Supplementary data:

Table 1: Primary reason for somatic hospital contact

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Disease/(ICD-10 group) | AAS-users | | Controls | | P |
|  | Contacts | Individuals | Contacts | Individuals |
| Infectious disorder (A+B) | 109 | 57 | 467 | 295 | <0.001 |
| Cancer and benign tumors(C+D00-D48) | 51 | 24 | 485 | 178 | 0.161 |
| Non-mailgnant hematological disorders (D48-89) | 11 | 7 | 82 | 36 | 0.100 |
| Endocrine disorders (E) | 49 | 27 | 440 | 172 | 0.025 |
| Psychiatric disorder (F) | 24 | 19 | 211 | 112 | 0.029 |
| Neurological disorders (G) | 92 | 40 | 568 | 263 | 0.011 |
| Diseases of the eyes or ears | 87 | 39 | 584 | 335 | 0.353 |
| Diseases of the circulatory system (I) | 79 | 37 | 487 | 186 | <0.001 |
| Diseases of the respiratory system (J) | 98 | 56 | 760 | 383 | 0.006 |
| Diseases of the digestive sytem (K) | 241 | 100 | 1481 | 620 | <0.001 |
| Diseases of the skin (L) | 237 | 91 | 621 | 332 | <0.001 |
| Diseases of musculoskeletal system (M) | 487 | 156 | 2302 | 1053 | <0.001 |
| Diseases of the genitourinary sytem (G) | 206 | 112 | 880 | 436 | <0.001 |
| Congenital malformations (Q) | 16 | 10 | 168 | 84 | 0.599 |
| Laboratory abnomalitites etc (R) | 322 | 133 | 1622 | 838 | <0.001 |
| Injury (S, T00-35, T66-T98, X,Y) | 1337 | 361 | 7107 | 2605 | <0.001 |
| Poisoning /Toxic effects (T36-65) | 42 | 27 | 244 | 121 | <0.001 |
| Other (Z) | 1621 | 394 | 8630 | 2852 | <0.001 |
| Missing | 6 | 5 | 28 | 27 | 0.197 |
| Total | 5115 | 545 | 27167 | 5450 |  |

Explanation: In total, the 545 AAS users had 5,115 hospital contacts during follow-up and 5,450 persons in the control cohort had 27,167 hospital contacts. Primary reason for hospital contact are found in the rows. The P-values are found in the last column, and are based ordinary chi-square tests calculated according to the number of individuals

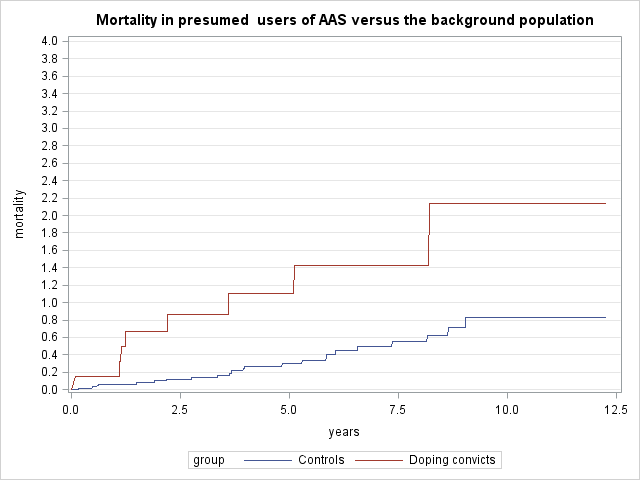
Table 2: Results of the hypothesis-free approach:

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Disease** | Incident cases | | Incidence rate, per 1000 person- years | | **Hazard ratio (95% CI) ref=controls** | **P** | **P Bonferroni** | Cumulative Prevalence | | P |
| AAS users | Controls | AAS -user | Controls | AAS-users | Controls |
| Testicular dysfunction (ICD-10:E29) | 11 | 5 | 2.74 | 0.12 | 21.86 (7.59-62.90) | <.0001 | <.0001 | 2.20% | 0.15% | <0.0001 |
| Umbilical hernia (ICD-10:K42) | 9 | 18 | 2.25 | 0.45 | 5.01 (2.25-11.16) | <.0001 | 0.030 | 2.02% | 0.50% | 0.0004 |
| Other abdominal hernia (ICD-10:K45) | 5 | 3 | 1.24 | 0.07 | 16.59 (3.96-69.41) | 0.0001 | 0.045 | 1.10% | 0.07% | <0.0001 |
| Other diseases of the digestive sytem ICD-10:K92 | 7 | 6 | 1.76 | 0.15 | 11.70 (3.93-34.81) | <.0001 | 0.0037 | 2.20% | 0.33% | <0.0001 |
| Cutaneous abscesses, furuncles, carbuncles (L02) | 22 | 70 | 5.81 | 1.78 | 3.27 (2.03-5.28) | <.0001 | 0.0005 | 8.62% | 2.44% | <0.0001 |
| Urticaria (ICD-10:L50) | 11 | 12 | 2.76 | 0.30 | 9.15 (4.04-20.75) | <.0001 | <.0001 | 2.39% | 0.66% | 0.0003 |
| Granulomatous disorders of skin and subcutaneous tissue (ICD-10:L92) | 6 | 5 | 1.49 | 0.12 | 11.91 (3.63-39.02) | <.0001 | 0.016 | 1.47% | 0.11% | <0.0001 |
| Other disorders of skin and subcutaneous tissue (ICD-10: L98) | 7 | 10 | 1.74 | 0.25 | 6.97 (2.65-18.31) | <.0001 | 0.031 | 1.47% | 0.29% | 0.0009 |
| Dorsalgia (ICD-10:M54) | 38 | 152 | 10.07 | 3.95 | 2.55 (1.79-3.64) | <.0001 | <.0001 | 10.46% | 5.21% | <0.0001 |
| Shoulder lesions (ICD-10:M75) | 30 | 126 | 7.86 | 3.22 | 2.44 (1.64-3.63) | <.0001 | 0.0043 | 8.44% | 3.41% | <0.0001 |
| Other acquired deformities of musculoskeletal system and connective tissue (ICD-10:M95) | 9 | 15 | 2.25 | 0.38 | 5.97 (2.61-13.63) | <.0001 | 0.0085 | 1.83% | 0.68% | 0.0084 |
| Male infertility (ICD-10:N46) | 28 | 117 | 7.21 | 2.98 | 2.42 (1.6-3.66) | <.0001 | 0.0099 | 6.61% | 3.06% | <0.0001 |
| Gynecomastia (ICD-10:N62) | 38 | 31 | 10.39 | 0.78 | 13.29 (8.27-21.35) | <.0001 | <.0001 | 13.94% | 1.30% | <0.0001 |

Explanation: Column 2 and 3 display incident cases from baseline (date of doping test/or enrollment as control) to the end of follow-up. Column 4 and 5 display the incidence rates per 1000 person-years, and column 6 the corresponding hazard ratio. Column 7 shows the P-value associated with the hazard ratio, and column 8 the Bonferroni adjusted P-value. Finally, the last three columns show the cumulative prevalence (cases known at baseline+incident cases) in AAS users and controls and the corresponding P-value for the null-hypothesis.

**Replication analysis,** using data on 644 males who received a doping sentence, because they refused to deliver a urine. Their data are compared 6440 male controls. See text. Average age for these strongly suspected AAS-user at enrollment 28.4 (SD 7.3), Average age among controls at enrollment 28.4 (SD 7.2)

Figure 1:



Explanation: The red line represents the user of Androgenic Anabolic Steroids (AAS) and blue line the controls. The mortality was significantly higher in the AAS cohort ( Log-rank test: P=0.0013). 8 users of AAS died during follow-up and 23 in the control group (HR 3.44 (1.54-7.70)).

Table 3- replication analysis

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Disease** | Incident cases | | Incidence rate, per 1000 person- years | | **Hazard ratio (95% CI) ref=controls** | **P** | **P Bonferroni** | Cumulative Prevalence | | P |
| AAS users | Controls | AAS -user | Controls | AAS-users | Controls |
| Male infertility | 22 | 99 | 6.81 | 3.07 | 2.22 (1.40-3.53) | 0.0007 | 0.011 | 5.12% | 2.89% | 0.0038 |
| Testicular dysfunction | 7 | 6 | 2.11 | 0.18 | 11.60 (3.90-34.51) | <.0001 | 0.0002 | 1.09% | 0.20% | 0.0013 |
| Testosterone supplementation | 7 | 4 | 2.48 | 0.14 | 17.53 (5.13-59.89) | <.0001 | 0.0001 | 1.16% | 0.27% | .00333 |
| Medication against erectile dysfunction | 47 | 124 | 18.10 | 4.47 | 4.06 (2.90-5.68) | <.0001 | <.0001 | 12.46% | 3.77% | <.0001 |
| Medication against acne | 29 | 80 | 13.97 | 3.31 | 4.21 (2.75-6.44) | <.0001 | <.0001 | 28.07% | 14.10% | <.0001 |
| Gynecomastia | 36 | 41 | 11.89 | 1.25 | 9.48 (6.06-14.83) | <.0001 | <.0001 | 12.11% | 1.46% | <.0001 |
| Surgery of the breast | 18 | 17 | 5.62 | 0.52 | 10.91 (5.62-21.18) | <.0001 | <.0001 | 4.97% | 0.57% | <.0001 |
| cancer excl non-melanoma skin cancer | <3 | 28 | . | 0.85 | . | 0.64 | 1 | 0.47% | 0.75% | 0.62 |
| Ischaemic heart disease | 9 | 19 | 2.74 | 0.58 | 4.76 (2.15-10.52) | 0.0001 | 0.0017 | 2.02% | 0.57% | .00038 |
| Other forms of heart diseases | 16 | 50 | 4.95 | 1.53 | 3.24 (1.84-5.68) | <.0001 | 0.0006 | 3.88% | 1.72% | .00070 |
| Thromboembolic disorders | 6 | 15 | 1.83 | 0.46 | 4.02 (1.56-10.36) | 0.0040 | 0.060 | 1.86% | 0.47% | .00025 |
| Diseases of the liver | <3 | 7 | . | 0.21 | . | 0.19 | 1 | 0.62% | 0.31% | 0.27 |
| Disease of gallblader, biliary tract and pancreas | 3 | 31 | 0.90 | 0.94 | 0.96 (0.29-3.14) | 0.95 | 1 | 0.93% | 0.81% | 0.65 |
| Diseases of the kidney | 8 | 14 | 2.41 | 0.43 | 5.65 (2.37-13.48) | <.0001 | 0.0014 | 1.86% | 0.65% | 0.0028 |
| Kidney stone | 11 | 50 | 3.33 | 1.53 | 2.18 (1.13-4.18) | 0.020 | 0.29 | 2.17% | 1.26% | 0.069 |

Explanation: Column 2 and 3 display incident cases from baseline (date of doping test/or enrollment as control) to the end of follow-up. Column 4 and 5 display the incidence rates per 1000 person-years, and column 6 the corresponding hazard ratio. Column 7 shows the P-value associated with the hazard ratio, and column 8 the Bonferroni adjusted P-value. Finally, the last three columns show the cumulative prevalence (cases known at baseline+incident cases) in AAS users and controls and the corresponding P-value for the null-hypothesis.