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1 Summary

1.1 Background

The global opioid crisis has prompted a re-evaluation of pain management practices, particularly in hospitals where opioid exposure is high. Despite increasing concerns about opioid-related harms in Switzerland, there is a lack of standardized protocols for tapering opioid therapy, leading to potential long-term opioid use and dependence. While previous studies have shown the potential benefits of opioid tapering interventions, their generalizability to the Swiss healthcare context remains unclear due to variations in practice and patient populations. This project aims to develop a novel, hospital-based opioid exit plan (OEP) to minimize opioid consumption and assess its effectiveness in a prospective trial.

1.2 Objectives

The clinical use of opioids for pain control is varied. First, we aimed to develop an opioid tapering tool that is adaptable to the different clinical situations of patients. Second, we are setting up a randomized controlled trial to assess the effectiveness of an interprofessional clinical counselling service to reduce opioid use. The primary objective of the trial is to reduce the number of treatment days with opioids, as prolonged use is a major risk factor for opioid dependence. The secondary objectives are to assess the morphine milligram equivalents needed for effective pain management and to monitor patient safety during the reduction process, focusing on withdrawal symptoms, and the impact of pain on daily activities.

1.3 Methods

Based on a systematic review of OEPs and current pain management guidelines, we conducted a focus group interview to synthesize elements of the key considerations for reducing opioids in patients with acute or chronic pain. These elements were then disseminated in a Delphi survey of physicians with different medical backgrounds. The qualitative research methods informed the development of an opioid reduction planner, a reduction plan template, and patient information on opioids. These elements will be central components of a single-center, investigator-initiated, prospective, open, randomized controlled trial.

1.4 Project status

	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	No
5	Trial completion	September 2026	No

1.5 Expenditure overview (Dec 2024)

Item	Expenditure (CHF)
Focus group: catering	123.70
Focus group: financial compensation of participants (CHF 200/ person)	1000.00
Focus group: MAXQDA® licenses	332.25
Delphi questionnaire: financial compensation of participants (CHF 50/ person)	200.00
ETH Digital Trial Intervention Platform: project management (1.5 h)	180.00
ETH Digital Trial Intervention Platform: data management (3.27 h)	392.40
ETH Digital Trial Intervention Platform: quality management (14.63 h)	1755.60
	Total: 3983.95

2 Subprojects

2.1 Systematic literature review of published opioid withdrawal plans

We wanted to know what OEPs have been developed, studied, and published. A systematic review of the literature was conducted to assess the effectiveness and design of OEPs for tapering postoperative pain management in noncancer patients. The main aim was to identify effective strategies for reducing opioid use after discharge from hospital. The review was conducted according to the PRISMA guidelines, and, with the help of a library specialist, the databases PubMed and Embase were searched for trials published between 1 January 2000 and 4 June 2024. A total of 2,585 abstracts were screened, of which eight studies met the selection criteria. Two independent reviewers assessed the abstracts and full texts. Data extraction focused on study characteristics, intervention components, and effectiveness. The included studies were primarily conducted in North America and focused on postoperative orthopedic or neurosurgical patients. Intervention designs varied, but often included patient education and individual tapering protocols based on predischarge opioid use. Six trials assessed the effectiveness of OEPs and four trials showed a statistically significant reduction in opioid use. The quality of the studies, which frequently used pre-post implementation study designs, was variable, with only three studies rated as high quality and none as low risk of bias. The results nevertheless suggest that OEPs are effective and safe for reducing postoperative opioid use, and encouraged us to develop an OEPs for our own hospital.

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 Conducting a focus group

To develop our own, locally adapted OEP, a stakeholder survey was conducted in the form of a focus group. The aim was to gather important opinions and expert knowledge about the current and best possible opioid treatment approach in our hospital. To this end, interactive discussions were held on prepared key questions and a representative case study was used. In addition to an overview of other patient brochures available in Switzerland, excerpts from current Swiss patient brochures were shown and discussed. Finally, the OEPs identified in the systematic literature review were presented and evaluated. The focus group was attended by five representatives of internal medicine (n=1), family medicine (n=1), pain medicine (n=1), and orthopedics (n=2). The focus group provided us with information on how to adapt the American models to local conditions and needs.

This step enabled a student to work on her practice-oriented master's thesis. A publication is in preparation.

2.3 Development of OpiTaper

Based on the focus group and the systematic literature review, a small tool was developed in Phyton to later assist the intervention team in the initial design of a reduction process. The tool allows the current opioids and dosages to be specified and a target opioid and dose to be set. Based on conversion factors and the reduction steps defined in the

focus group, a plan is generated for a daily adjusted dose and an adjusted pain reserve. The reduction steps can be slowed down by patient-specific factors such as opioid use prior to hospital admission, chronic opioid use, and catastrophizing behavior The reduction process generated in this way should be further individualized by the intervention team together with the case-leading ward physicians, so that a holistic therapy concept is developed for each individual patient, but with the clear aim of reducing opioids to the preadmission dose as consequently as possible.

2.4 Development of the patient brochure

The patient brochures, which serves as the basis for patient education for patients leaving hospital on opioids, was based on existing brochures. These are published on the “PEPra – Prevention with Evidence in Practice”, PEPra.ch, for further use. We checked the comprehensibility of the leaflet according to the recommendations of Lampert and colleagues from Heidelberg (Lampert A, et al. Guidance on how to achieve comprehensible patient information leaflets in four steps. Int J Qual Health Care. 2016;28(5):634-638), and improved it in incremental steps that can be verified using the Flesch Reading Ease Score. The revised text fragments were tested on a local patient collective of 10 subjects and further improved through patient feedback. We will be working with the Zurich University of the Arts on the illustration and design of the brochure. This collaboration also plans to create an educational video so that patients can review key information about their opioid therapy at home after an already busy discharge day. The final patient brochure will then be tested again on a local patient collective of 10 subjects before a final evaluation by us and other stakeholders, as recommended by Lampert and colleagues.

A publication is in preparation.

2.5 Conducting a Delphi survey

Important elements of our intervention, the opioid reduction process using the OpiTaper and the need for patient education, as well as the embedding of our project in the overall structure of our hospital, were examined for consensus in an extended Delphi survey. Eleven representatives from pain medicine (n=2), internal medicine (n=4), rheumatology (n=1), visceral surgery (n=2), orthopedics and traumatology (n=1), and spine surgery (n=1) participated in the Delphi survey. Fifty statements were tested in two rounds of questioning, with six statements being modified after the first round to improve consensus. This step allowed us to show that the elements of our project were supported by different medical disciplines who are involved in the prescription of opioids in our hospital.

This step enabled a student to work on her practice-oriented master's thesis. A publication is in preparation.

2.6 Developing a dashboard to identify patients with opioid prescriptions

We needed a way to identify patients with an opioid prescription in our hospital. We used a dashboard developed by our infectious disease department and our IT department as a template: Qlik-Sense® is used to retrieve and aggregate data from our hospital information system (KISIM®) based on ATC codes. Our infectious disease department uses it to generate the required reports on antibiotic use. We have adapted this dashboard to our needs by preparing and importing drug data for opioids and relevant concomitant medications (other analgesics, laxatives, antiemetics, antidotes). Our own dashboard allows us to export aggregated data for all administrations of these drugs, including administrative information such as prescriber and ward, and medical data such as primary diagnosis. The dashboard has enabled us to identify the main prescribers of opioids, and therefore the main points of intervention, and to create patient profiles. We used the 2023 data to conduct a feasibility analysis for our planned clinical trial. Based on the top prescribers and the different patient profiles, we decided to define the potential study population as broadly as possible: All patients receiving opioids for more than three consecutive days should be considered for the trial. In 2023, this meant almost 600 patients.

This step allowed a student to work on his practice-oriented master's thesis.

2.7 Preparation of the clinical trial

We aim to evaluate the effectiveness of our intervention. According to Swiss law, a Chapter 4 clinical trial is required for studies using a parallel design to estimate effect sizes with a control cohort. This confirmatory, single-center, prospective, two-arm, open, randomized controlled trial is designed to address this requirement. The study population includes adults who have initiated or increased opioid doses during hospitalization, with planned cessation of opioid therapy. Eligibility criteria include patients with at least three consecutive days of opioid use, excluding those unable to follow educational interventions (e.g., non-German speakers, cognitive impairment, or dementia), those with metastatic cancer requiring treatment within the last 12 months, pregnant or breastfeeding individuals, patients in critical or intermediate care, and those with a life expectancy under one year. The primary endpoint is the time required to return to prehospitalization morphine milligram equivalents (MMEs), illustrated in a mock survival curve (Figure 1). Secondary endpoints include pain interference scores, subjective opioid withdrawal symptoms, MMEs required for analgesia, and satisfaction with pharmacological treatment. Preliminary power calculations estimate the sample size required to detect a significant difference to be of 84 participants per arm, for a total of 168 participants. Seven administrative documents have been prepared for the ethics application: Study protocol, informed consent form, monitoring plan, data management plan, investigator's brochure, staff & delegation list, adverse events reporting file.

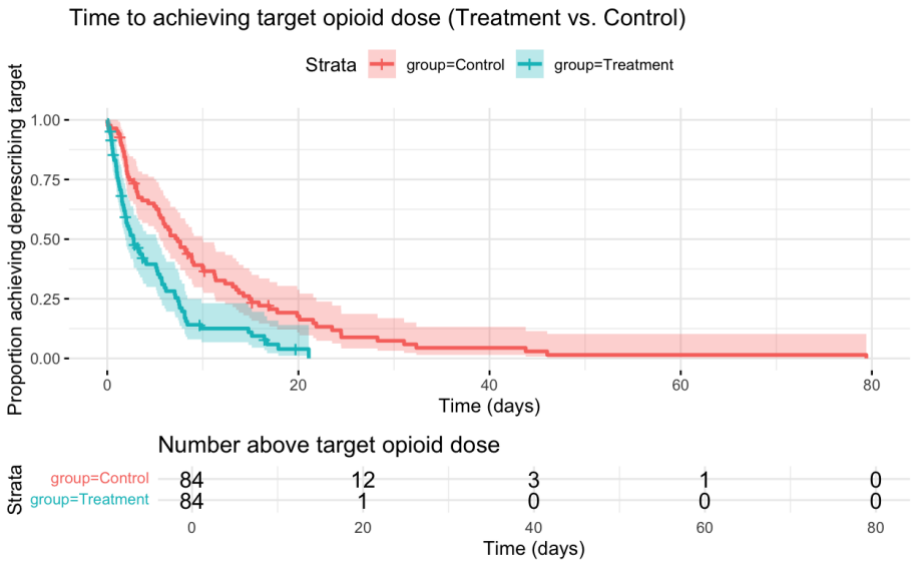

Figure 1 Mock survival curve of time to target opioid dose of a hypothetical study population after study inclusion.

3 Outlook

We will next proceed with the ethics submission to the "Ethikkommission Nordwest- und Zentralschweiz / EKNZ". An agreement will also be signed with the ETH Digital Trial Intervention Platform (dTIP), which will act as the designated clinical trial unit (CTU). The hospital's internal CTU will support patient recruitment. The trial is expected to start at the end of Q2 2025.

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

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