**Effectiveness of interventions to increase safe and appropriate medicine disposal: systematic review.**

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**Introduction.** Reducing the availability of unused medicines is a component of ensuring medication safety. However, current literature on how best to increase medicine disposal is unclear.

**Aims**. To investigate the effectiveness of interventions designed to increase safe and appropriate medicine disposal.

**Methods**. Electronic databases and trial registries were searched from inception to 16th February 2024 for randomised trials of interventions aiming to increase medicine disposal (of any drug class) compared to any control. The primary outcome was the change in the proportion of participants that disposed their unused medicines. Secondary outcomes were changes in patient (e.g. knowledge of disposal strategies), population (e.g. poisonings), environmental and economic outcomes. The original Cochrane tool was used to assess risk of bias. Random-effects meta-analysis was conducted. Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of evidence. PROSPERO registration: CRD42023491797.

**Results.** Twenty-three studies were included (18 studies published from 2016 to 2023 plus 5 ongoing trials). The mean age of the 5,347 participants was 43.2 years (SD 13.6). All studies were conducted in North America and targeted opioid analgesic disposal. Interventional strategies of providing disposal kits (Risk Ratio [RR] 1.42, 95% Confidence Interval [CI] 1.13 to 1.79, moderate evidence), education alone (RR 1.47, 95%CI 1.03 to 2.09, low evidence), education plus reminder prompts (RR 2.51, 95%CI 1.30 to 4.83, moderate evidence), and education plus disposal kits (RR 2.00, 95%CI 1.03 to 3.87, moderate evidence) increased disposal compared to routine practice. Secondary outcomes were infrequently reported.

**Discussion.** There is low to moderate quality of evidence supporting the use of interventions to increase the disposal of unused medicines compared to routine practice. Secondary outcomes were recorded infrequently and may be a pathway for future research.