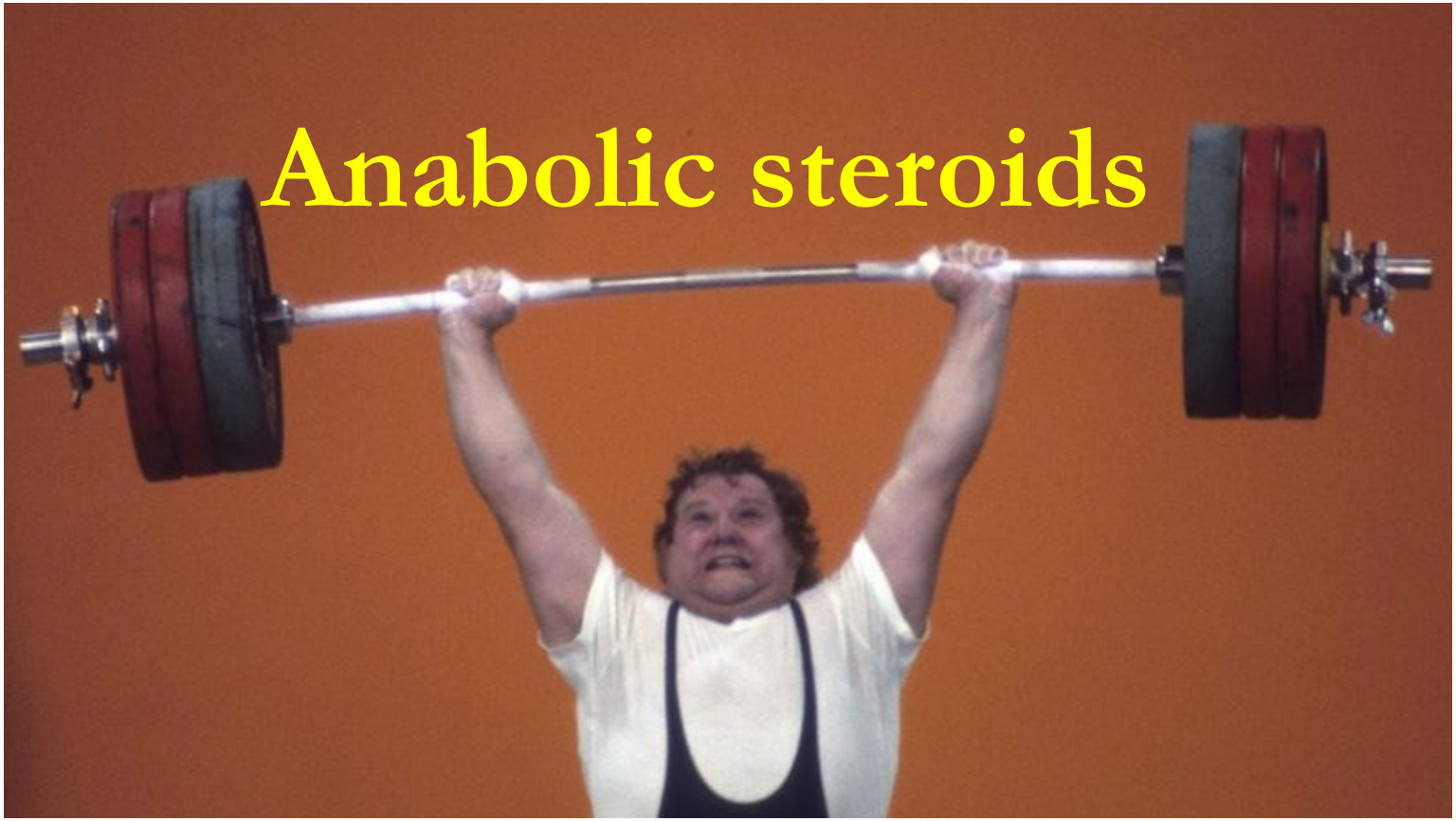
Anabolic steroids



Henrik Horwitz, MD, PhD

Bispebjerg Hospital

Disclosures

Received a research grant from
Antidoping Danmark

Agenda

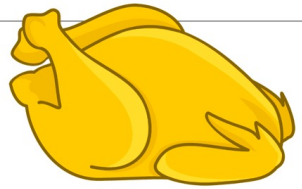
Historical Notes

General Physiology

Danish Data

Chickens vs. Chicks.

"If it crows, it's a rooster. If it lays an egg, it's a hen."

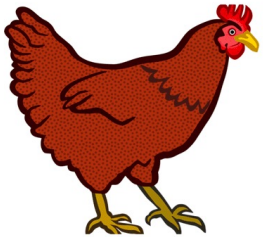


Roast chicken

(Most of the chicken we eat is hen meat.)

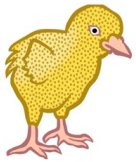
Rooster/Cock

(an adult male)



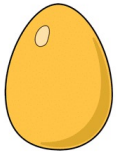
Hen

(an adult female)



Pullet

(a juvenile female)



An egg

Capon

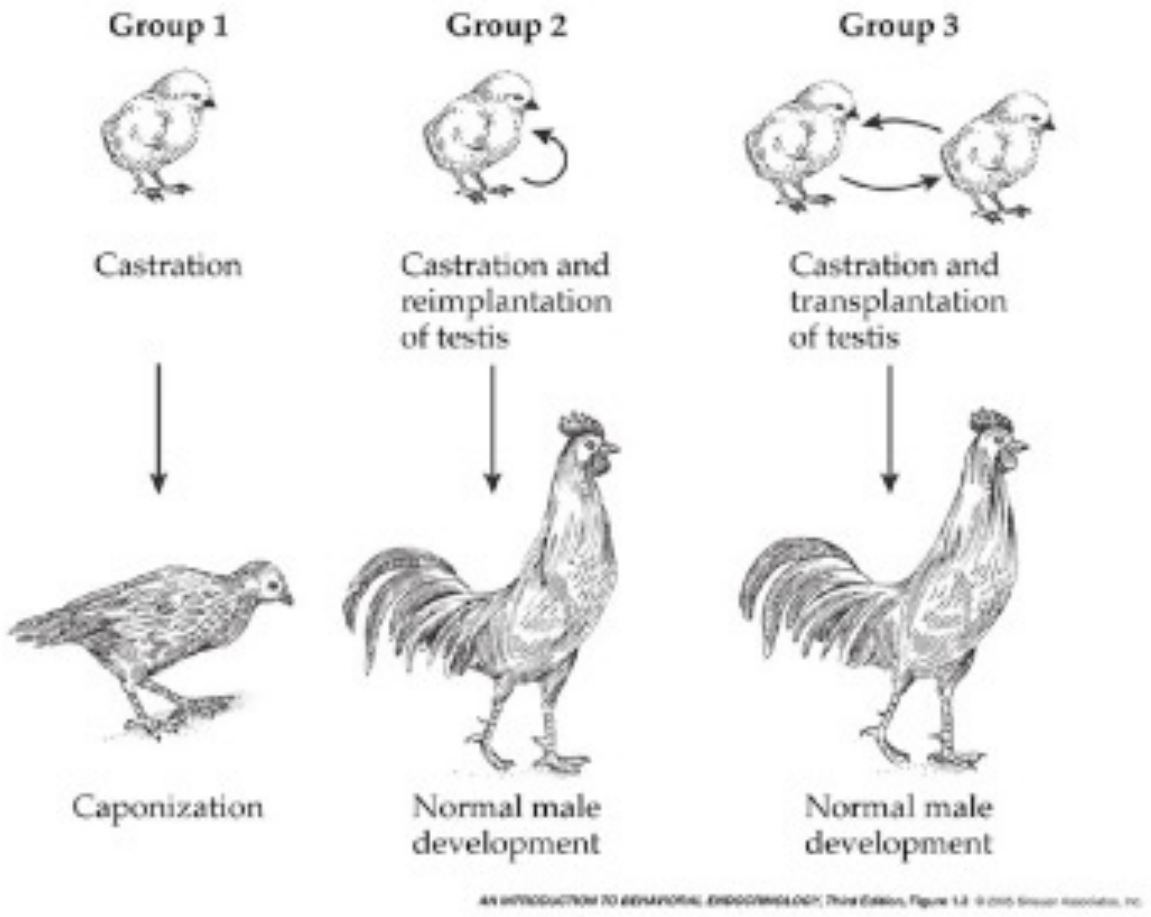
(a castrated male)

Cockerel

(a juvenile male)

- Chickens live together in flocks.
- Young chickens are called chicks.
- Roosters crow: cock-a-doodle-doo.
- Hens cluck.

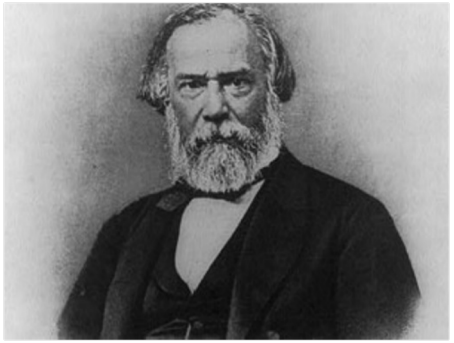
All roosters, hens, cockerels, pullets and capons are chickens. They are subcategories of age and gender, but all the same species.



Arnold Adolph Berthold 1803-61

In 1849 Arnold Adolph Berthold demonstrated that it was possible to transplant testicles to castrated cockerels, and that this procedure ensured their normal development; and thus, he concluded that testicles secreted a blood-bound substance with masculinizing properties.

Charles-Edouard Brown-Sequard 1817-94



A

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NOTE ON

THE EFFECTS PRODUCED ON MAN BY SUB-CUTANEOUS INJECTIONS OF A LIQUID OBTAINED FROM THE TESTICLES OF ANIMALS.

By DR. BROWN-SÉQUARD, F.R.S. &c.

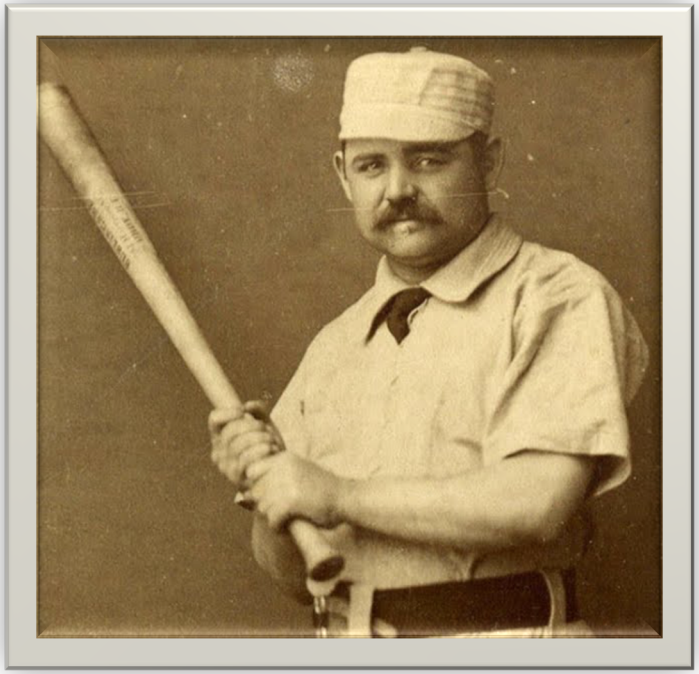
On the 1st of June last I made at the Société de Biologie of Paris a communication on the above subject, which was published in the *Comptes Rendus* of that Society on June 21st (No. 24). I will give here a summary of the facts and views contained in that paper and in two subsequent ones, adding to them some new points.

There is no need of describing at length the great effects produced on the organisation of man by castration, when it is made before the adult age. It is particularly well known that eunuchs are characterised by their general debility and their lack of intellectual and physical activity. There is no medical man who does not know also how much the mind and body of men (especially before the spermatic glands have acquired their full power, or when that power is declining in consequence of advanced age) are affected by sexual abuse or by masturbation. Besides, it is well known that seminal losses, arising from any cause, produce a mental and physical debility which is in proportion to their frequency. These facts and many others have led to the generally admitted view that in the seminal fluid, as secreted by the testicles, a substance or several substances exist which, entering the blood by resorption, have a most essential use in giving strength to the nervous system and to other parts. But if what may be called spermatic

in favour of that conclusion. It is known that well-organised men, especially from twenty to thirty-five years of age, who remain absolutely free from sexual intercourse or any other causes of expenditure of seminal fluid, are in a state of excitement, giving them a great, although abnormal, physical and mental activity. These two series of facts

Pud Galvin 1856-1902

The same year the baseball player Pud Galvin experimented with this elixir as a performance enhancing agent



Brown-Séquard revisited: a lesson from history on the placebo effect of androgen treatment

Andrea J Cussons, Chotoo I Bhagat, Stephen J Fletcher and John P Walsh

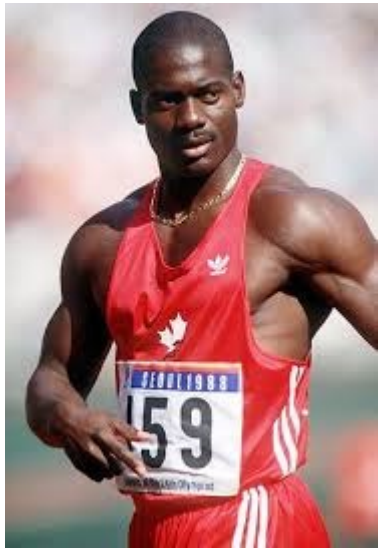
Results

The mean testosterone concentration in the testicular extracts was 390 nmol/L (SD, 306 nmol/L), equivalent to 112 µg/L (SD, 88 µg/L). The Box gives the concentration found in each of the five extracts.

Testosterone concentration in testicular extracts prepared from five dogs

Dog	Breed	Age (months)	Dog weight (kg)	Testicular weight (g)	Testosterone (nmol/L)
1	Great dane	12	31.9	26.6	790
2	Pointer cross German shepherd	10	28.0	17.0	40
3	Kelpie cross German shepherd	24	21.9	17.9	580
4	Bull terrier	18	18.0	21.0	150
5	Papillon	18	2.2	4.7	390

Anabolic steroids enter the world of sports



Ben Johnson stanozolol 1988

Gerd Bonk 1951-2014

DDR had a succesful program

Effects

THE EFFECTS OF SUPRAPHYSIOLOGIC DOSES OF TESTOSTERONE ON MUSCLE SIZE AND STRENGTH IN NORMAL MEN

SHALENDER BHASIN, M.D., THOMAS W. STORER, PH.D., NANCY BERMAN, PH.D., CARLOS CALLEGARI, M.D., BRENDA CLEVENGER, B.A., JEFFREY PHILLIPS, M.D., THOMAS J. BUNNELL, B.A., RAY TRICKER, PH.D., AIDA SHIRAZI, R.PH., AND RICHARD CASABURI, PH.D., M.D.

VARIABLE	NO EXERCISE		EXERCISE	
	PLACEBO	TESTOSTERONE	PLACEBO	TESTOSTERONE
Body weight (kg)				
Base line	79.5±4.3	82.2±1.9	85.5±3.3	76.0±3.0
10 wk	80.8±4.4	85.7±1.5	86.4±2.9	82.0±2.8†
P value	—	0.004	—	<0.001
Fat-free mass (kg)				
Base line	65.1±2.5	69.9±1.3	72.1±2.3	65.3±1.8
10 wk	65.9±2.7	73.1±2.2	74.1±2.2	71.4±1.8‡
P value	—	—	0.017	<0.001
Triceps area (mm^2)				
Base line	3621±213	3579±260	4,052±262	3483±217
10 wk	3539±226	4003±229§	4,109±230	3984±239§
P value	—	0.003	—	<0.001
Quadriceps area (mm^2)				
Base line	8796±561	9067±398	9,920±569	8550±353
10 wk	8665±481	9674±472§	10,454±474§	9724±348¶
P value	—	<0.001	—	<0.001
Bench-press exercise (kg lifted)				
Base line	88±5	96±8	109±12	97±6
10 wk	88±5	105±8§	119±11§	119±6‡
P value	—	—	0.005	<0.001
Squatting exercise (kg lifted)				
Base line	102±6	103±8	126±13	102±5
10 wk	105±6	116±5	151±13§	140±5¶
P value	—	0.004	<0.001	<0.001

600 mg Testosterone weekly vs placebo

Adverse effects

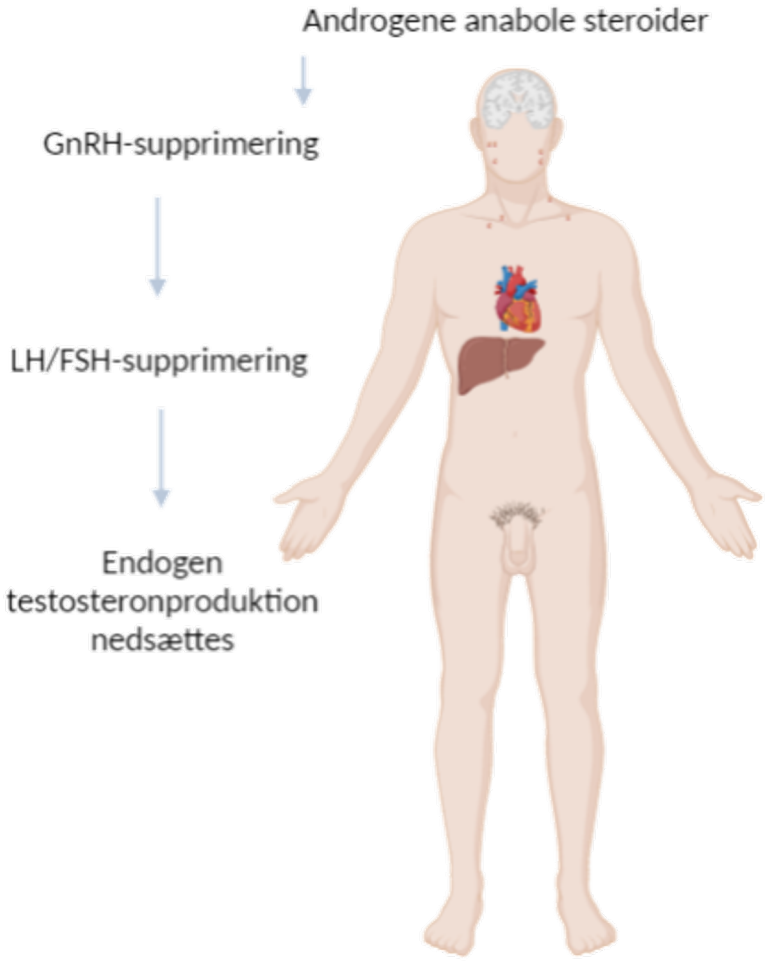
Experiences from DDR

Table 3. Some of the documented damaging side effects observed in male and female GDR athletes during treatment with anabolic-androgenic steroids, notably Oral-Turinabol.

Damaging side effect	% of athletes affected	Dosage category[a]
Side effects observed in athletes of jumping events, heptathlon, and decathlon [7]		
Muscle tightness	65	1, 4, 5
Body weight increase	23	1, 4, 5, 6
Muscle cramps	15	1, 3
Irregular menstruation, including amenorrhea	15	1, 6, 7
Acne and hirsutism	10	7, 8
Alteration of libido, sexual potency, fertility	8	1, 5, 7, 8
Edema	2	1
Diarrheas, constipation	2	1, 6
Functional/structural liver damage	0–1	7, 8, 5
Other damaging side effects reported by "Unofficial Collaborators" in Stasi reports		

Kilde: Franke WW, Berendonk B. Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic government. *Clin Chem* 1997;43(7):1262-79

Expected adverse effects



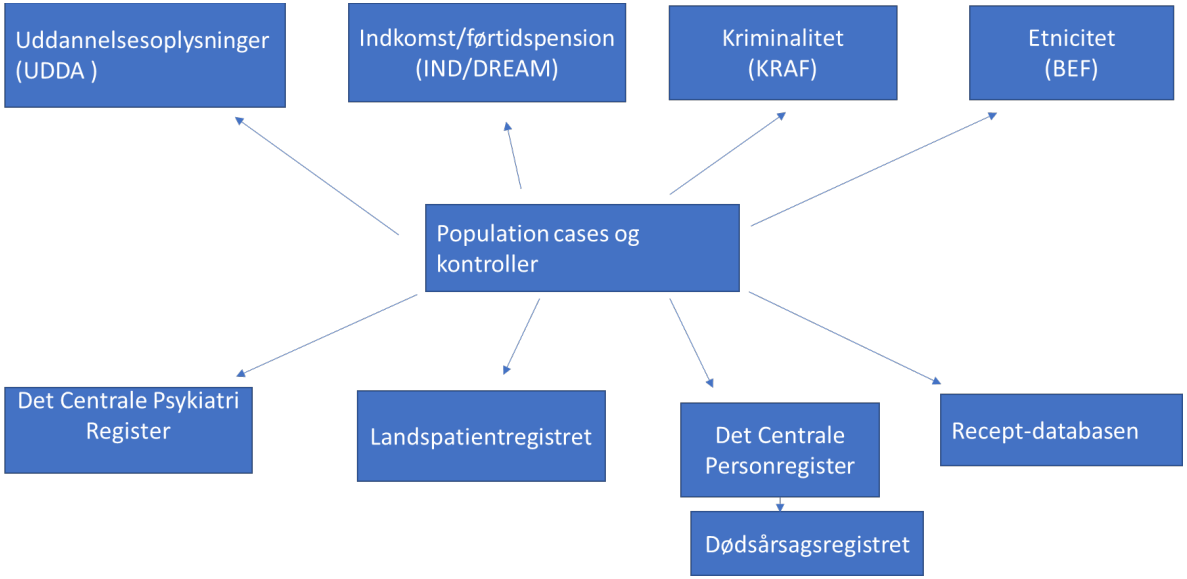
Klinisk manifestation	Undersøgelser
Psykisk påvirkning	Psykiatrisk vurdering med screening for både depression, mani og angst
Hudpåvirkning	Aknepræg, abscesdannelse
Gynækomasti	
Kardiel påvirkning, brystsmerter, hjertebanken	EKG, iskæmimarkører, evt. ekkokardiografi
Leverpåvirkning	Levermarkører
Hypogonadisme, infertilitet	Objektiv undersøgelse, fertilitetsmarkører, ejakulatundersøgelse
Øget muskelstyrke	Objektiv undersøgelse, evt. kreatinkinase

Data from Antidoping Denmark

- 1219 doping sanctioned individuals in Danish fitness centres: 2006-2018
- 1189 of these were males living in Denmark
- 545 with a positive urine sample and 644 refused to deliver a urine sample

Study design

- Cohort study
- 10-50 age and sex matched controls



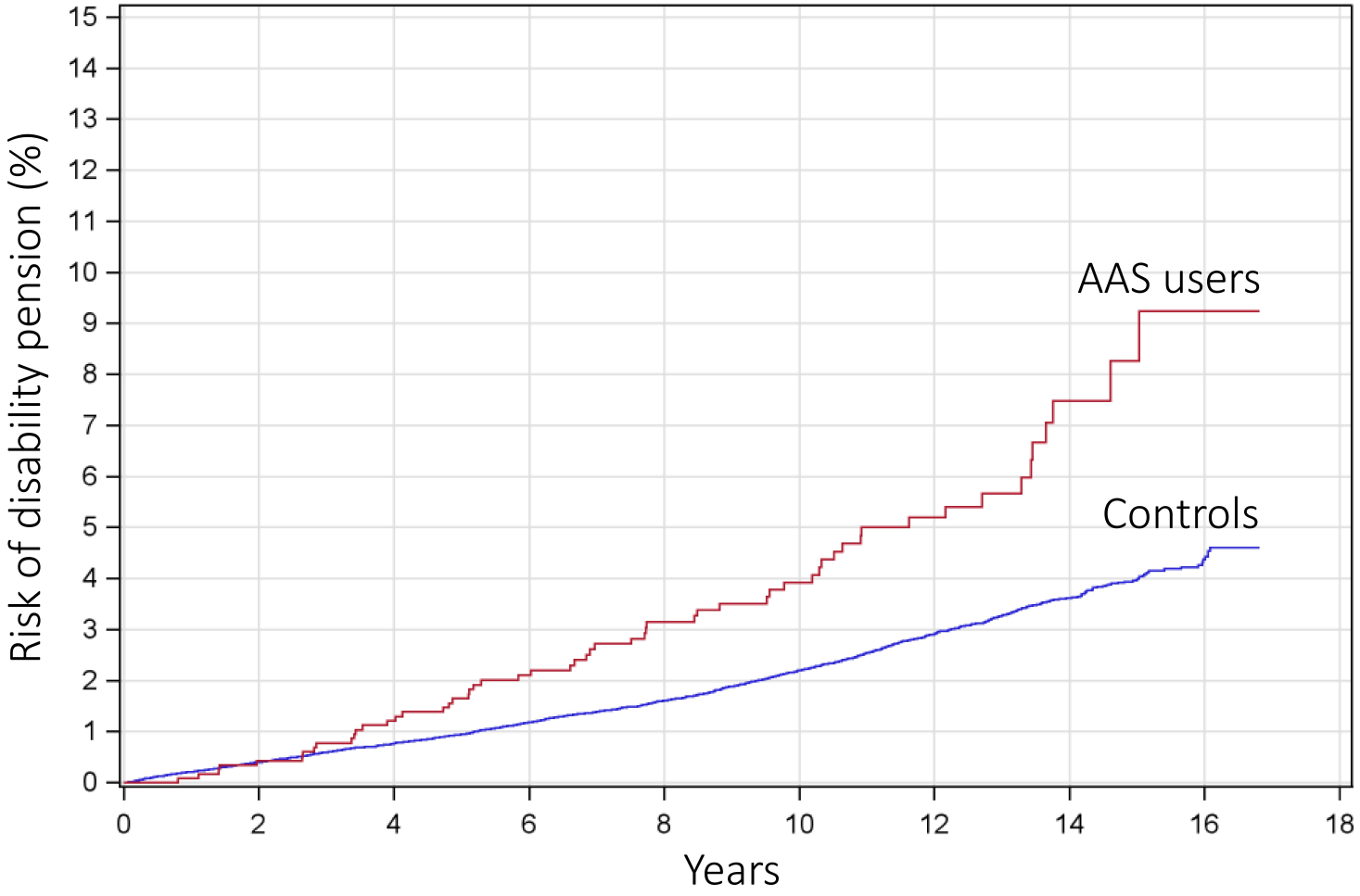
Demograhics

		AAS users (n=1189)	Control participants (n=59450)
Age at baseline	Mean (SD), years	27.4 (6.9)	27.4 (6.9)
Education level at baseline			
10 years or less	N (%)	300 (25.2)	9,290 (15.6)
10 to 15 years	N (%)	782 (65.8)	36,087 (60.7)
15 years or more	N (%)	72 (6.1)	12,023 (20.2)
Missing	N (%)	35 (2.9)	2,050 (3.4)

Occupational status

Occupational Status at baseline		AAS-users	Controls
Self-supporting	N (%)	880 (74.0)	50,319 (84.6)
Sick leave – temporarily	N (%)	44 (3.7)	1,159 (2.0)
Sick leave – permanently	N (%)	38 (3.2)	1,513 (2.5)
Unemployed	N (%)	208 (17.5)	5,916 (10.0)
Missing	N (%)	19 (1.6)	543 (0.9)

Risk of becoming being disability pension



Anabolic-androgenic steroids and the risk of imprisonment

Thea Christoffersen[a,*], Jon Trærup Andersen[a,b], Kim Peder Dalhoff[a,b], Henrik Horwitz[a,b]

[a] *Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, Bispebjerg Bakke 23, 2400 Copenhagen NV, Denmark*
[b] *Department of Clinical Medicine, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark*

Table 3
Time to first prison sentence, within different domains of crime.

Law offense	baseline AAS user	baseline control	*P* Value[a]	Follow-up AAS-users	Follow-up controls
Property crime (i.e. theft, burglary, robbery)	8.07%	1.54%	< .0001	11.01%	2.15%
Violation of the traffic law	0.92%	0.42%	0.11	2.57%	0.70%
Violation of the law on narcotics	1.47%	0.26%	< .0001	2.02%	0.51%
Violent crime	13.58%	2.02%	< .0001	18.53%	2.72%
Violation of the weapon law	0.55%	0.11%	0.011	1.47%	0.22%
Other	6.97%	0.79%	< .0001	12.11%	1.34%
Any prison sentence	20.55%	3.65%	< .0001	29.54%	4.90%

Health effects

Depression and Anxiety

RESEARCH REPORT | Open Access

Psychiatric morbidity among men using anabolic steroids

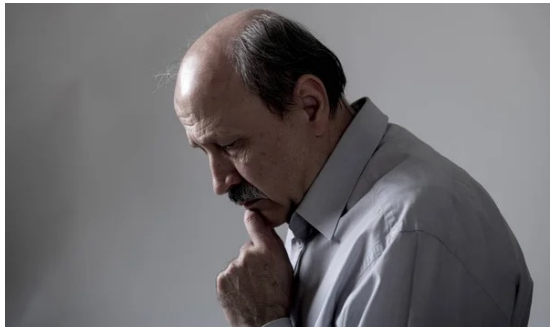
Josefine Windfeld-Mathiasen, Thea Christoffersen, Niels August Willer Strand, Kim Dalhoff, Jon Trærup Andersen, Henrik Horwitz

First published: 25 October 2022 | https://doi.org/10.1002/da.23287

Psychiatric effects

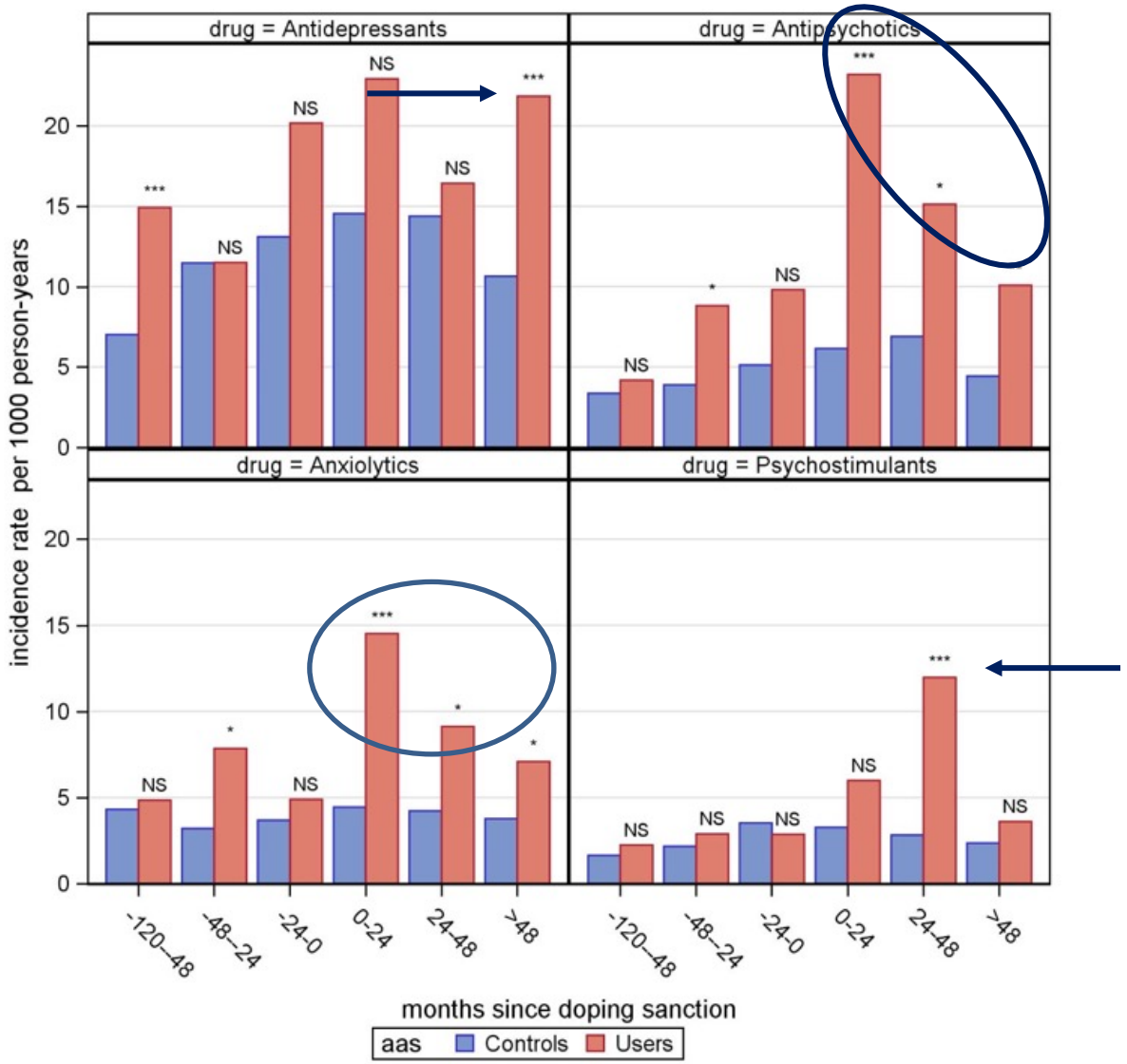
"Three women could be bouncing naked on a trampoline in front of you, and all you'd want is a cup of tea."

Testosterone improves mental well-being in hypogonadal men. Castration in prostate cancer leads to depression



- Walther A, Breidenstein J, Miller R. Association of Testosterone Treatment With Alleviation of Depressive Symptoms in Men: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2019 Jan 1;76(1):31-4
- McHenry J, Carrier N, Hull E, et al.: Sex differences in anxiety and depression: role of testosterone. Front Neuroendocrinol 2014; 35:42–57
- Nead KT: Androgens and depression: a review and update. Curr Opin Endocrinol Diabetes Obes 2019; 26:175–179
- Fischer S, Ehlert U, Amiel Castro R: Hormones of the hypothalamic-pituitary-gonadal (HPG) axis in male depressive disorders - A systematic review and meta-analysis. Front Neuroendocrinol 2019; 55:10079

Incidence of psychopharmacological treatment



Psychiatric disorders

TABLE 3 Chronic psychopharmacological treatment and diagnoses

	AAS (%)	Control (%)	OR (unadjusted)	*p* Value	OR (adjusted)	*p* Value
Medication						
Five or more prescriptions of antipsychotics (N05A)	6.6	3.5	1.94 (1.34–2.80)	.0004[a]	1.71 (1.15–2.55)	.008[a]
Five or more prescriptions of anxiolytics (N05B)	3.3	1.4	2.35 (1.40–3.96)	.001[a]	2.1 (1.19–3.70)	.01[a]
Five or more prescriptions of antidepressants (N06A)	12.5	9.2	1.41 (1.08–1.85)	.01[a]	1.28 (0.96–1.70)	.09
Five or more prescriptions of psychostimulants (N06B)	4.0	2.9	1.43 (0.91–2.25)	.13	1.08 (0.67–1.75)	.74
Diagnoses						
F00–F09 Organic, including symptomatic, mental disorders	NA	NA	2.00 (0.44–9.17)	.37	2.13 (0.44–10.43)	.35
F10–F19 Mental and behavioral disorders due to psychoactive substance use	5.1	2.2	2.41 (1.58–3.67)	<.0001[a]	1.93 (1.24–2.99)	.004[a]
F20–F29 Schizophrenia, schizotypal and delusional disorders	1.7	1.9	0.85 (0.43–1.70)	.65	0.74 (0.36–1.51)	.40
F30–F39 Mood [affective] disorders	3.3	3.1	1.08 (0.66–1.77)	.76	0.9 (0.54–1.52)	.71
F40–F48 Neurotic, stress-related, and somatoform disorders	7.5	5.5	1.41 (1.00–1.97)	.048[a]	1.13 (0.80–1.61)	.49
F50–F59 Behavioral syndromes associated with physiological disturbances and physical factors	NA	NA	2.74 (0.76–9.84)	.12	3.84 (1.00–14.69)	.05[a]
F60–F69 Disorders of adult personality and behavior	1.3	1.7	0.75 (0.35–1.62)	.47	0.62 (0.28–1.37)	.24
F70–F79 Mental retardation	NA	NA	0.53 (0.07–3.93)	.53	0.37 (0.05–3.02)	.35
F80–F89 Disorder of psychological development	NA	NA	0.45 (0.11–1.87)	.27	0.38 (0.09–1.60)	.19
F90–F99 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	5.0	3.2	1.59 (1.05–2.41)	.029[a]	1.22 (0.79–1.89)	.38
Any psychiatric hospital contact	18.0	13.5	1.41 (1.12–1.78)	.004[a]	1.15 (0.9–1.48)	.27

Effects on skin

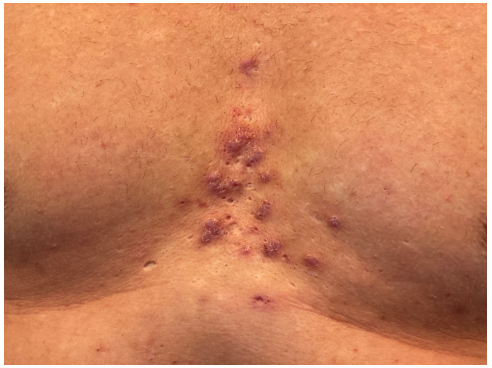


Table I. Dermatologic treatments and hospital-diagnosed skin conditions in anabolic androgenic steroids users (a total of 1189) and controls (a total of 11,890) from baseline and 1 year forward

Clinical category	Number		Relative risk (95% CI)	*P* value
	AAS users	Controls		
Dermatologic treatment				
At least one prescription of antifungals	98	626	1.57 (1.28-1.92)	<.0001
At least one prescription of antipsoriatics	<5*	58	NA*	NA*
At least one prescription of topical antibiotics	36	196	1.84 (1.29-2.61)	.0007
At least one prescription of topical antivirals	57	158	3.61 (2.68-4.85)	<.0001
At least one prescription of topical steroids	78	729	1.07 (0.85-1.34)	.557
At least one prescription of topical antiacne treatment	52	178	2.92 (2.16-3.96)	<.0001
At least one prescription of systemic antiacne treatment	21	50	4.20 (2.53-6.97)	<.0001
Hospital-diagnosed skin condition				
Acne	<5*	<5*	NA*	NA*
Alopecia	<5*	<5*	NA*	NA*
Bullous disorders	<5*	<5*	NA*	NA*
Dermatitis and eczema	<5*	12	NA*	NA*
Granulomatous disorders of skin and subcutaneous tissue	<5*	<5*	NA*	NA*
Hypertrichosis	<5*	<5*	NA*	NA*
Other follicular disorders	<5*	<5*	NA*	NA*
Infections of the skin and subcutaneous tissue	23	69	3.33 (2.09-5.32)	<.0001
Papulosquamous disorders	<5*	<5*	NA*	NA*
Pigmentation disorders	<5*	<5*	NA*	NA*
Ulcers	<5*	7	NA*	NA*
Urticaria and erythema	<5*	<5*	NA*	NA*

Effects on the heart

	Users	Controls	P
Ischaemic heart disease	**1.10%**	**0.68%**	**0.28**
Other forms of heart diseases	3.67%	1.76%	0.0048
Thromboembolic disorders	1.83%	0.39%	0.0003

Internal organs

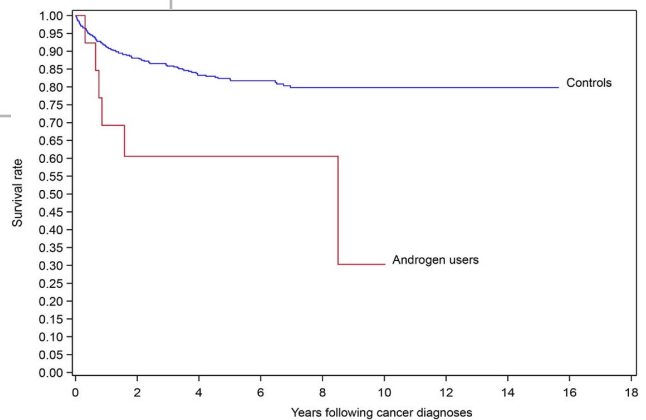
	Users	Controls	P
Diseases of the liver	**0.92%**	**0.15%**	**0.0042**
Disease of gallblader, biliary tract and pancreas	1.83%	1.16%	0.21
Diseases of the kidney	1.65%	0.61%	0.012
Kidney stone	2.57%	1.34%	0.036

Reproductive organs

Disease	AAS-users	controls	P
Male infertility	6.61%	3.06%	<.0001
Testicular dysfunction	2.20%	0.15%	<.0001
Testosterone supplementation	1.90%	0.23%	<.0001
Medication against erectile dysfunction	11.20%	3.76%	<.0001
Gynecomastia	13.94%	1.30%	<.0001
Surgery of the breast (surgery code: KH)	6.79%	0.53%	<.0001

Cancers

Malignancy type	Incident numbers (95% CI)		Incidence, per 100,000 person-years (95% CI)		IRR (95% CI)	
	Androgen users	Controls	Androgen users	Controls		*p*-value
Malignant neoplasm of prostate	0 (0–3.7)	17 (9.9–27.2)	0 (0–27.8)	2.6 (1.5–4.2)	0 (0–11.93)	1
Malignant neoplasm of breast	0 (0–3.7)	0 (0–3.7)	0 (0–27.8)	0 (0–0.6)	NA	NA
All cancers but non-melanoma skin cancer	13 (6.9–22.2)	612 (564.5–662.5)	98 (52–167)	93 (86–101)	1.05 (0.55–1.81)	0.9



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Clinical Research Article

Clinical Research Article

Male Fertility Before and After Androgen Abuse

Josefine Windfeld-Mathiasen,[1] Kim Peder Dalhoff,[1,2] Jon Trærup Andersen,[1,2] Marc Klemp,[2,3] Anna Horwitz,[4,5] and Henrik Horwitz[1,2]

[1]Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, 2400 Copenhagen, Denmark; [2]Department of Clinical Medicine, University of Copenhagen, 2200 Copenhagen, Denmark; [3]Population Studies & Training Center, Brown University, Providence, Rhode Island 02912, USA; [4]Department of Drug

Fertility = fecundity * sex appeal

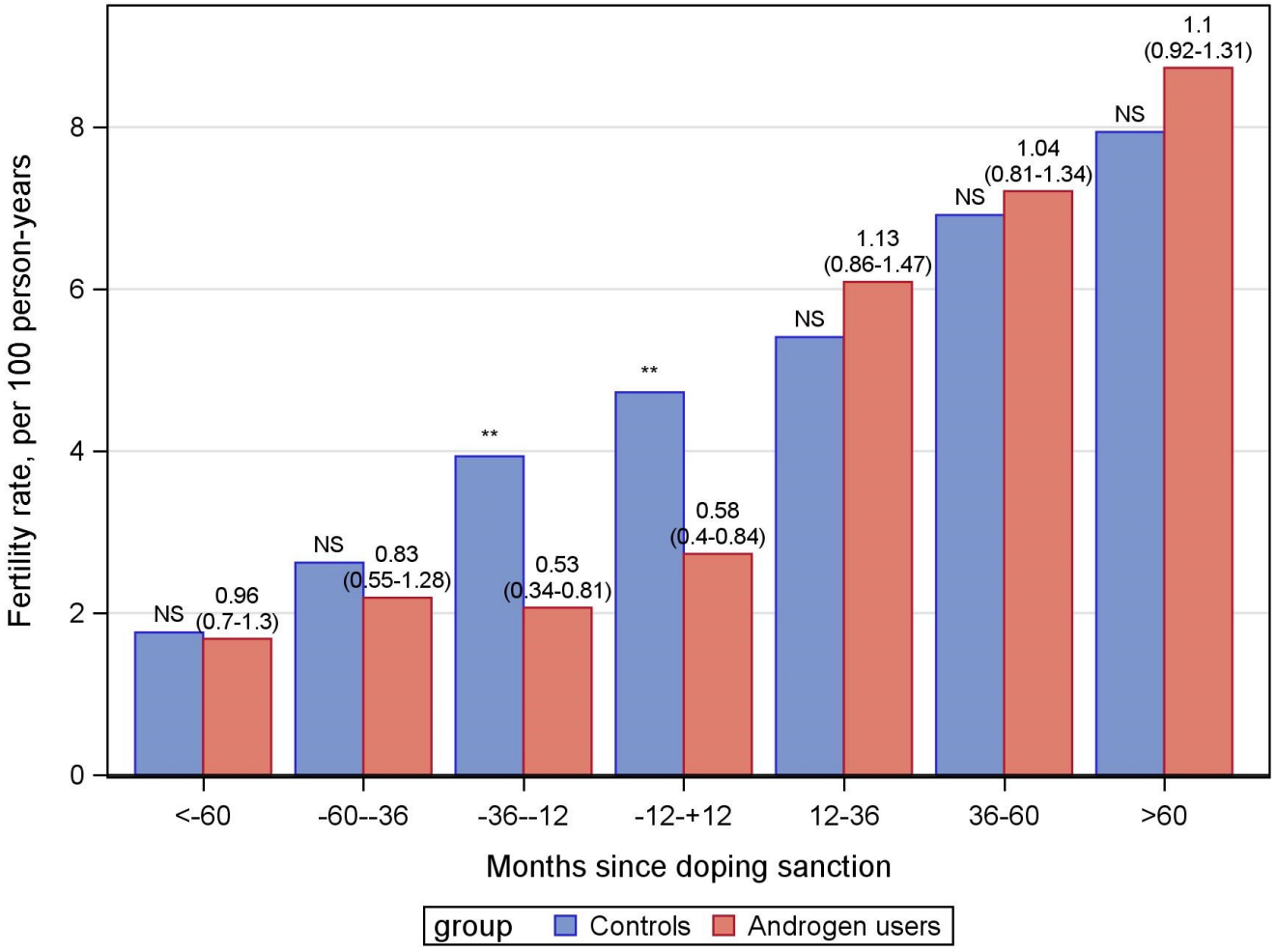
Male fertility before and after androgen abuse

Research endpoints:

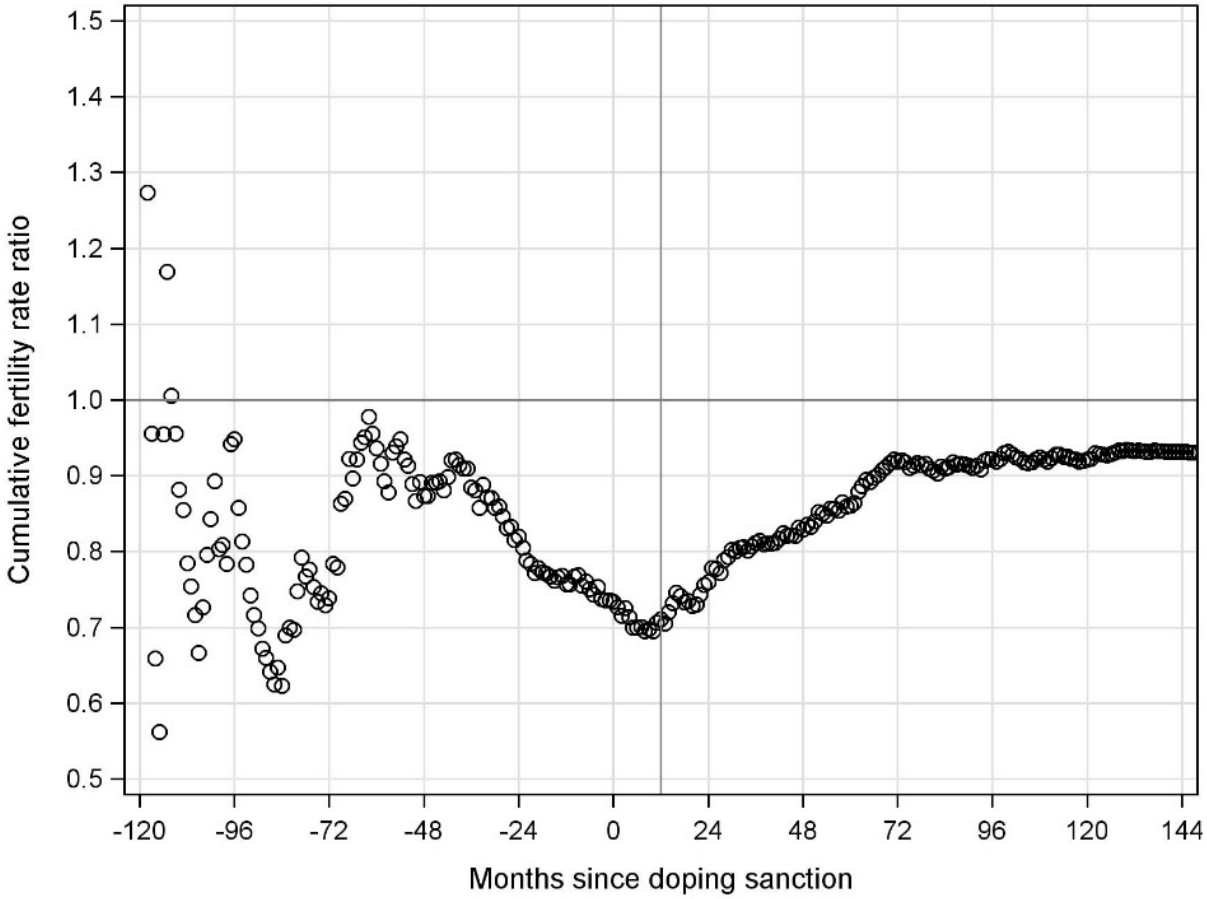
- To compare the fertility rate in androgen users with that of a cohort of age matched male controls.
  - To estimate the difference in fertility rates between the two groups.
  - To estimate the difference in the prevalence of assisted reproduction between the two groups.
- To estimate the change in fertility following a positive test in an anti-doping intervention program.

	Baseline			Follow-up		
	AAS	Control	*p*-value	AAS	Control	*p*-value
Age in years (SD)	26.2 (6.3)	26.2 (6.3)	0.99	33.6 (6.4)	33.5 (6.5)	0.74
Person-years	5265	50975	NA	9276	90611	NA
Average follow-up in years (SD)	9.7 (1.4)	9.4 (2.1)	0.0007	17.0 (3.9)	16.6 (4.1)	0.03
Number of children	102	1343	NA	382	4008	NA
Fertility rate per 100 person-years	1.94	2.63	0.0028*	4.12	4.42	0.18
Childless	86.24%	83.14%	0.064	54.50%	56.73%	0.31
Assisted reproduction	0.55%	1.41%	0.11	5.69%	5.28%	0.69
A diagnosis of infertility	1.47%	0.94%	0.23	6.61%	3.08%	<0.0001*
No. of observations	545	5450		545	5450	

Fertility rate

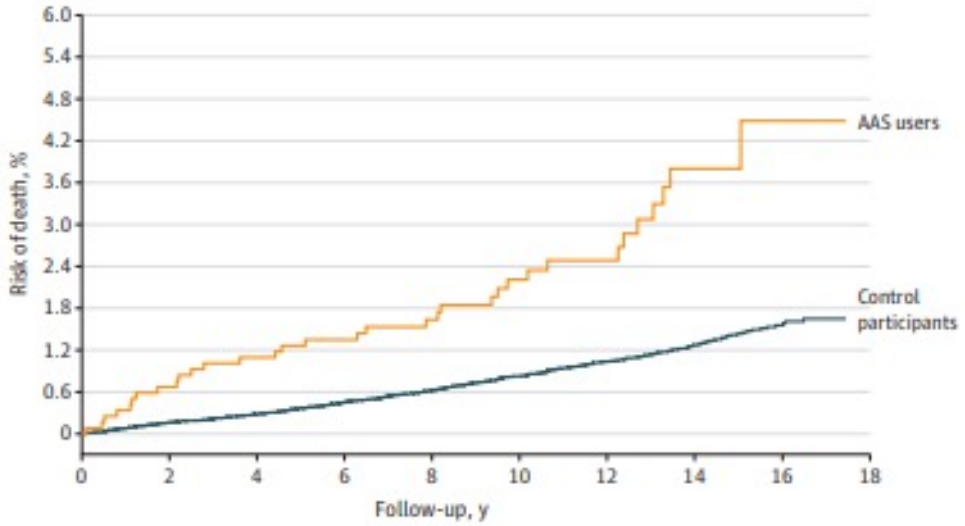


Cumulative fertility rate



Mortality in users of anabolic steroids

Figure. Time to Death for Users of Androgenic Anabolic Steroids and Control Participants



No. at risk									
AAS users	1189	1178	1169	1107	935	750	547	294	77
Control participants	59 450	58 130	57 474	54 047	45 617	36 765	27 096	14 708	3784

Table. Cohort Characteristics and Study Outcomes

	AAS users (n = 1189)	Control participants (n = 59 450)
Age at baseline, mean (SD), y	27.4 (6.9)	27.4 (6.9)
Duration of follow-up, mean (SD), y	11.2 (3.4)	11.0 (3.6)
Follow-up time, person-y	13 305	654 938
Death, No.	33	578
Cause of death, No.		
Unnatural	17	208
Natural	16	334
Unknown	0	36

Abbreviation: AAS, androgenic anabolic steroids.

Conclusion

- Anabolic steroids
  - provide an efficient shortcut to achieve muscle growth
  - is also associated with a range of side effects and premature death
- Most common somatic adverse drug reactions:
  - gynaecomastia
  - infertility
  - testicular dysfunction
  - acne
- Use of anabolic steroid use is strongly associated with anti-social behaviour

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