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Thirteen years of the fight against doping in figures

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and Juan Del Coso^{a*} 

Every year, the World Anti-Doping Agency (WADA) publishes the main statistics reported by the accredited laboratories, which provide very valuable information for assessing changes in the patterns of doping in sports over time. Using the information provided since 2003 as the basis for the analysis, the evolution of doping/anti-doping figures over the last decade can be examined in reasonable detail, at least in reference to samples analyzed and categories of substances more commonly found in athletes' samples. This brief analysis of the WADA statistical reports leads us to the following outcomes: the increase in anti-doping pressure from 2003 to 2015, as evidenced by increased numbers of samples analyzed and banned substances, has not directly produced a higher frequency of adverse/atypical findings. Although this could be interpreted as steady state in the capacity to detect doping through this whole period, it also resulted in a significant increase in the absolute number of samples catalogued as doping (from 2247 in 2003 to 5912 in 2015). Anabolic agents have been the most common doping substances detected in all statistics reports while the remaining groups of substances are much less frequently found in doping control samples. Given that one might have expected the enhancement of the anti-doping programme led by WADA over this last decade to have increased the percentage of adverse/atypical findings, the fact that it did not might indicate the need to take another step in sampling strategies, such as 'more intelligent testing' based on the differences in the prevalence of doping substances among sports. Copyright © 2017 John Wiley & Sons, Ltd.

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The globalization of the fight against doping

In 1928, the International Association of Athletics Federations (IAAF) became the first ever sports federation to ban the use of doping products in sport. During the 1960s, the International Olympic Committee collected the first anti-doping samples in the Rome Olympic Games while the International Cycling Union (Union Cycliste Internationale; UCI) and the International Federation of Football Associations (Fédération Internationale de Football Association, FIFA) planned their first anti-doping programmes during the World Championships celebrated that decade. However, the most significant step forward for the harmonization of the fight against doping in all sports worldwide occurred in 1999 with the creation of the World Anti-Doping Agency (WADA). WADA was established as a single independent international agency with the aim of promoting a universal Anti-Doping Code that synchronized anti-doping policies among all stakeholders. Since its creation, WADA has improved the coordination of national and international anti-doping organizations, implemented the cooperation with law enforcement, monitored compliance with the anti-doping rules, and increased the relevance of education as a key aspect in the fight against doping. However, till now, the most relevant milestone reached by WADA in terms of harmonization has been the development of a single list of banned substances together with the enhancement of the methodologies employed to detect their use.^[1]

WADA measures to increase reliance on doping testing

Based on WADA policies and actions implemented in the last few years, the agency can be presumed to be aware that the overall strategy in the fight against doping must rely on the scientific evidence produced by the detection methods and analyses of data on the prevalence of doping in sports. In this respect, WADA maintains strict norms for accrediting specialized anti-doping laboratories in different countries to ensure the production of reliable and uniform results from athletes' samples.^[2] These norms include the mandatory application in the laboratories of the ISO/IEC 17025 and WADA Technical Documents. Moreover, WADA periodically assesses the degree of fulfilment of these norms by the accredited laboratories through recurrent audits that assure full confidence in the results reported by the laboratories wherever they are located. Additionally, every year on its website, WADA publishes the

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main statistics reported by these accredited laboratories, which provides valuable information for assessing changes in the patterns of doping in sports over time. WADA published the first Testing Figures Report in 2003 and since then the report has evolved from merely presenting the numbers of samples analyzed and the substances found, to a complex document that provides information on different sports, laboratories, methodologies and sample matrices (e.g. urine and blood) regarding all the samples analyzed in WADA-accredited laboratories.^[3]

Data from testing figures reported since 2003

Using the information provided since 2003 as the basis for the analysis, the evolution of doping/anti-doping figures over the last 13 years can be examined in reasonable detail, at least in reference to samples analyzed and categories of substances more commonly found in athletes' samples. It is important to keep in mind that not all the adverse analytical findings imply a violation of the anti-doping rules as an authorized therapeutic use exception (TUE) permits the use of banned substances when certain health problems are demonstrated by the athlete. Figure 1 depicts the quantity of samples analyzed in WADA-accredited laboratories for the years 2003 to 2015 in both Olympic and non-Olympic sports. In general, the number of anti-doping controls has increased on a yearly basis, with a slight reduction in the number of samples analyzed coinciding with the worst years of the worldwide financial crisis. Most of the samples ($\sim 71.5 \pm 5.0\%$) analyzed corresponded to Olympic sports, while the remaining samples were from other non-Olympic sports.

From 2003 to 2015, there was a 101% increase in the number of samples analyzed together with the improvement of detection methodologies and the increase in the number of substances/methods included in the List of Prohibited Substances in Sport^[4] (a $\sim 270\%$ increase in the number of substances to be controlled). Nevertheless, the percentage of adverse plus atypical analytical findings has remained relatively stable at $\sim 1.9 \pm 0.2\%$ during this whole period (Figure 2). Although this could be interpreted as steady state in the capacity to detect doping through this whole period, it also resulted in a significant increase in the absolute number of samples catalogued as doping (from 2247 adverse/atypical samples in 2003 to 5912 samples in 2015). This information suggests the efficacy of increasing the number of

samples analyzed per year to enhance the detection of doping, although it also advises the necessity of implementing other testing strategies to fight against doping in a more efficient manner such as non-random/targeted testing and unannounced controls out of competition.

Initially, WADA identified as an 'adverse analytical finding' the presence of a prohibited substance, or its metabolites, and also the presence of abnormal quantities of endogenous substances that might constitute the use of prohibited substances. However, since the report in 2008, the agency has discriminated between adverse and atypical findings, to provide a more detailed description of the results reported by the laboratories. In any case, the differentiated percentages of adverse and atypical findings (refer to note under Figure 2) did not change significantly from 2008 to 2015. This very interesting outcome reflects a stable percentage of adverse analytical findings despite the economic and technical efforts made by anti-doping organizations and laboratories in the fields of education and testing methodologies.^[5] On the other hand, the percentage of atypical findings should be interpreted cautiously because of the modifications in the thresholds and techniques used to determine the use of several banned substances (e.g. the variation in the testosterone/epitestosterone ratio or the threshold to consider the use of carboxy-THC). The stability in the percentages of adverse and atypical findings during these last thirteen years may also be a reflection of a testing policy that needs to be fine-tuned.^[6] Nevertheless, these outcomes could also be interpreted by others as confirming the effectiveness of the deterrent policies implemented by WADA.

Another interesting aspect which emerges from analyzing the historical series of the WADA statistical reports is related to the groups of substances that are more commonly found in adverse and atypical analytical samples. Figure 3 depicts the percentage of substances identified in adverse/atypical samples, although the names of the groups have changed slightly over the years, for example in 2003 the group named 'Peptide Hormones' is now (in 2015) 'Peptide Hormones, Growth Factors and Related Substances and Mimetics'. Anabolic agents that include exogenous anabolic androgenic steroids, endogenous anabolic androgenic steroids when administered exogenously and other anabolic substances such as clenbuterol, represent the group of substances more commonly found in all the statistical reports. Figure 3 shows an increase in the proportion of findings related to anabolic agents from 2003 to 2009, mainly due to the reduction by WADA of the

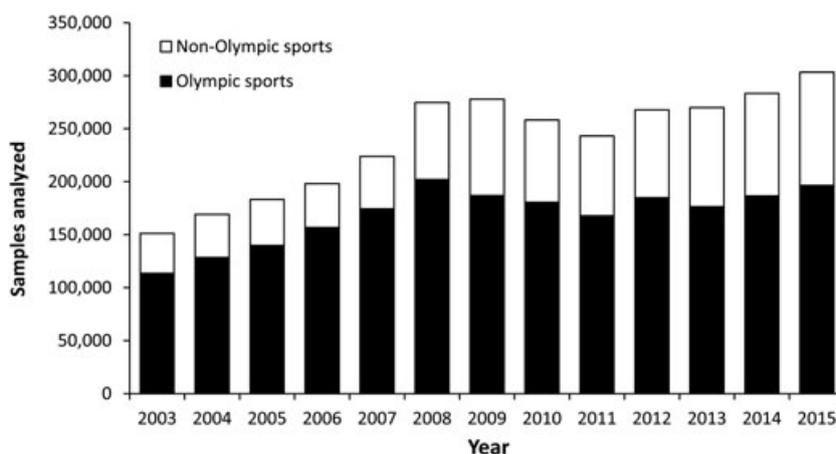


Figure 1. Total number of samples analyzed by WADA-accredited laboratories per year.

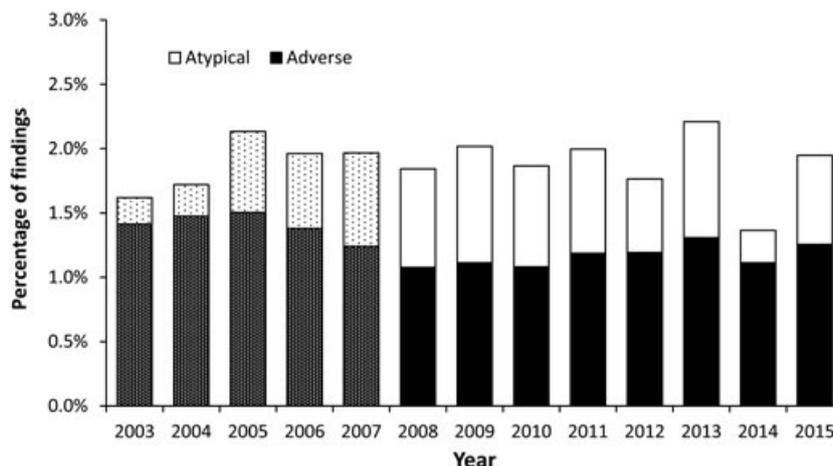


Figure 2. Percentage of adverse and atypical findings in the samples analyzed by WADA-accredited laboratories. Note: In the reports from 2003 to 2007, WADA only reported adverse analytical finding as: 'a report from a laboratory or other WADA-approved entity that, consistent with the International Standard for Laboratories and related Technical Documents, identifies in a Sample the presence of a Prohibited Substance or its Metabolites or Markers (including elevated quantities of endogenous substances) or evidence of the Use of a Prohibited Method. From 2008 to 2014, WADA also included atypical findings in its reports as "a report from a laboratory or other WADA-approved entity which requires further investigation as provided by the International Standard for Laboratories or related Technical Documents prior to the determination of an Adverse Analytical Finding'. To construct this Figure, we have estimated the percentage of atypical findings from 2003 to 2007 using the data on anabolic agents that constituted atypical findings (such as testosterone/epitestosterone ratio, androsterone, or ethiocholanolone, etc.).

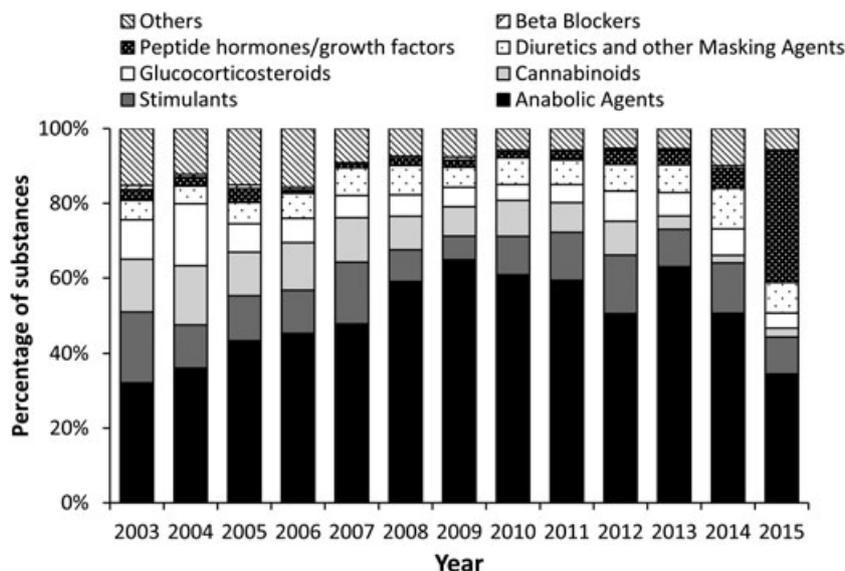


Figure 3. Percentage of the groups of substances from the List of Prohibited Substances in relation to the total number of adverse/analytical findings found by WADA-accredited laboratories.

testosterone/epitestosterone threshold from 6/1 to 4/1. Since then, the proportion of findings associated with anabolic substances has remained at $\sim 58.2 \pm 6.1\%$ till 2015 when a noteworthy decrease to 34.5% in 2015 was produced likely due to the new implementation of the steroidal module of the ABP. Stimulants represent the second group of substances found in adverse samples in most years although their proportion (on average $\sim 12.1 \pm 3.4\%$ from 2003 to 2015) is much lower when compared to anabolic agents. With this analysis, the importance of stimulants as doping substances is in part 'underestimated' because this group of substances is only considered as adverse finding when they are found in the samples obtained in-competition, while anabolic agents are prohibited at all times (in samples obtained in and out of

competition). Other groups of substances that represent proportions lower than 10% of all the adverse analytical/atypical findings are glucocorticosteroids, diuretics/masking agents, peptide hormones/growth factors and beta-blockers, and their frequencies remained relatively constant from 2003 to 2015. Of note, cannabinoids have progressively decreased from 13.9% of the total adverse findings in 2003 to 2.4% in 2015 due to the changes in the threshold proposed for carboxy-THC.^[7] while the percentage of peptide hormones and growth factors has rocketed in 2015 due to the changes proposed for the detection of the luteinizing hormone. Despite these small changes observed in a sequence of 13 years of anti-doping analyses, most of them promoted by WADA technical modifications rather than changes in the patterns of use,

it can be objectively concluded that the proportion of findings of the different groups of prohibited substances has been relatively constant over the last years.

Athlete biological passport

Over the last few years, WADA has developed the Anti-Doping Administration and Management System (ADAMS) that has permitted the implementation of the athlete biological passport (ABP; first issued by UCI in 2008, although WADA implemented this anti-doping method in 2009). The ABP aims to establish the misuse of forbidden substances or methods based on the measurement of physiological variables without relying entirely on the detection of particular banned substances and/or methods. Additionally, based on abnormal values or profiles, athletes can be targeted for traditional anti-doping tests to detect prohibited substances or methods. Although the ABP was initially proposed to monitor haematological variables to primarily detect blood doping (haematological module), this approach will be also used to detect the misuse of growth factors and anabolic steroids.^[8,9] At present, the ABP is a key tool for carrying out target testing, especially in endurance sports disciplines.^[10] Although WADA's data of adverse findings based on the ABP are not summarized in the anti-doping laboratories' testing figures, the UCI reported a total of 26 athletes who were found positive by using the ABP blood parameters from a total of more than 1000 athletes tested between 2008 and 2010.^[11] The implementation of the ABP by the UCI enhanced the numbers obtained in 2007 by this federation, when the atypical changes in athletes' blood parameters were not used for the detection of blood doping. Perhaps, it is still too early to be able to analyze the efficacy of the ABP and we will have to wait a few more years to evaluate this WADA strategy.

Roadmap for the future

This brief analysis of the WADA statistical reports leads us to the following conclusions: (1) the increase in anti-doping pressure from 2003 to 2015, as evidenced by increased numbers of samples analyzed per year and the number of banned substances, has not directly produced a higher percentage of adverse/atypical findings, even when the detection capacity of the laboratories has improved remarkably in terms of sensibility for identifying prohibited substances. While the fight against doping has been effective to increase by 142% the absolute number of samples detected as doping (from 2003 to 2015), other more efficient policies should be implemented in the following years to allow a higher detection of adverse/atypical findings without the necessity of increasing the number of samples analyzed. (2) Anabolic agents remain the most common doping substances detected while the remaining groups of substances are much less frequently found in doping control samples.

Given that the enhancement of the anti-doping programme led by WADA over these last 13 years minimally affected the percentage of adverse/atypical findings, it is likely necessary to take another step in sampling strategies, such as 'more intelligent testing'^[12] based on the differences in the prevalence of doping

substances and patterns of use among different sports disciplines.^[13] This more intelligent anti-doping testing requires the doping authorities to target athletes/sports/countries with higher risks of doping, the increase in the number of unannounced out-of-competition testing and the enhancement of the use of retroactive analysis of blood and urine samples. On the other hand, the enhancement of the deterrent power of the anti-doping strategies together with the educational policies has probably contributed to a lower doping prevalence that has affected the percentage of adverse findings.

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