KS_B Kantonsspital Baden Ort der Gesundheit

ETH zürich

GSASA Forschungsprojekt nationaler Tragweite 2023
iPROACTIVE (Ausschreibung Nr. 14)
Interim report 2, November 2025

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1 Summary

1.1 Project achievements

Since the previous, first iPROACTIVE project report, we have completed all foundational development milestones and successfully transitioned to trial implementation. Specifically, we: (1) conducted a systematic review of opioid exit plans that informed the design of our intervention; (2) synthesized determinants of successful deprescribing of hospital-initiated opioid analgesics and operationalized them partially in a Python-based dose-reduction calculator; (3) developed an evidence-based intervention framework, including a reproducible workflow blueprint for interprofessional collaboration; (4) produced and user-tested a patient brochure to enhance comprehensibility of safe opioid use recommendations; (5) built an automated dashboard within our hospital information system to identify and characterize inpatients receiving opioid therapy; and (6) finalized a study protocol to evaluate the efficacy of an interprofessional opioid deprescribing service in hospitals, which has been approved by the responsible ethics committee. Achievements 1–4 have been disseminated by publication, whereas dissemination of achievements 5 and 6 is currently underway.

1.2 Status

The iPROACTIVE trial was initiated on 23 June 2025, and patient recruitment is ongoing at the Kantonsspital Baden AG. An interprofessional team of hospital pharmacists and physicians has been established to deliver individualized opioid reduction plans to participants randomized to the intervention arm. This team applies the evidence and tools developed in earlier project phases, including deprescribing determinants, the dose-reduction calculator, and the patient brochure, to formulate individualized deprescribing protocols.

1.3 Next steps

The trial will continue until the target sample size is reached (N = 86) and all participants have completed follow-up (three months). Thereafter, the dataset will be analyzed, and the results will be disseminated and reported to GSASA.

1.4 Project status overview

	Milestones	Planned time to completion	Completed
1	Development of an opioid tapering intervention	August 2024	Yes
2	Development of an opioid dashboard to screen patients	September 2024	Yes
3	Development of a study protocol and trial documents	December 2024	Yes
4	Ethics submission, trial initiation, recruitment of participants	March 2025	Yes
5	Trial completion	September 2026	No

The details of the achievements and status of the iPROACTIVE subprojects are described below.

1.5 Expenditure overview (Nov 2025)

Item	Expenditure (CHF)
Focus group: catering	123.70
Focus group: financial compensation of participants (CHF 200/ person)	1’000.00
Focus group: MAXQDA licenses	332.25
Delphi questionnaire: financial compensation of participants (CHF 50/ person)	200.00
ETH Digital Trial Intervention Platform: study counselling	2’328.00
ETH Digital Trial Intervention Platform: study support (data management, monitoring, etc.)	13’772.60
Statistics counselling	650.00
GCP training team members	58.00
Licenses questionnaires (PROMIS pain, SOWS, SATMED-Q, PCS)	3’801.40
Development patient information material	6’000.00
Print patient information material	185.95
Ethics approval	1’000.00
	Total: 29’451.90

2 Subprojects

2.1 Systematic literature review of published OEPs

As previously reported, we aimed to identify effective strategies for reducing postoperative opioid use at hospital discharge through a systematic review of the literature in noncancer patients (1 January 2000 - 4 June 2024). Eight studies met eligibility criteria from 2,585 abstracts screened. Of the six trials that assessed OEP effectiveness, four showed statistically significant reductions in opioid use. Studies were primarily conducted in North America focusing on orthopedic or neurosurgical patients, with interventions typically including patient education and individualized reduction protocols. Study quality was variable (three rated as high quality, none as low risk of bias) due to study design (pre-post implementation) that limit causal inference. However, results suggest OEPs are effective and safe for reducing postoperative opioid use. This step allowed a student to work on her practice-oriented master's thesis.

Publication:

Rainer M, Ommerli SM, Burden AM, Betschart L, Stämpfli D. Opioid exit plans for tapering postoperative pain control in noncancer patients: a systematic review. Patient Saf Surg. 2024;18(1):25. doi:10.1186/s13037-024-00408-w

2.2 Intervention development for the deprescription of hospital-initiated opioid analgesics

To develop a locally adapted OEP, we conducted a multi-level consensus study with prescribers of opioid analgesics and patients who had received opioid analgesic therapy. This study employed focus group discussions, a Delphi survey, and structured individual interviews. We synthesized clinical determinants of successful deprescription of hospital-initiated opioids across six medical subspecialties (Figure S1a), developed an opioid reduction calculator programmed in Python (Figure S1b), and created a patient brochure. These components were integrated into a practical blueprint (Figure S1c) that outlines a collaborative workflow between an opioid deprescribing service and the treating physician to safely reduce opioid analgesics in hospitalized patients with planned tapering or discontinuation of opioid therapy.

Publication:

Rainer M, Sebesta E, Wertli MM, Burden AM, Stämpfli D. Optimizing deprescribing of hospital-initiated opioids: a multi-level consensus study bridging evidence, expertise, and patient perspectives. Sci Rep. 2025;15(35850). doi:10.1038/s41598-025-19823-9

The patient brochure elements were turned into a template in collaboration with the «Zürcher Hochschule der Künste» and is available online via the [pain medicine] subsection of «PEPra - Unterstützung zur Prävention in der Praxis».

2.3 Developing a dashboard to identify patients with opioid prescriptions

We aimed to map the prevalence of opioid use at Kantonsspital Baden AG as a prospective study site for the actual iPROACTIVE trial. Using electronic health records, we defined variables to aggregate patient-level and physician-level data in an automated dashboard based on a template provided by our infectious diseases and informatics department. The dashboard software Qlik-Sense® was used to retrieve and aggregate data from our hospital information system (KISIM®) based on ATC codes. We identified over 600 inpatients in 2023 receiving prolonged opioid therapy (three or more consecutive days) primarily in orthopedics, internal medicine, and neurosurgery who were potential candidates for an opioid deprescribing intervention. We characterized their clinical profiles to inform eligibility criteria for a planned clinical trial. Publication is in preparation. This step allowed a student to work on his practice-oriented master's thesis.

2.4 Preparation of the clinical trial

We designed the iPROACTIVE trial to evaluate the effectiveness of the intervention developed in Subproject 2.2 in the patient population identified in Subproject 2.3 as being at risk for persistent opioid use. In accordance with Swiss regulations, a Chapter 4 clinical trial is required for parallel-group studies intended to estimate treatment effects. To meet this requirement, we developed a confirmatory, single-center, prospective, two-arm, open-label, stratified, randomized controlled trial. Eligible participants are adult inpatients who initiated or escalated opioid therapy during hospitalization and have a planned opioid taper or cessation, with at least three consecutive days of inpatient opioid use. Exclusion criteria include inability to follow educational interventions (e.g., non-German speakers, cognitive impairment or dementia), cancer-related pain, pregnancy or breastfeeding, critical or intermediate care, and life expectancy under one year. The primary endpoint is time to return to prehospitalization morphine milligram equivalents, analyzed using the exact log-rank test applied to Kaplan–Meier curves. Secondary endpoints include pain interference scores, opioid withdrawal symptoms, opioid requirements for analgesia, and satisfaction with pharmacological treatment. Power calculations yielded a required sample size of 86 participants (43 per arm). The trial was approved by the responsible ethics committee "Ethikkommission Nordwest- und Zentralschweiz" (EKNZ) on 21 March 2025, and is registered with the [Swiss National Clinical Trials Portal (SNCTP000006418)] as well as the WHO-approved [German Clinical Trials Register (DRKS00036364)]. The study protocol has been submitted for publication.

2.5 Conducting the opioid deprescribing trial

The iPROACTIVE trial commenced as projected in late Q2, beginning on 23 June 2025, following delays in finalizing the clinical study agreement between ETH Zurich and the hospital. Patient screening at Kantonsspital Baden AG has proceeded weekly without interruption. The site maintains a weighted monthly average of 336 opioid-treated inpatients, of whom approximately 19 meet eligibility criteria monthly. To date, 24 participants have been enrolled (28% of the target sample size), with a mean recruitment rate of 5.11 participants per month (June–October 2025). Nine participants have been randomized to the intervention arm, each receiving an individualized opioid reduction plan developed collaboratively by a hospital pharmacist and physician. Eight participants have completed the study to date. Figure 1 summarizes recruitment metrics and ongoing trial progress.

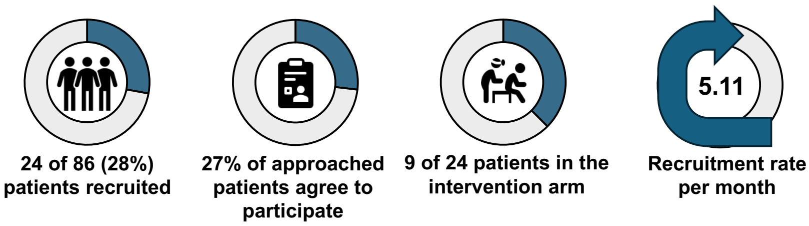

Figure 1 Study recruitment key metrics and progress indicators.

3 Outlook

Based on the present recruitment rate, we project the completion of the iPROACTIVE trial in February 2027, corresponding to the final participant's last 3-month visit following enrollment through November 2026. This amounts to a delay of + 29 weeks compared to our original schedule. However, the financing is secured.

Following a somewhat unexpected restructuring at ETH Zurich, the ETH Digital Trial Intervention Platform is being dissolved. Although a newly created department will continue to provide support in data management, it will no longer be responsible for study monitoring. Discussions are underway with the Department of Clinical Research at the University Hospital of Basel, and a favorable offer has been made. However, and again, difficulties in agreeing on the general terms and conditions of two institutions remain.

We would like to thank GSASA and its partners once again for their support of the iPROACTIVE project. It is only thanks to this financial support that the development of the various elements and the ongoing clinical trial are possible.

Written by: Dominik Stämpfli, Marcel Rainer, Peter Wiedemeier
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4 Supplement

Figure S1a

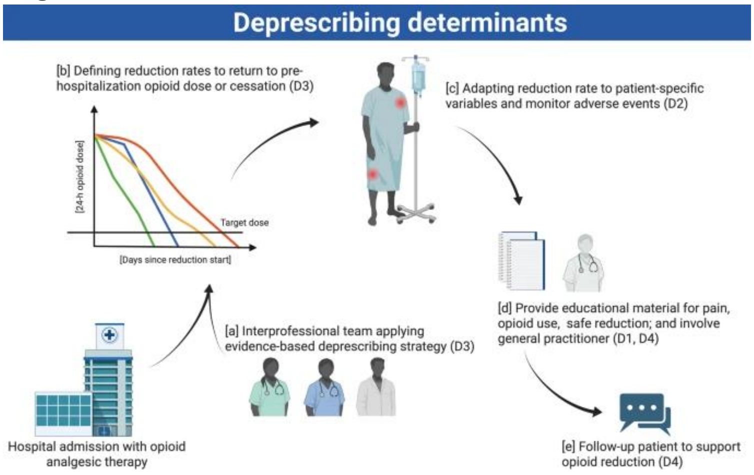

Figure S1b

OpiTaper

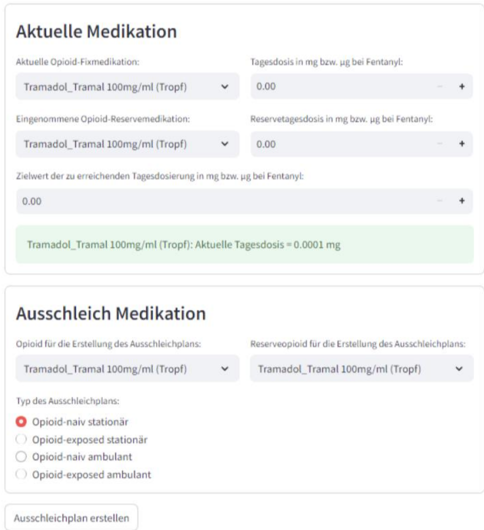

Figure S1c

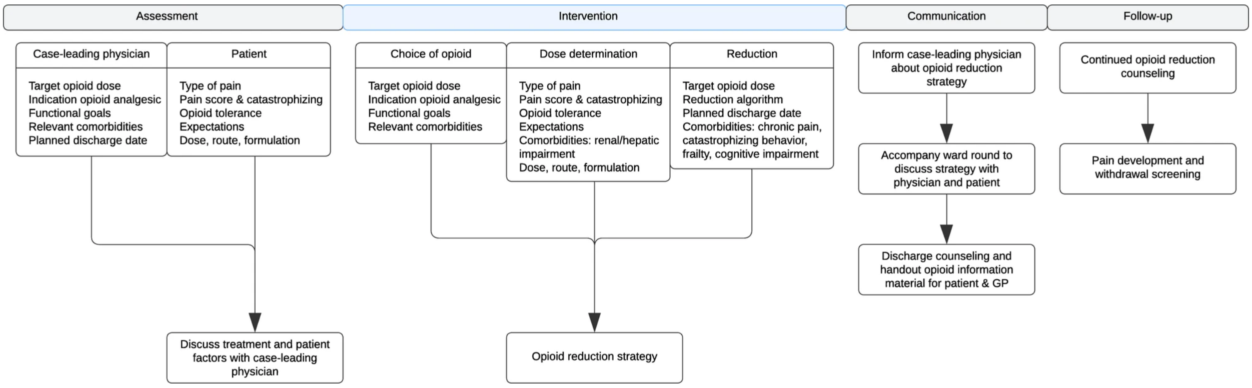

Figure S1a-c Foundational elements synthesized within the iPROACTIVE project to develop a deprescribing intervention suitable for clinical trial evaluation, adapted from the dissemination of Subproject 2.2.[1]

S1a: Key determinants for implementing an interprofessional deprescribing service, arranged in their preferred sequence from hospital admission through individualized pain management to structured follow-up.[1]

S1b: "OpiTaper", a Python-programmable opioid dose-reduction calculator that proposes reduction trajectories based on patient opioid use history (chronic vs. new use) and distinguishes between initiating deprescribing in the hospital versus the community.

S1c: Workflow blueprint outlining the structured collaboration between hospital pharmacists and physicians for delivering an opioid deprescribing intervention.[1]

[1] Rainer M, Sebesta E, Wertli MM, Burden AM, Stämpfli D. Optimizing deprescribing of hospital-initiated opioids: a multi-level consensus study bridging evidence, expertise, and patient perspectives. Sci Rep. 2025;15(35850). doi:10.1038/s41598-025-19823-9