Juli 2023

Forschungsprojekte nationaler Tragweite
Vorlage für das Einreichen eines Projekts

Ausschreibung Nr. 14

Titel des Projekts	**iPROACTIVE: I**nterprofessional **P**artnership in **R**eduction of **O**pioid-related **A**dverse **C**onsequences **T**hrough **I**nno**V**ative **E**fforts	**Datum** 28.07.2023
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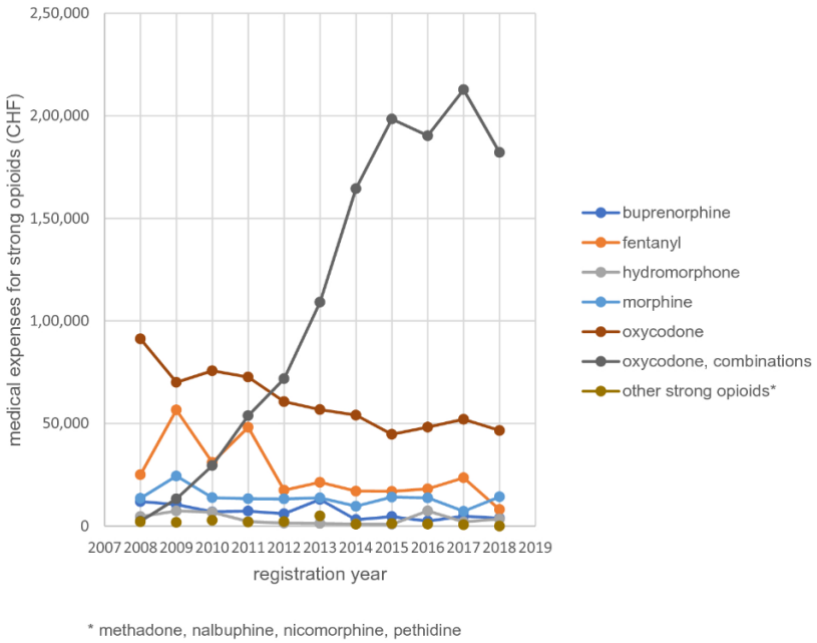
Literatur **Analyse von Literaturdaten**	Opioid misuse has emerged as a major public health epidemic in North America over the last two-decades. The burden of this crisis has had dire socio-economic and financial consequences[1]. While the opioid crisis in North America is well known, recent European studies have demonstrated a rise in opioid drug misuse in Europe as well. The Netherlands[2], France[3], and the United Kingdom[4] have all seen a trend in the use and harms of opioids. Switzerland is no exception, with studies showing rising use[5,6], poisonings[5], hospitalizations[7], and costs[8]. Additionally, recent Swiss studies have revealed an increase in the use of prescription opioids since 2006, as well as an increase in misuse, particularly for musculoskeletal injuries[6-8]. Importantly, these trends are driven by increasing use of strong opioids, such as oxycodone, which is also associated with significant increases in medical expenses [Figure 1]. These developments are worrying, as opioids were found to be the most prevalent primary drug among all visits to a	

large Swiss emergency department[9].



* methadone, nalbuphine, nicomorphine, pethidine

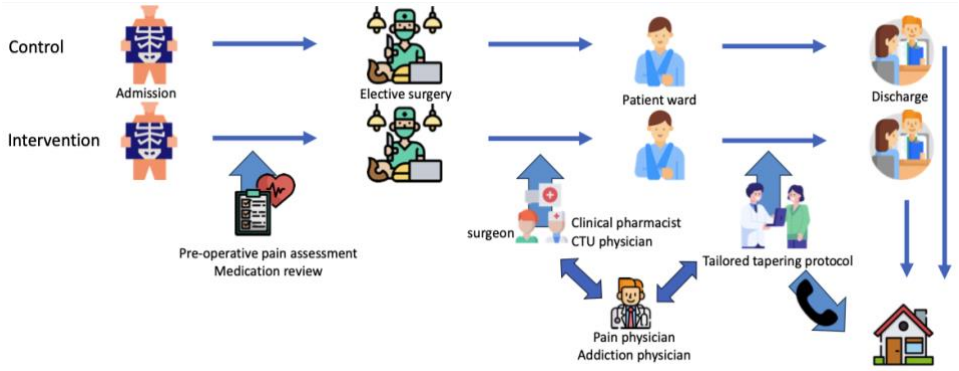
Figure 1 Change in analgesic-treated injuries per 1000 injuries that used at least one analgesic from 2008 to 2018[8].

In general, one-size-fits-all prescribing practices can lead to large quantities of unused opioids, which in turn can increase the risk of non-medical use and overdose[11]. Data from the US show that 67-92% of patients still have unused opioids at home and 42-71% of originally prescribed tablets are not used[12]. These findings emphasize the need for opioid stewardship strategies that establish strong guidance for new users to thwart opioid misuse, decrease the number of potential persistent opioid users, and minimize the potential for unintended harm.
General guidelines for de-prescribing opioid analgesics are being developed[13], but require complementary local efforts to help patients taper newly prescribed opioids after discharge from hospital. Within North America, opioid stewardship programs have been shown to reduce the number of opioid prescriptions or the number of prescribed tablets without compromising patient well-being, failing to achieve analgesia, or increasing requests for repeat prescriptions[14, 15, 16]. Furthermore, post-operative patients involved in opioid stewardship programs have fewer subsequent visits to the emergency department[15]. In response, US hospitals introduced multidisciplinary teams to install a transitional pain service[16-17]. These have been effective in reducing opioid prescriptions at discharge and facilitating sustained outpatient tapering[18].

Zielsetzungen des Projekts

Hypothese
Begründung
Erwartete Ergebnisse
Auswirkung für die Praxis

Hypothesis: We propose an interprofessional project targeting post-operative pain management with a focus on opioids. The primary objective of this new transitional pain service is a standardization to improve medication safety, patient care, and post-operative satisfaction. This is the first opioid stewardship program in Switzerland to involve physicians, nurses, and pharmacists. We expect that the development of an interprofessional team will result in optimized pain management and reduced outpatient opioid consumption without compromising patient satisfaction.
Rationale: Among all post-operative patients, more than 70% are prescribed opioids after discharge[19]. Specially, these patients are vulnerable to adverse drug events. Nearly 30% of all discharged patients experience adverse events, more than two-thirds of which would have been either preventable or manageable[20]. We have therefore chosen a setting that is vulnerable to drug-related problems, the transition of care, which the World Health Organization has identified as one of three key areas for action[21]. Both opioid-naïve and tolerant patients may receive opioids on discharge without information about the duration of analgesic therapy and/or clear tapering strategies[22-23]. Various trials have consistently shown significant reductions of persistent opioid use for non-cancer pain at hospital discharge[24], of prescription sizes and of unnecessary opioid prescribing[18]. Implementations were mainly supported by a pharmacist and study nurses. Thus, as an interprofessional team, we aim to intervene at the stage of hospital discharge, which has neither been shown to be associated with a “spill-over effect”[25] to other potentially inappropriate drugs nor worse pain outcomes[26].

	Expected results: A standardized discharge of post-operative patients can reduce the number of opioid prescriptions, persistent opioid drug use, oral morphine milligram equivalent doses, and aid in patient satisfaction and monitoring of analgesic efficacy as well as possible adverse drug reactions. **Impact on practice:** This interprofessional project enables surgeons, physicians, nurses, and pharmacists to provide a safe patient discharge with improved post-operative patient experience and appropriate prescribing of opioid analgesics. The established protocols, tapering strategies, and patient information will serve as inspiration or template for other Swiss hospitals.
Beschreibung der Methode **Protokoll, Methode, Analyse der Ergebnisse, Statistik**	**Study protocol** A tapering team is formed between physicians from different specialties, nurses, and hospital pharmacists. We will develop internal guidelines for the pain management in surgical patients with a focus on opioid-sparing. These will be based on a systematic review of opioid exit plans that our research group recently performed. Current deprescribing guidelines and evidence-based recommendations on multimodal pain management are used for refinement. A panel consisting of all relevant stakeholders including the pain service team, surgery department, internal medicine, hospital pharmacy, general practitioners, and patient representatives will be formed to reach consensus on the final opioid exit plan. **Design** This prospective study will be conducted as a two-armed randomized clinical trial.  **Figure 2** Scheme of the stratified RCT "iPROACTIVE" **Intervention arm** Patients scheduled for surgery are interviewed about their previous medication, pre-operative pain using the Morton PQRST pain assessment tool, and are educated about post-operative pain as well as opioid agonist therapy. Information is gathered about their current analgesic therapy, potential opioid tolerance and pain. After surgery, a clinical pharmacist or CTU physician participates in daily ward rounds of the assessed surgical patients to monitor medication therapy and pain management. Changes to the daily pain regimen are recommended using a pain medication classification with an approximate analgesic equivalence tool, focusing on early switch-to-oral and dose reductions. Opioid-tolerant patients receive a tailored multimodal therapy, while opioid-naïve patients are treated according to a standardized protocol. Pain or addiction specialists are involved in the management of complex cases. Patients will receive an informational sheet, and an individualized tapering plan created by the tapering team. Opioid usage in prior 24 hours will determine the maximum amount of opioids prescribed[27], a modified SOAPP-R questionnaire will detect problematic drug-related behavior, and a modified pain catastrophizing scale to detect patients at risk of chronic pain. Patients will be asked whether their concluded supply of prescription pain medication after discharge is sufficient or not. This counseling will be communicated to the patient upon discharge and in a letter to their general practitioner or responsible provider. Patients will be followed up after discharge by phone calls. **Control arm** A comparison group of two-to-one patients will be used as control group receiving standard care. These patients will not receive the pre-operative assessment, the informational sheet, the tapering plan, nor discharge counseling. However, they will be followed up with the same series of phone calls. **Selection and exclusion of subjects** All patients 18 years of age or older who are opioid-naïve defined as no intake of

	opioid drugs 30 days prior to surgery or opioid-tolerant are included. Exclusion criteria are cancer, sickle cell disease, substance use disorder, suicidality, palliative and end-of-life care. Although the proportional hazard ratio may not be met due to potentially differing follow-up times, we expect robust results due to consistent accrual patterns in patient recruitment[28]. Eligible patients are allocated in the treatment or control group by stratified randomization based on pre-operative opioid use. We will assess the balance of relevant confounding factors such as education level, employment status, marital status, smoking history, surgical approach, outpatient use of benzodiazepines or gabapentinoids. Unbalanced grouping will be adjusted in the analysis. We expect high patient engagement as robust participation was shown in similar US interventional studies[15]. **Adverse Events** Adverse events whether related or unrelated to the multimodal management of post-operative pain will be recorded and reported to the responsible authorities according to good clinical practice (GCP) guidelines. **Statistics** An a priori power calculation based on a binomial test (type I error (alpha) = 0.05, type II error (beta) = 0.2) yielded 80% power assuming the same effect size as in previous studies[22, 29, 30] recruiting 30 patients in the control group and 50 in the treatment group. To avoid attrition bias, an intention-to-treat analysis will be included in addition to statistical tests. **Data handling, recordkeeping** The digital Trial Intervention Platform (dTIP) will support all aspects of data collection, management, storage, and processing according to GCP guidelines.
Ort (e) der Studie **Institute, die am Forschungsprojekt teilnehmen**	Kantonsspital Baden, Im Ergel, 5404 Baden Rehaklinik Baden-Dättwil, Im Ergel, 5404 Baden
Outcomes **Erwartete Hauptergebnisse**	**Primary outcome:** Reduction of oral morphine equivalents to pre-hospitalization dosage after three weeks of discharge **Secondary outcomes:** • Time to zero oral morphine equivalents • Withdrawal symptoms or adverse drug reactions • Pain control and patient satisfaction
Nationale Tragweite **Aspekte hervorheben, die einen nationalen Impact rechtfertigen (z.B. Bedeutung der Ergebnisse, multizentrisch, interdisziplinär)**	This study proactively addresses a potential opioid crisis, ultimately reducing opioid burden in post-operative patients, avoiding unnecessary opioid therapy continuation, and opioid poisonings. Also, this study is in line with the National Strategy for the Development of Quality in Health Care for 2022-2024 proposed by the Federal Office of Public Health, which promotes the implementation of the "Medication Without Harm" action plan as a management tool to mitigate clinical risks[21, 31]. In addition, this project will further strengthen the interprofessional collaboration between physicians, nurses, and pharmacists, and establish a nationally emerging opioid stewardship in a Swiss hospital, with hospital pharmacists at the forefront of a patient-centered service.
Planung **Vorgesehener Zeitplan Etappen (milestones)**	**Mar-Aug 2024:** Interprofessional development of internal guidelines to reduce opioid prescribing at discharge and ensure safe outpatient tapering. Design of an informational sheet to inform and visualize opioid tapering to patients. **Sep-Nov 2024:** Ethics approval, implementation of recommendations **Jan-Jul 2025:** Initiation of the trial, recruitment of patients, study monitoring **Aug-Sep 2025:** Outcomes and data collection of preliminary results to compare percentage of persistent opioid use. Continuous analysis of results. **Jan-Mar 2026:** Completion of patient recruitment, data analysis
Finanzierung **Notwendiger Betrag** **Verwendung** **Andere Finanzierungsquellen**	ETH doctoral student salary — Paid by ETH + KSB Ethics approval — 1'000 CHF Insurance conducting Clinical Trials — Paid by ETH Panel development tapering protocol — 5'000 CHF Study nurse CTU KSB (Screening & Recruitment, 2 h/ day) — 26'000 CHF FPH Cand. KSB team member Tapering Team (2 h/ day) — 18'000 CHF Consultations pain specialists KSB or addiction specialists PDAG in difficult cases — 10'000 CHF Print patient information material — 5'000 CHF Digital Trial Intervention Platform ETH Zurich — 10'000 CHF

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