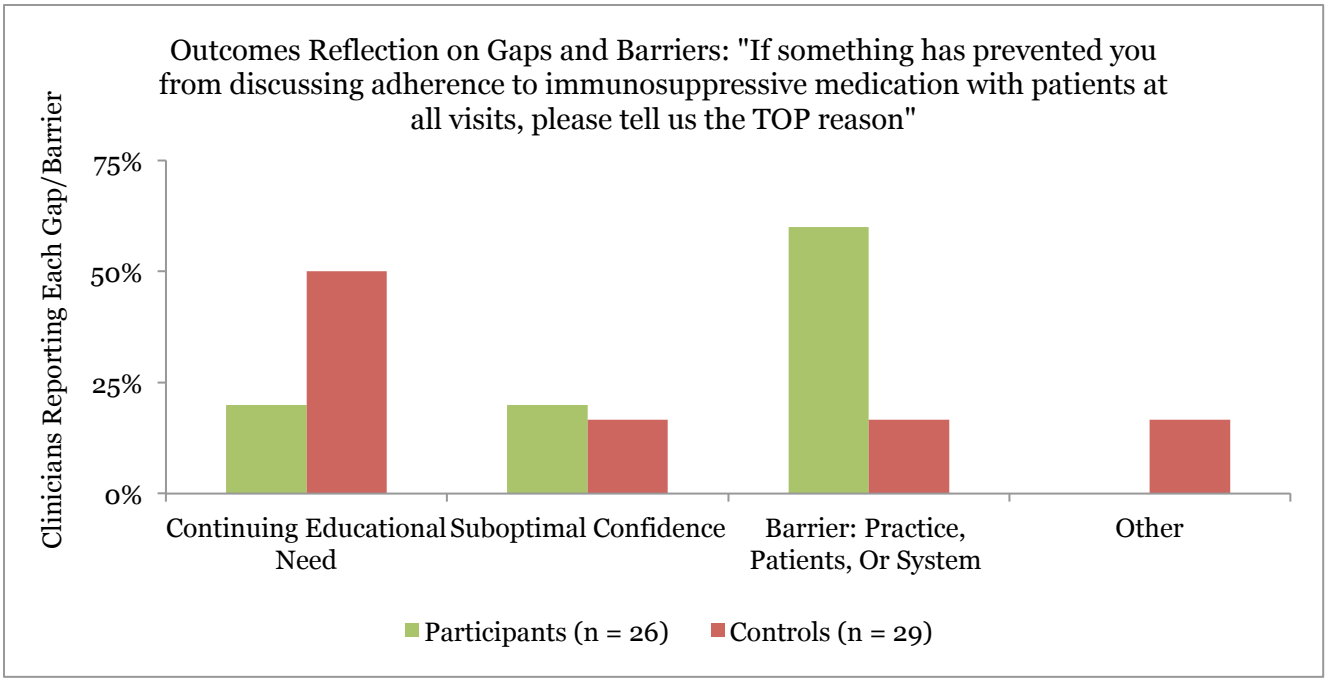
Overall, participants' strong consideration of all available therapies for tailoring ISM to individual patients, as well as the desire for more education in the future, is an indication that participants are seeking improved awareness that the choice of ISM regimen does affect the five-year survival of the graft.

Discussing adherence to ISM with patients at all visits

Change over time by participants, as well as differences between participant and control groups, were great in magnitude (see Figure, below). In the outcomes survey, *all responding participants* had been discussing adherence to ISM with *many to most patients at all visits*: 58.3% with over three quarters of patients, another 25.0% with over half of patients, and the remaining 16.7% with at least one quarter of patients (n = 26). Meanwhile, performance among controls was virtually no different from that of participants with the highest proportion of patients (76% – 100% of patients), yet 23.1% of controls were discussing adherence with at least one quarter of patients, and 15.4% of controls were discussing adherence with less than one quarter of patients (n = 29).



Participants provided reasons for not increasing their performance even further, and controls (see Figure, below) more often cited a need for additional education or lack of confidence with discussing adherence at all visits than participants did:

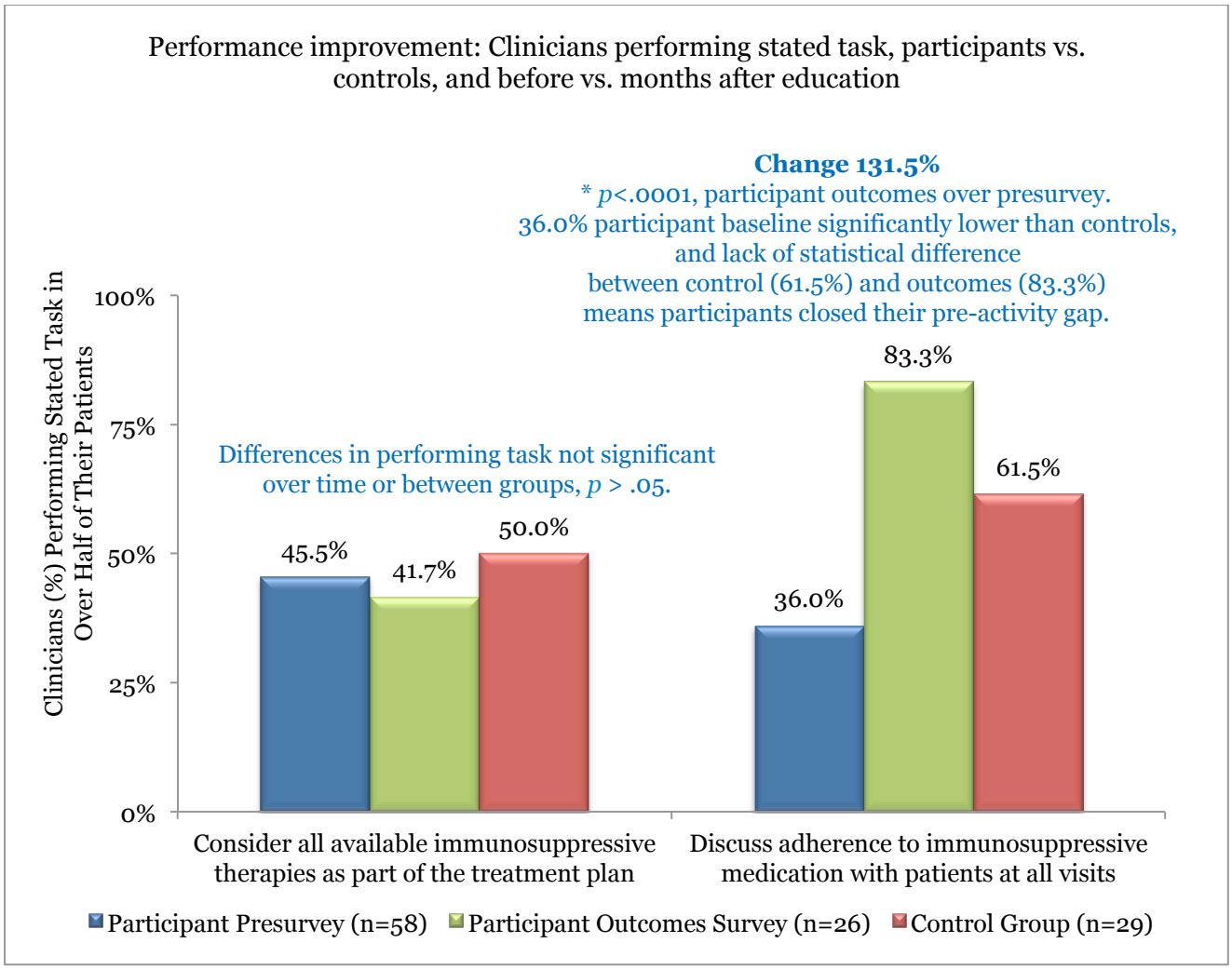


This shows that participants are ready and able to discuss adherence and to partner with patients.

Educational Activity Impact

CME Outfitters faculty and content helped clinicians no longer blame patients' presumed willfulness, ignorance, or misunderstanding of the importance of ISM, and they responded with appropriate performance at eight months after participating in education: 1) participants are more ready than controls to switch agents or to once-daily formulations to help individual patients remain adherent, and a higher percentage of participants than of controls overall stated that they actually were considering all available ISM therapies over the months; and 2) all responding participants had been discussing adherence to ISM with many to most patients at all visits. They are actively helping patients overcome forgetfulness with technologies and considering different agents and once-daily formulations to help patients with side effects that reduce adherence to graft- and life-saving ISM. They further comprehend patient needs and attitudes regarding ISM, the role of ISM-selection in graft rejection, and supportive technologies to enhance patient adherence to ISM.

Participation in this activity reduced clinicians' pre-activity practice gaps in discussing adherence to immunosuppressive medication with patients at all visits, producing a 131.5% change ($p < .0001$), in participant outcomes over presurvey data (see Figure, below). Because the participant baseline was significantly lower than controls ($p = .0125$), the lack of statistical difference between control data (61.5%) and outcomes data (83.3%) means participants selected appropriate education to address self-identified needs.

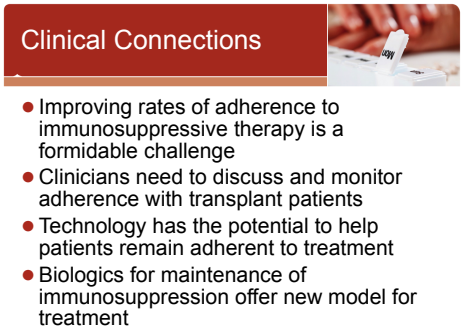


Although differences in considering all available immunosuppressive therapies as part of the treatment plan were not statistically significant across time periods or between groups ($p > .05$), competence data suggest that participants actually were behaving differently: consider evidence from the outcomes case vignette showing that participants were more likely than controls to switch the therapeutic regimen when a case patient ("Robin") with lifelong adherence to ISM had been experiencing GI issues with MMF that could have led her to reduce her adherence to medication.

Clinicians who masterfully communicate with patients about treatment needs AND technologies to support self-administration of ISM will help patients achieve longer survival of the graft, with fewer complications, emergencies, and needs for regrafting. With the modern focus on documenting positive patient outcomes from clinical encounters, clinicians can use their better preparation to support ISM adherence—this is true both for specialized clinicians who frequently see patients with history of transplant AND for primary care clinicians who must care for the whole patient and coordinate care in a patient-centered medical home model.

Continued Education Is Needed

As stated in the *Clinical Connections* during the CME activity, improving rates of adherence to immunosuppressive is a formidable challenge, but a challenge that is essential to positive long-term outcomes in transplant recipients. ISM adherence is associated with clinicians' understanding of patients' needs, support network, barriers to medication, and attitudes toward both graft survival and immunosuppressive medication. The first step to better care is to use appropriate communication methods on a frequent basis to improve the clinician-patient relationship, treatment-optimization, and patient adherence, and the second is to recommend that patients use modern tools and technologies to fit chronic self-administration into their daily habits.



Ensuring adherence to medication is an ongoing process that requires continual education and reinforcement. Future education is needed to sustain the benefits to patients that occur when clinicians consistently incorporate whichever of the available agents and formulations best suit each patient's needs for efficacy and safety. Participants stated a clear desire for more education on available therapies to help them tailor ISM to individual patients to improve adherence and improve long-term patient outcomes.