

INPLASY PROTOCOL

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eligibility criteria.

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None declared.

INTRODUCTION

Review question / Objective: With this systematic literature review we aim to assess published data on the quality and quantity of anabolic androgenic steroids (AAS) found on the black market to further determine the proportions of original,

Quantitative and qualitative analysis of anabolic androgenic steroids found on the black market – A protocol for a systematic review

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Review question / Objective: With this systematic literature review we aim to assess published data on the quality and quantity of anabolic androgenic steroids (AAS) found on the black market to further determine the proportions of original, substandard, and counterfeit drugs. To our knowledge this is the first systematic literature review analyzing the quality and quantity of blackmarked anabolic steroids within the published literature.

Condition being studied: AAS are synthetic, or human-made, variations of the male sex hormone testosterone that are widely abused by athletes for its anabolic effect on the muscle, thus are a convenient and easy method to improve body image and sport performance goals. Fake AAS, commonly acquired from the black market, pose a significant risk to individual and public health.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 November 2021 and was last updated on 13 November 2021 (registration number INPLASY2021110042).

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Rationale: The effect of supraphysiologic doses of anabolic androgenic steroids

(AAS) on the muscle has been widely described and recognized in literature for decades (Bhasin et al. 1996). AAS belong to the broader group of image and performance enhancing drugs (IPEDs) and are widely abused to improve body image and sport performance goals (Mullen et al. 2020). Global lifetime prevalence of AAS use is estimated to be as high as 3.3% (Sagoe et al. 2014). Due to lack of reporting, precise prevalence and demographic information on the use of these substances is difficult to estimate (Bates 2016). The most common source of anabolic steroid acquisition is the internet, which provides the perfect foundation for a counterfeit drug market (McBride, Carson and Coward 2018, Rahnema et al. 2014, Mullen et al. 2020). Those blackmarket substances may contain no active ingredient (inert), a wrong active ingredient (substituted), not all active ingredients or more active ingredients than are labelled (adulterated), or the labelled active ingredient(s) in another amount than labelled (substandard). Mislabeled products can potentially lead to negative health outcomes and are considered an individual and public health threat (Nieschlag and Vorona 2015, Solimini et al. 2017, Christou et al. 2017).

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METHODS

Search strategy: We will conduct a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA) statement. We will search Pubmed/MEDLINE and Google Scholar for studies published before October 2021 that analyzed the quality and quantity of AAS to determine the proportions of original,

substandard, and counterfeit found on the black market. We will use the following search strategy with Boolean operators: ((fake) OR (counterfeit)) AND (anabolic steroids). For Google Scholar the same search terms are used without Boolean operators. Furthermore, we will continue to pursue relevant references of references and tracked electronic citations related to the topic manually to identify sources in obscure locations, also called snow-ball method (Greenhalgh and Peacock 2005).

Participant or population: Blackmarket anabolic steroids. Articles that analyze AAS can include substances that were acquired from different sources, such as directly from the black market (e.g. bought online), acquired from gym owners or athletes, or substances that were seized and analyzed by authorities.

Intervention: Not applicable for this systematic literature review.

Comparator: Not applicable for this systematic literature review.

Study designs to be included: One author (RM) will conduct the initial database search, extract the initial articles, and remove double records. PB will independently crosscheck the initial search. Two reviewers (RM and PB) will screen each study independently by title and abstract based on the predefined eligibility criteria. Full texts of eligible studies will be reviewed independently by two reviewers (RM and PB) for data extraction. Disagreements in search results and study eligibility are resolved by consensus between the two reviewers. One author (AC) will assess the analytical methods used within eligible articles.

Eligibility criteria: Inclusion criteria are: (i) peer-reviewed original articles with full-text available; (ii) no restriction regarding country and date, (iii) articles in English language or with English abstracts, (iv) included a qualitative and/or quantitative analysis of blackmarket anabolic steroids and presented proportions of original and/or counterfeit and/or substandard drugs,

(v) articles where the majority of analyzed substances (>75%) are AAS, if the analysis includes different classes of IPED's. We will exclude (i) abstract-only papers as preceding papers, conferences, editorials, and author response theses and books, (ii) articles without full text available, (iii) articles where the exact composition of analyzed IPEDS's is not provided by the author, if the analysis doesn't include exclusively AAS, (iv), articles where the minority of analyzed substances (<25%) are AAS, if the analysis includes different classes of IPED's.

Information sources: The following electronic databases will be included in the search: PubMed and Google Scholar. We will include studies up to October 2021.

Main outcome(s): The proportion of original, substandard, and counterfeit AAS found in qualitatively and quantitatively analyzed samples from the black market. Definitions are available in section "other relevant information".

Additional outcome(s): - The proportion of adulterated, substituted, and inert AAS for counterfeit substances. - The proportion of over- or under-concentrated AAS for substandard substances. - Assessment of the different analytical methods used to determine the quality and quantity of blackmarket AAS. Definitions are available in section "other relevant information".

Data management: Extracted information will include first author's name, year of publication, country, sample collection period, analysis methods, sample information, analyzed classes of compounds and sample size, proportion of original, substandard, and counterfeit products and other remarks. Disagreements in data extraction are resolved by consensus between the two reviewers. Two team members (RM and LF) will review all data to ensure accuracy before analysis. Classification of prohibited substances are done according to the world anti-doping agency (WADA) prohibited list (Updated version as of 01 January 2021). We will further classify

compounds according to the suggested classification of Neves (Neves and Caldas 2017), and Weber and colleagues (Weber et al. 2017) with adaptations into "original", "substandard" and "counterfeit". A sub-classification of "counterfeit" substances into "adulterated", "substituted" and "inert", and "substandard" substances into "over- or under-concentrated" will be done. Definitions are available in section "other relevant information".

Quality assessment / Risk of bias analysis: Study quality will be assessed by two reviewers (RM and PB) independently. Quality assessment for bias of analytical studies will be conducted using the ToxRtool for in vitro studies (Schneider et al. 2009). Disagreements in quality assessment are resolved by consensus between the two reviewers.

Strategy of data synthesis: Although a meta-analysis is favourable, this will only become apparent when the research team can determine what data is extracted and made available from the systematic review.

Subgroup analysis: If sufficient data is available, we will perform subgroup analyses to further evaluate differences in outcomes between countries and/or continents.

Sensitivity analysis: Although a sensitivity analysis is not planned at this stage, this may become apparent when the research team can determine what data is extracted and made available from the systematic review.

Language: Articles in English language or with English abstracts are considered for this systematic review.

Country(ies) involved: This systematic review is carried out in Switzerland.

Other relevant information: Definitions 1. Original anabolic steroids • Formulation detected fully matches the one declared on the label (Qualitative) • Levels of active pharmaceutical ingredients (AI) detected are between the defined range of the

declared formulation provided by the individual article (Quantitative) 2. Substandard anabolic steroids • Formulation detected fully matches the one declared (Qualitative) • Levels of AI detected are not between the defined range of the declared formulation provided by the individual article (Quantitative) • Subclassification (Quantitative): - Over-concentrated: AI detected above the defined range - Under-concentrated: AI detected below the defined range 3. Counterfeit anabolic steroids • Formulations detected does not match the label (Qualitative) • Subclassification (Qualitative): - Inert: no AI present in the sample - Substituted: different AI than labelled present in the sample - Adulterated: not all or more AI than the labelled AI present in the sample.

Keywords: Anabolic androgenic steroids; AAS; fake; counterfeit; original; substandard; quality; quantity; black market; systematic review.

Dissemination plans: Dissemination will occur through publication of results in a peer-reviewed journal. Additional dissemination will occur through presentations at conferences regionally and nationally/internationally. Furthermore, this project will serve as a foundation for future prevention and harm reduction services within this field and will be disseminated on the respective web site when implemented.

Contributions of each author:

Author 1 - Raphael Magnolini - RM conceived the original idea. RM planned the literature search, data extraction and quality assessment. RM created the manuscript draft. RM contributed to refinement of the manuscript.

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