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Evaluating the Effectiveness of a Medication Adherence Module on Immunosuppressant Adherence: Secondary Analysis of Two Hybrid Implementation–Effectiveness Randomized Control Trials (RCTs)

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Background

Reduced medication adherence (MA) to immunosuppressants (IS) (31-89%)(1) after allogeneic stem cell transplantation (alloSCT) is linked to poor clinical outcomes(2). MA support for the 3-6 months post-alloSCT is needed.

MA is defined as *"the process by which patients take their medications as prescribed"* (p. 697)(3); implementation MA (*"the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen[…]"* p. 697)(3) is the key phase post-alloSCT.

Theory-based, multilevel interventions utilizing behavior change techniques (BCTs)(4) and eHealth delivery(5), embedded in integrated care models (ICM), showed efficacy in trial settings to improve MA, yet barriers remain in translating this evidence to real-world setting(6).

Implementation science methods help embed MA interventions into routine care(6).

Aim

To evaluate the **effectiveness** and the **delivery** & **app usage** of an advanced practice nurse (APN)-led, eHealth-facilitated MA module within the SMILe-ICM on IS implementation MA in the first 3 months post-alloSCT.

Intervention description

Intervention functions. Education, training, modeling, persuasion, and enablement, spanning 24 BCTs.

Two delivery modes. Face to face during routine visits, and eHealth via SMILeApp (patient) & SMILeCare (APN).

Delivery during routine visits.

- *Pre-discharge (Visit 1):* Focused education on IS regimen and consequences of non-adherence; set up medication routine (pillbox/app/cues); co-create a concrete goal and action plan; demonstrate and rehearse key steps.
- *Early outpatient (Visits 2–3):* Review the goal & give brief reinforcement; if present, troubleshoot barriers & adjust the plan.
- *Subsequent visits (Visits 4+):* Compare behavior with goals using self-reported data; provide feedback; target lapses with problem-solving.

SMILeApp. Patients log daily IS intake in SMILeApp; APNs monitor entries and, if needed, initiate phone/clinic follow-up with tailored BCTs.

Tailoring & escalation rules. In case of MA challenges → step-up support (extra BCTs, additional phone contacts/visits).

Methods

Design. Secondary analysis of two single-site hybrid effectiveness–implementation RCTs (Freiburg [FiB], Basel [USB]; 2020–2023).

Setting. FiB and USB perform 80-110 adult alloSCTs annually. Neither has implemented systematic MA support in their routine follow-up care.

Participants. 152 (n_{FiB} = 72, n_{USB} = 80) adults undergoing alloSCT; 1:1 randomization to intervention group (**IG**) and usual care group (**UCG**), stratified by age, sex, and living status; allocation via secuTrial®; no blinding.

Outcomes. Trajectory of *implementation adherence* over the first 3 months, operationalized as the proportion of adherent patients at each visit.

Measures & definitions. *Primary:* BAASIS© self-report, monthly (all sites), MA defined as no missed doses, no drug holidays (>2 doses), dosing within ±2 hours, no dose reductions. *Secondary*: MEMS® Button electronic monitoring (EM; USB only), MA defined as all expected doses taken within ±2 hours of schedule. Daily values aggregated to monthly proportions.

Analysis.

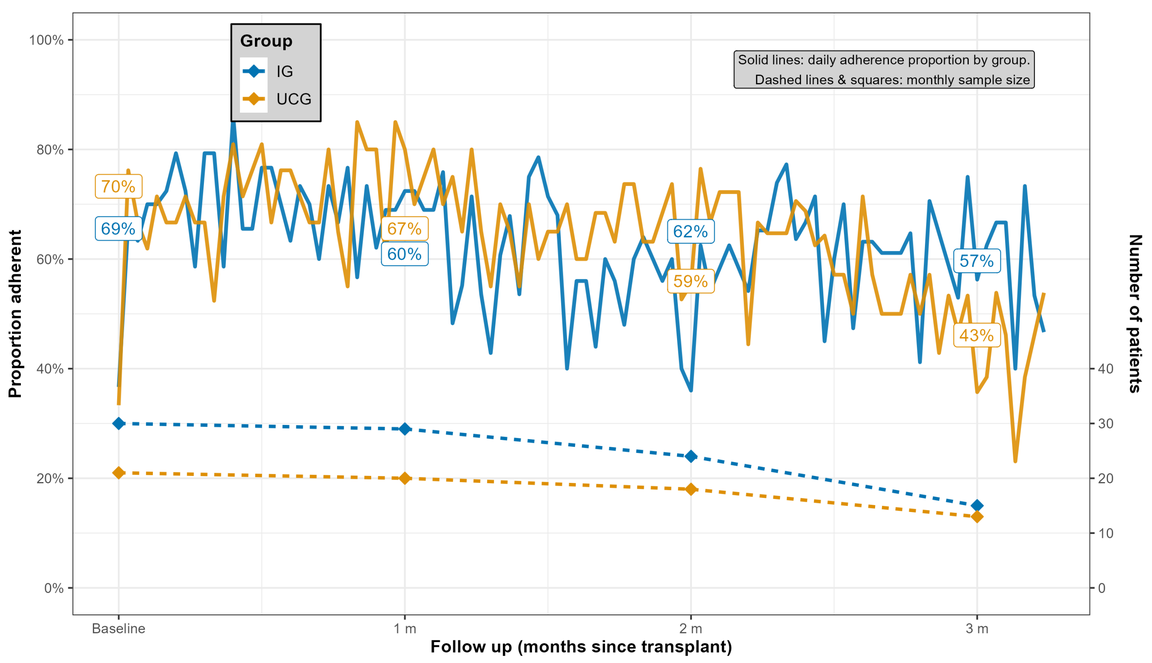
1) Descriptive analysis & generalized estimating equations (GEE, binomial logit) with group × time (months) interaction, adjusted for center, age, sex, living status, education for the patients still on IS.
2) Descriptive analysis of BCT delivery and app usage.

Results - Effectiveness

BAASIS©, both centers, descriptive: IG trended higher at 1 month (94% vs 86%) and 2 months (84% vs 73%). By 90 days post-alloSCT, MA converged (77% vs 78%).
Adjusted GEE: No significant IG–UCG differences at any month; MA decreased over time in both groups; group × time interaction not significant (NS).

MEMS®, USB, descriptive, Fig 1. Baseline MA was similar (69% vs 70%). Both groups declined over 3 months, with slightly higher IG levels (57% vs 43% at 3 months).
Adjusted GEE: Group × time interaction NS.

Figure 1. Proportion of adherent patients at each visit (MEMS®)



Results - BCT Delivery and App Usage

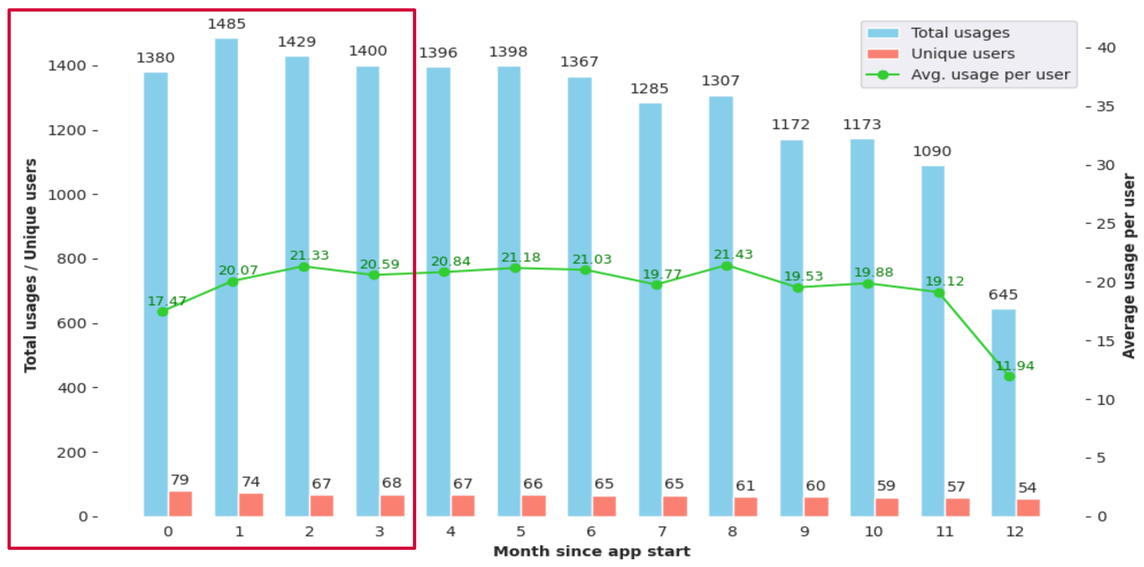
Delivery rate of BCTs over all visits was 84%; FiB had higher delivery rate (92%) than USB (78%).

Most frequently delivered BCTs in both centers:

- **Social reward**: 444/471 (94%);
- **Monitoring of behavior by others without feedback**: 323/347 (93%);
- **Information about health consequences**: 161/196 (82%).

~20 usages each month of the SMILeApp throughout the trial (Fig. 2).

Figure 2. SMILeApp usage over entire study period, first 3 months highlighted



Conclusions

The results showed a positive trend in self-reported MA in first two months, though this effect did not sustain over time. No significant group differences found as measured by EM.

The majority of BCTs was implemented as planned during routine visits, with differences between centers; patients used SMILeApp regularly.

Enhancing the MA module by incorporating the most effective BCT, i.e., EM-outprint feedback, should guide intervention planning, while ensuring feasibility and cost-effectiveness in daily clinical practice.

References

(1) Visintini C, Mansutti I, Palese A. Medication Adherence among Allogeneic Haematopoietic Stem Cell Transplant Recipients: A Systematic Review. Cancers. 2023;15(9):2452. doi:10.3390/cancers15092452; (2) Gresch B, Kirsch M, Fierz K, et al. Medication nonadherence to immunosuppressants after adult allogeneic haematopoietic stem cell transplantation: a multicentre cross-sectional study. Bone Marrow Transplant. 2017;52(2):304-306. doi:10.1038/bmt.2016.262; (3) De Geest S, Zullig LL, Dunbar-Jacob J, Hughes D, Wilson IB, Vrijens B. Improving medication adherence research reporting: ESPACOMP Medication Adherence Reporting Guideline (EMERGE). Ann Intern Med. 2018;169(1):30-35. doi:10.7326/M18-0543; (4) Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews. 2014;(11). doi:10.1002/14651858.CD000011.pub4; (5) Pouls B, Vriezekolk J, Bekker C, et al. Effect of Interactive eHealth Interventions on Improving Medication Adherence in Adults With Long-Term Medication: Systematic Review. Journal of Medical Internet Research. 2020;23(1):e18901. doi:10.2196/18901; (6) Kostalova B, Ribaut J, Dobbels F, et al. Medication adherence interventions in transplantation lack information on how to implement findings from randomized controlled trials in real-world settings: A systematic review. Transplantation Reviews. 2022;36(1):100671. doi:10.1016/j.trre.2021.100671