Practical efficacy of prior checks on athletes' medication use for the prevention of unintentional doping

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Abstract

Background: Athletes are subjected to disciplinary action for even unintentional doping. This study aimed to clarify the effectiveness of prior checks on athletes' drug regimens by medical personnel with knowledge of anti-doping to prevent unintentional doping. *Methods*: This is a retrospective evaluation of the inquiries to the Anti-Doping Committee by the Japan Table Tennis Association national team athletes and athlete support personnel between 2011 and 2019 regarding whether the drug in question was permitted and whether it contained any prohibited substance. Discrete evaluations were performed for ethical and over-the-counter drugs, in addition to the evaluation of all drugs. Additionally, we evaluated the drugs according to therapeutic category and World Anti-Doping Agency's classification. *Results*: Overall, 85/1238 (6.9%) ethical drugs, 49/259 (18.9%) over-the-counter drugs and 134/1497 (9.0%) total drugs were considered as not allowed for use. The proportion of over-the-counter drugs judged as not allowed for use was higher than that of ethical drugs ($P < 0.001$). When tabulating the drugs not allowed for use in the therapeutic category, numerous prohibited substances were identified in adrenal hormone preparations, Kampo products, synthetic narcotics, antitussives, antihemorrhoidals, and bronchodilators among ethical drugs and in cold remedies, gastrointestinal drugs, and antitussives and expectorants among over-the-counter drugs. *Conclusions*: Of the ethical and over-the-counter drugs that elite athletes wanted to use, approximately 10% were not allowed because of the risk of unintentional doping. These results suggest that conducting prior checks of the athletes' drug regimens by medical personnel with anti-doping knowledge are effective measures to prevent unintentional doping.

Keywords

Anti-doping, Unintentional doping, Doping in sports, Table tennis, Medical personnel

Introduction

Doping in sports is a social issue that has been reported worldwide. Violations of anti-doping rules impact individual athletes, as well as the team, sponsor, and the value of the athlete's sport. Although the sanction imposed on individuals who intentionally perform doping is standard, there are instances where athletes are punished for unintentional doping caused by medical drug use for purposes other than improving athletic performance (Pluim, 2008). Therefore, athletes need to pay special attention to medical drug use, and some preventive measures are required. The World Anti-Doping Agency (WADA) discloses statistical figures on Anti-Doping Rule Violations (ADRVs) annually (World Anti-Doping Agency, 2020); however, they do not distinguish between intentional and unintentional doping during data collection and classification. A sole available report estimated the proportion of athletes who were punished because of unintentional doping by analyzing the data in ADRVs (de Hon & van Bottenburg, 2017), and no studies have analyzed the potential risks of unintentional doping that could lead to its prevention. Accordingly, evidence is lacking on the ways to effectively control unintentional doping, and formative research is required on effective interventions for preventing unintentional doping (Chan et al., 2019). Hence, we examined the potential risks of

65 unintentional doping and effective methods to prevent them by investigating the long-term
66 history of drug use in a population of elite athletes in sports where intentional doping is
67 extremely rare.

68 Table tennis is considered a sport with minimal intentional doping, with only two
69 ADRVs in 2018 according to the statistics from WADA (World Anti-Doping Agency, 2020).
70 Moreover, the Japan Table Tennis Association (JTTA) has long emphasized unintentional
71 doping prevention in parallel with intentional doping prevention activities and has undertaken
72 countermeasures in this regard. Athletes on the national team are counseled to contact the JTTA
73 Anti-Doping Committee which consists of doctors and pharmacists with anti-doping
74 knowledge before using drugs to confirm that they do not contain any prohibited substances. As
75 such, this is formally an athlete-initiated inquiry system, although it is almost mandatory. When
76 handling inquiries from athletes, the Anti-Doping Committee advises athletes to discontinue
77 the use of drugs or proposes alternatives if the presence of a prohibited substance is confirmed,
78 or if the ingredients in the drug of interest cannot be identified. Additionally, the Anti-Doping
79 Committee provides advice on submitting Therapeutic Use Exemptions (TUE) applications.
80 The records of this long-term advisory service in a group with extremely low levels of
81 intentional doping are considered the most appropriate materials for investigating the potential
82 risks and preventive measures of unintentional doping. Therefore, this study aimed to clarify
83 the risks of unintentional doping and effectiveness of prior checks of athletes' drug regimens

through ethical and over-the counter (OTC) drugs by analyzing 9 years' worth of records of responses to inquiries by the JTTA Anti-Doping Committee.

Materials and Methods

Survey period and target population

In this study, the records of responses to inquiries received by the JTTA Anti-Doping Committee between 2011 and 2019 were retrospectively evaluated. Inquiries were evaluated if they met all of the following inclusion criteria: (1) inquiries were from athletes who were members of the JTTA national team or had previous affiliations or from athlete support personnel and (2) inquiries were on the acceptability of use of ethical or OTC drugs. Cases in which the drug could not be identified were excluded. National team athletes were defined as those who participated in international events on the Japanese team. This study, including the opt-out method of consent available to all athletes, was approved by the Ethical Review Board of Juntendo University Faculty of Medicine (Approval numbers: 2019103, 2020042) and was conducted in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects and the Declaration of Helsinki. The committee waived the requirement for a written informed consent because of the retrospective design of the study.

Survey items

The survey items were drugs for which inquiries were received; the number of individuals who

sent inquiries; and the age and sex of the inquiring individual and the number of drugs included in inquiries received. Regarding drugs for which inquiries were received, the presence or absence of prohibited substances, the classification of the drug as ethical or OTC and the therapeutic category were investigated. Moreover, if a prohibited substance was confirmed, its classification was determined based on the WADA Prohibited List (World Anti-Doping Agency, 2010; World Anti-Doping Agency, 2011; World Anti-Doping Agency, 2012; World Anti-Doping Agency, 2013; World Anti-Doping Agency, 2014 [https://www.wada-ama.org/sites/default/files/resources/files/WADA-Revised-2014-Prohibited-List-EN.PDF]; World Anti-Doping Agency, 2014 [https://www.wada-ama.org/sites/default/files/resources/files/wada-2015-prohibited-list-en.pdf]; World Anti-Doping Agency, 2015; World Anti-Doping Agency, 2016; World Anti-Doping Agency, 2017; World Anti-Doping Agency, 2018). The age of individuals sending inquiries at the time of the first inquiry were tabulated. Prohibited substances were determined according to the WADA Prohibited List that was in effect at the time of the inquiry. Drugs that were judged to not contain any prohibited substances were labeled as “Not prohibited.” If the presence of a prohibited substance was confirmed, the drug was classified as “Prohibited”. However, the substance content could not be identified, and the drug was labeled “Indeterminate.” Prohibited substances, such as beta-2 agonists and glucocorticoids, which were allowed to be used in exceptional cases, labeled as “Not prohibited” only if they were administered via the routes

approved in the WADA Prohibited List, e.g., inhalation, intranasal spray and topical application. Only drugs that were not found to contain any prohibited substances were handled as "Allowed," whereas all others were handled as "Not allowed." Drugs prescribed by a physician were classified as ethical drugs, and all others were classified as OTC drugs. For the therapeutic category, the Standard Commodity Classification Number of Japan was used for ethical drugs (Ministry of Internal Affairs and Communications, Japan, 1990) and the Classification Criteria from the Ministry of Health, Labour and Welfare were used for OTC drugs (Kyoto Encyclopedia of Genes and Genomes, 2021). After classifying the drugs based on therapeutic category, whether the use of the drug was allowed and whether the drug contained any prohibited substances were tabulated for each group.

Endpoints

Separate evaluations were performed for ethical and OTC drugs in addition to the evaluation of all drugs. The primary endpoint was the percentage of drugs classified as not allowed. The secondary endpoints were the proportion of prohibited substances, of drugs in the therapeutic category classified as not allowed and of prohibited substances by category based on the WADA Prohibited List.

Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR). Categorical

variables were expressed as total values and percentages. Group comparisons were assessed using the Mann–Whitney *U* test for continuous variables and the chi-squared test or Fisher's exact test for categorical variables. All *P*-values were two sided and *P*-values ≤0.05 were considered statistically significant. All statistical analyses were performed with EZR version 1.50 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R version 4.0.1 (The R Foundation for Statistical Computing, Vienna, Austria) (Kanda, 2013). Specifically, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.

Results

Target drugs and background characteristics of individuals making inquiries

Between 2011 and 2019, the JTTA Anti-Doping Committee responded to 1813 inquiries (**Figure 1**). Overall, 112 inquiries were received from individuals other than JTTA national team athletes or athlete support personnel, and 202 inquiries received were on non-ethical and non-OTC drugs, which did not meet the inclusion criteria. Of the 1499 drugs that met the inclusion criteria, two were excluded because the drugs could not be identified. Ultimately, 1238 ethical drugs and 259 OTC drugs were analyzed, totaling 1497 drugs evaluated. **Table 1** lists the background characteristics of individuals who made the inquiries.

[Figure 1 near here]

[Table 1 near here]

One athlete and one athlete support personnel had missing age values. In total, 106 individuals submitted inquiries on all drugs. The median (IQR) age of the athletes was 19 years (16–22 years) and the median number of inquiries per individual was 5 drugs (3–13 drugs). There were no differences in terms of sex ratio or age of the individuals making inquiries between the ethical drugs and OTC drugs.

Determination of the allowability for use of drugs for which inquiries were received

Of the 1497 drugs evaluated, 81 (5.4%) contained prohibited substances. The substances contained in 53 drugs (3.5%) could not be identified. In total, 134 drugs (9.0%) were classified as not allowed for use (**Table 2**).

[Table 2 near here]

Based on the type of drug, of the 1238 ethical drugs, 85 drugs were not allowed (6.9%). The breakdown of the drugs not allowed for use were 52 (4.2%) that contained prohibited substances and 33 (2.7%) for which the substance content could not be identified. Of the 259 OTC drugs, 49 (18.9%) were not allowed for use. The breakdown of the drugs not allowed for use were 29 (11.2%) that contained prohibited substances and 20 (7.7%) for which the substance content could not be identified. The proportion of OTC drugs determined as not allowed for use was higher than that of ethical drugs ($P < 0.001$).

Tabulation of drugs not allowed for use by therapeutic category

When tabulated by therapeutic category, the most common categories of ethical drugs not allowed for use were Kampo products (n = 22; 25.9%), followed by crude drugs (n = 18; 21.2%), adrenal hormone preparations (n = 13; 15.3%), synthetic narcotics (n = 11; 12.9%), antitussives (n = 5; 5.9%), antihemorrhoidals (n= 4; 4.7%) and bronchodilators (n = 2; 2.4%) (**Table 3**).

[Table 3 near here]

Among ethical drugs, the therapeutic categories that contained two or more prohibited substances were adrenal hormone preparations (n = 13; 25.0%), Kampo products (n = 11; 21.2%), synthetic narcotics (n = 11; 21.2%), antitussives (n = 5; 9.6%), antihemorrhoidals (n= 4; 7.7%) and bronchodilators (n = 2; 3.8%). The most common therapeutic category of OTC drugs not allowed for use were cold remedies (n = 18; 36.7%); gastrointestinal drugs that incorporated two or more of antacids, stomachics, digestives, and intestinal regulators (n = 10; 20.4%); vitamin preparations (n = 6; 12.2%); antidiarrheals (n = 4; 8.2%); antacids (n = 4; 8.2%) and antitussives and expectorants (n = 2; 4.1%) (**Table 4**).

[Table 4 near here]

Among OTC drugs, the therapeutic categories that contained two or more prohibited substances were cold remedies (n = 18; 62.1%); gastrointestinal drugs that incorporated two or more of antacids, stomachics, digestives, and intestinal regulators (n = 7; 24.1%); and

antitussives and expectorants (n = 2; 6.9%). The prohibited substances in 18 cold remedies were all ephedrine and its derivatives. Higenamine in crude drugs was the prohibited substance in the seven gastrointestinal drugs that incorporated two or more of antacids, stomachics, digestives, and intestinal regulators.

Classification of prohibited substances according to the WADA Prohibited List

Confirmed prohibited substances were substances prohibited in-competition, except for S3 beta-2 agonists in 11 drugs (13.6%). Of the 81 prohibited substances, substances classified as S6 stimulants were most common (n = 40; 49.4%) (**Table 5**). Differences were noted in the composition of identified prohibited substances between ethical and OTC drugs ($P < 0.001$). Prohibited substances identified among ethical drugs were categorized in the following order: S6 stimulants in 20 (38.5%), S9 glucocorticoids in 17 (32.7%), S7 narcotics in 12 (23.1%) and S3 beta-2 agonists in 3 (5.8%). For OTC drugs, S6 stimulants were identified in 20 drugs (69.0%), S3 beta-2 agonists in 8 (27.6%) and S9 glucocorticoids in 1 (3.4%). No S7 narcotics were noted.

[Table 5 near here]

Discussion

Risks of unintentional doping and the effectiveness of prior check of athlete's drugs

To our knowledge, this is the largest study of drug use among elite athletes in accordance with anti-doping guidelines. This study revealed that 9.0% of ethical and OTC drugs that elite athletes wanted to use were not allowed for use and that the proportion of OTC drugs not allowed for use was higher than that of ethical drugs. In a 1-year survey of domestic-level Japanese athletes reported by Yokoi et al. (2016), 15% of ethical drugs and 38% of OTC drugs were classified as not allowed for use. Similar to the present study, the proportion of OTC drugs determined not allowed for use was higher than that of ethical drugs. The tendency was the same in the present study; however, the percentage of drugs determined as not allowed for use was low. This was possibly because the target population of this study was national team athletes, who were highly likely to undergo doping tests, and their athlete support personnel, all of whom received regular education and training from the JTTA Anti-Doping Committee. However, even among elite athletes with adequate education and training, 9.0% of the drugs these individuals wanted to use were drugs that athletes should avoid, and at least 5.4% of the drugs could have been considered doping by ingestion. Athletes can verify their medication using Global Drug Reference Online, a search-based website that complies with the Prohibited List (Global drug reference online [https://www.globaldro.com/Home]) however, not all products and ingredients are listed on the website. Moreover, individuals who are not familiar

with the website may experience difficulty while performing searches. Thus, the present research showed that the risk of unintentional doping among athletes was by no means small. Moreover, prior checks of athletes' medical drug use by medical personnel with knowledge of anti-doping are an effective method of identifying prohibited substances and preventing unintentional doping.

Risks of unintentional doping based on therapeutic category

Domestic criteria in Japan were used for the therapeutic category to allow classification of traditional medicines. In the evaluation by therapeutic category of ethical drugs that were not allowed for use, the most common categories were Kampo products, which are traditional medicines, and crude drugs. Because drugs in these categories are composed of natural materials, identifying all the ingredients is difficult, and determining whether they contain prohibited substances is occasionally not feasible. Some crude drugs contain higenamine, a prohibited substance (Japan Anti-Doping Agency, 2016). In addition to higenamine, ephedrine and its derivatives are known to be contained in crude drugs, such as *Pinelliae ternate* (Oshio et al., 1978). Therefore, to avoid unintentional doping, athletes are recommended to avoid using these classes of drugs.

In the OTC drugs evaluated, prohibited substances were most frequently identified in cold remedies. Tseng et al. (2003) reported that several OTC cold remedies contained ephedrine and cautioned regarding the risk of ADRVs associated with their misuse. All 18

248 prohibited substances identified in cold remedies in this study were ephedrine and its
249 derivatives, and the risks indicated were confirmed even in the actual use of the drugs. The
250 second largest number of OTC drugs confirmed to contain prohibited substances was drugs
251 classified as gastrointestinal drugs. The presence of higenamine was confirmed in all seven
252 prohibited drugs. Because crude drugs and supplements sometimes contain higenamine,
253 anti-doping organizations have been issuing alerts (Japan Anti-Doping Agency, 2016; World
254 Anti-Doping Agency [https://www.wada-ama.org/en/prohibited-list#faq-anchor]). For
255 respiratory drugs such as bronchodilators, antitussives, and expectorants, the frequency of
256 verifications for prohibited drugs is high for both ethical and OTC drugs. Respiratory diseases,
257 such as asthma, have frequently been reported as the most common diseases in elite-level
258 athletes (Fitch, 2012; Engebretsen et al., 2013; Soligard et al., 2015); thus, these athletes would
259 need to be alerted on unintentional doping from respiratory drug use.

260 ***Risks of unintentional doping based on the WADA Prohibited List***

261 In the Prohibited List, substances and methods, excluding those prohibited in particular sports,
262 are broadly classified into “Substances & methods: prohibited at all times” and “Substances &
263 methods prohibited in-competition.” The former is further classified into S1–S5 prohibited
264 substances and M1–M3 prohibited methods, and the latter is classified into S6–S9 prohibited
265 substances. Notably, 86.4% of prohibited drugs identified in the present study corresponded to
266 the latter, and these substances were considered as drugs frequently used in daily life. Among

the “Substances & methods prohibited in-competition,” S6 stimulants were the most common. For OTC drugs in particular, approximately 70% of the prohibited substances identified were in this drug category, and most of these were ephedrine and its derivatives. These are components of common cold medicines and are prohibited substances about which athletes must be most cautious.

S7 narcotics and S9 glucocorticoids are drugs for high therapeutic need. Of the 30 prescribed drugs evaluated in this study, 29 were prescribed by medical institutions, such as hospitals. Of these drugs, evaluating the allowability of use and the necessity of submitting TUE applications during the checking process prior to drug use is necessary. All drugs classified as “Substances & methods prohibited at all times” were S3 beta-2 agonists, accounting for 13.6% of all prohibited drugs. In a survey by de Hon & van Bottenburg (2017) analyzing ADRVs between 2010 and 2012, 81.1% of instances wherein beta-2 agonists were detected were associated with a reduced sanction period and were considered unintentional doping. Considering the high prevalence of asthma in elite-level athletes (Fitch, 2012; Engebretsen et al., 2013; Soligard et al., 2015), beta-2 agonists are thought to be one of the most likely causes of unintentional doping.

Limitations

This study has several limitations. First, because the study was retrospective and observational,

286 unknown confounding factors may have influenced the results. The most desirable study design
287 for evaluating the effectiveness of prior checks on athletes' medical drug use is determining
288 differences in the incidence of ADRVs with or without prior checks on drug use. However,
289 conducting a comparative study was difficult because it was not ethical to have a control group
290 and the percentage of ADRVs in the number of doping tests is extremely low at 0.62% in 2018
291 for all sports (World Anti-Doping Agency, 2020). Second, this study was limited to Japanese
292 athletes. Because pharmaceutical regulatory systems vary across countries, the differences
293 between regulatory systems in each country should be considered. Third, all "Substances &
294 methods prohibited in-competition" were handled as prohibited drugs. Medications falling
295 under the category of "Substances & methods prohibited in-competition" can theoretically be
296 used outside of competition. The 2021 revision of the International Standard for Therapeutic
297 Use Exemptions (ISTUE) allows for retroactive TUEs if an athlete uses a prohibited substance
298 out-of-competition for therapeutic purposes, which is prohibited only in-competition (World
299 Anti-Doping Agency, 2021). However, the conditions in Article 4.2 of ISTUE must be met,
300 including the condition on no reasonable permitted therapeutic alternative. Moreover, the risk
301 of athletes using drugs accessible to them during competition cannot be ruled out, and, to
302 prevent unintentional doping, explaining the list of "Substances & methods prohibited
303 in-competition" as prohibited drugs to athletes regardless of the period is preferable, as was
304 performed in this study. Fourth, the Prohibited List is revised at least once a year (World

Anti-Doping Agency, 2009; World Anti-Doping Agency, 2019). However, during 2011 and 2019, which was the study period, no major revisions to the Prohibited List and no changes in the substances detected as prohibited drugs in this study were made.

The risk of unintentional doping among athletes is by no means small. Among the ethical and OTC drugs that elite athletes wanted to use, 9.0% were not allowed for use. OTC drugs were associated with a higher risk of unintentional doping than ethical drugs. Cold remedies and gastrointestinal drugs among OTC drugs and Kampo products, crude drugs and respiratory drugs among ethical drugs were associated with a high risk of unintentional doping. To reduce these risks, prior checks on athletes' medical drug use by medical personnel with anti-doping knowledge is considered an effective method of prevention.

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Declaration of interest statement

The authors report no conflict of interest

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Data availability statement

The data sets will not be publicly available because athlete consent does not allow for such publication. The corresponding author will respond to inquiries on data analyses.

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Tables

Table 1. Background characteristics of individuals making inquiries

Variable	All drugs	Drug classification	
		Ethical drugs	OTC drugs
Number of inquiries, n (%)			
Athletes	92 (86.8)	86 (93.5)	46 (80.7)
Athlete support personnel	14 (13.2)	6 (6.5)	11 (19.3)
Age, median (IQR), years			
Athletes	19 (16–22)	19 (16–22)	19 (16.0–21.75)
Athlete support personnel	37 (33–43)	44.5 (35.5–46.75)	35.5 (31.5–37.75)
Female, n (%)			
Athletes	50 (54.3)	46 (53.5)	25 (54.3)
Athlete support personnel	5 (35.7)	1 (16.7)	5 (45.5)
Number of inquiries per individual, median (IQR)	5 (3–13)	6 (3–13)	2 (1–5)

436 Table 2. Determination on allowability of use and breakdown of drugs for which inquiries were

437 received

	Drug, n (%)			
		Drug classification		
	All drugs (n = 1497)	Ethical drugs (n = 1238)	OTC drugs (n = 259)	*P* value*
Whether use was allowed/not allowed for drugs for which inquiries were received				
Allowed	1363 (91.0)	1153 (93.1)	210 (81.1)	<0.001[a)]
Not allowed	134 (9.0)	85 (6.9)	49 (18.9)	
Breakdown of whether use was allowed/not allowed for drugs for which inquiries were received				
Not prohibited	1363 (91.0)	1153 (93.1)	210 (81.1)	
Prohibited	81 (5.4)	52 (4.2)	29 (11.2)	<0.001[a)]
Indeterminate	53 (3.5)	33 (2.7)	20 (7.7)	

438 * Comparison between ethical and OTC drugs. a) Chi-squared test.

439

Table 3. Tabulation of ethical drugs not allowed for use by therapeutic category

Therapeutic category	Drug, n (%)		
	Not allowed		
		Prohibited	Indeterminate
Kampo products	22 (25.9)	11 (21.2)	11 (33.3)
Crude drugs	18 (21.2)	0 (0)	18 (54.5)
Adrenal hormone preparations	13 (15.3)	13 (25.0)	0 (0)
Synthetic narcotics	11 (12.9)	11 (21.2)	0 (0)
Antitussives	5 (5.9)	5 (9.6)	0 (0)
Antihemorrhoidals	4 (4.7)	4 (7.7)	0 (0)
Bronchodilators	2 (2.4)	2 (3.8)	0 (0)
Antitussives and expectorants	1 (1.2)	1 (1.9)	0 (0)
Other agents affecting respiratory organs	1 (1.2)	1 (1.9)	0 (0)
Antipyretics, analgesics, and antiinflammatory	1 (1.2)	1 (1.9)	0 (0)
Cardiotonics	1 (1.2)	1 (1.9)	0 (0)

Stomachics and digestives	1 (1.2)	0 (0)	1 (3.0)
Other agents for uro-genital and anal organ	1 (1.2)	0 (0)	1 (3.0)
Other antiallergic agents	1 (1.2)	1 (1.9)	0 (0)
Coca alkaloids preparations	1 (1.2)	1 (1.9)	0 (0)
Unclassified	2 (1.2)	0 (0)	2 (6.1)

441

442

443 Table 4. Tabulation of over-the-counter drugs not allowed for use by therapeutic category

Therapeutic category	Drug, n (%)		
	Not allowed		
		Prohibited	Indeterminate
Cold remedies	18 (36.7)	18 (62.1)	0 (0)
Gastrointestinal drugs that incorporated two or more of antacids, stomachics, digestives, and intestinal regulators	10 (20.4)	7 (24.1)	3 (15.0)
Vitamin preparations [b)]	6 (12.2)	0 (0)	6 (30.0)
Antidiarrheals	4 (8.2)	0 (0)	4 (20.0)
Antacids	4 (8.2)	0 (0)	4 (20.0)
Antitussives and expectorants	2 (4.1)	2 (6.9)	0 (0)
Hemorrhoid drugs for external use	1 (2.0)	1 (3.4)	0 (0)
Stomatitis remedies	1 (2.0)	0 (0)	1 (5.0)
Herbal preparations (not belonging to other categories)	1 (2.0)	0 (0)	1 (5.0)

Drugs for women’s health	1 (2.0)	0 (0)	1 (5.0)
Unclassified	1 (2.0)	1 (3.4)	0 (0)

[b)] Vitamin preparations include vitamin B_2 based drugs; vitamin B_1, B_6, and B_{12} based drugs; vitamin B_2 and B_6 based drugs; and vitamin-containing health drugs.

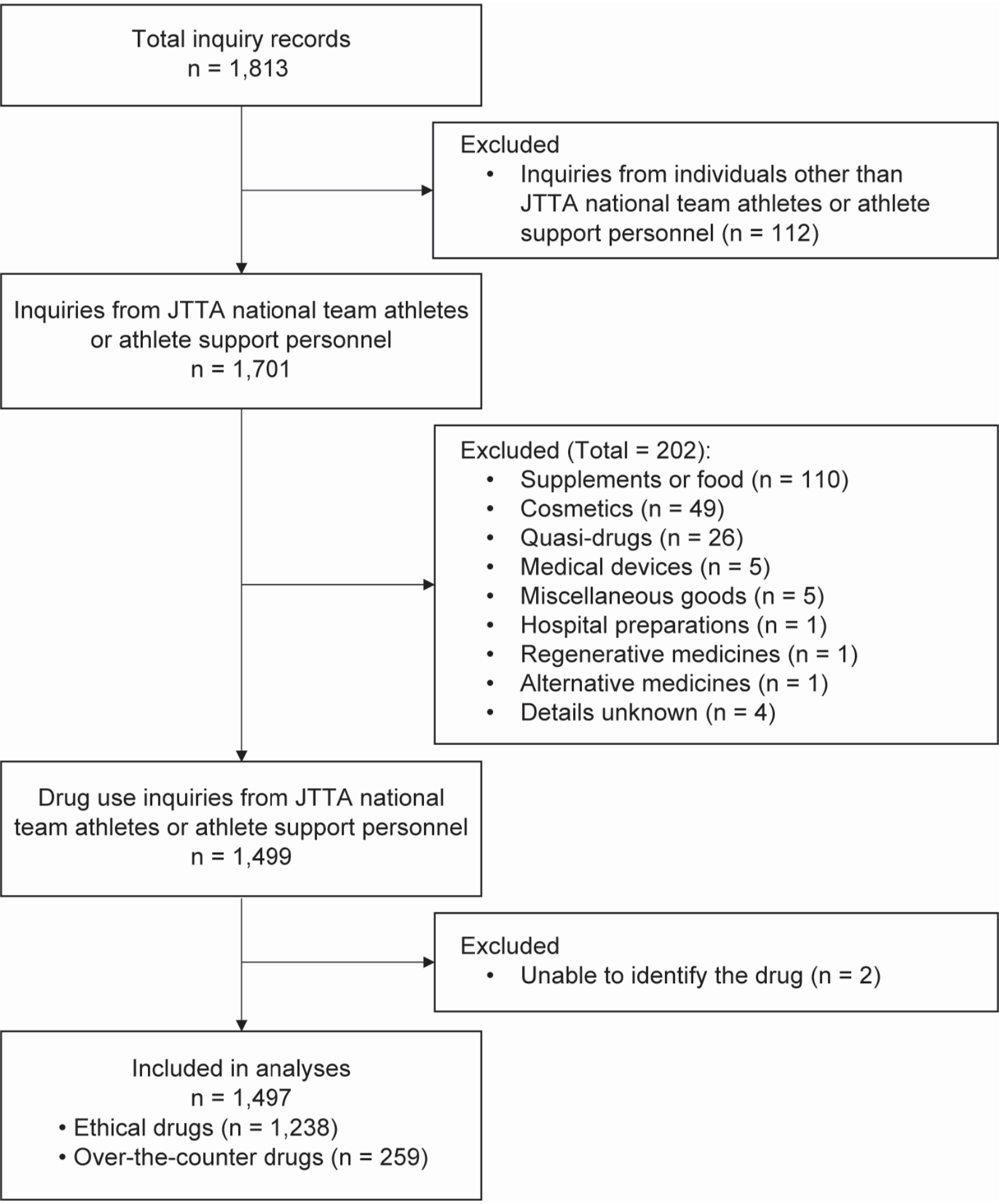
Table 5. Classification based on the WADA Prohibited List of prohibited drugs identified among those for which inquiries were received

	Prohibited drug, n (%)			
		Drug classification		
Group on Prohibited List	All drugs (n = 81)	Ethical drugs (n = 52)	OTC drugs (n = 29)	*P* value**
S3 Beta-2 agonists	11 (13.6)	3 (5.8)	8 (27.6)	
S6 Stimulants	40 (49.4)	20 (38.5)	20 (69.0)	
S7 Narcotics	12 (14.8)	12 (23.1)	0 (0)	<0.001 c)
S9 Glucocorticoids	18 (22.2)	17 (32.7)	1 (3.4)	

** Comparison between ethical and OTC drugs. c) Fisher's exact test.

Figure caption

Figure 1. Detailed flow chart of the study design


Total inquiry records
n = 1,813
Excluded
• Inquiries from individuals other than JTTA national team athletes or athlete support personnel (n = 112)
Inquiries from JTTA national team athletes or athlete support personnel
n = 1,701
Excluded (Total = 202):
• Supplements or food (n = 110)
• Cosmetics (n = 49)
• Quasi-drugs (n = 26)
• Medical devices (n = 5)
• Miscellaneous goods (n = 5)
• Hospital preparations (n = 1)
• Regenerative medicines (n = 1)
• Alternative medicines (n = 1)
• Details unknown (n = 4)
Drug use inquiries from JTTA national team athletes or athlete support personnel
n = 1,499
Excluded
• Unable to identify the drug (n = 2)
Included in analyses
n = 1,497
• Ethical drugs (n = 1,238)
• Over-the-counter drugs (n = 259)