

Maintaining Sexual Function in Later Life



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Maintaining Sexual Function in Later Life – An Overview



There have been major advances in helping sexual, and particularly erectile, function in men in the past 15 years

In women advances are less clear: HRT's benefits are limited; the clinical use of Testosterone is recently licensed while neuro-hormones are being researched.

Maintaining Sexual Function in Later Life – An Overview



PDE5 inhibitors and male and female sex hormones are major aids to the maintenance of sexual function.

Maintaining Sexual Function in Later Life – An Overview



Other factors which may effect continuing sexual activity:

- Psychological health and well-being
- Physical health
- Socio-economic factors.

Maintaining Sexual Function

Social Aspects



What are the findings from large Population Surveys in the past 50 years?

Can we trace the changes in expectations about sex and sexual activity over time?

The Kinsey Report

Kinsey A, Pomeroy W, Martin C. Sexual Behaviour in the Human Male. Saunders, 1948

Kinsey A, Pomeroy W, Martin C, Gebhard P. Sexual Behaviour in the Human Female, Saunders, 1953

Pros:

Ground-breaking

Fresh insights

Showed variety of sexual behaviours

Cons:

Unrepresentative

Few old, old people

(Cochran et al, 1953)

Baltimore Longitudinal Aging Study 1975

Men reporting the highest frequency of sexual activity when they were younger had the slowest decline in sexual activity as they got older

Martin C. Arch Sex Behav 1981;10:399-420

The US Consumer's Report

Becker 1976

Surveyed population over age 50

Termed them 'The Silent Generation'

Reported increasing range of sexuality with age

Poor correlation of satisfaction/dysfunction

Sexual activity declined with interest

Importance of intimacy despite absence of SI

The National Council on Aging Report

1988

Report on 1300 Americans over 60:

Sexually Active: 61% of men, 37% of women

- An active sex life important men 79% women 66%
- Men>women wanted more frequent sexual activity 60%
- Sex more emotionally satisfying than aged 40 in 66%
- Qualities sought in a partner: 90% cited high moral character, pleasant personality, humour and intelligence. Men>women cited sex; women>men cited financial security

Social Factors in Maintaining Sexual Function



The most common reason for older people to stop having sex is because they have either divorced or their partner has died

Studies of Sexual Lifestyles

NatSal Survey 1994

Frequency of sexual activity:

- Related to availability of a partner
- Inversely related to age
- Inversely related to duration of relationship

ie Sixty year old in new relationship may be more sexually active than 40 year old in 15 year relationship

AARP/Modern Maturity Sexuality Survey 1999

- Quality of interpersonal relationships rated more highly than good sexual relationships
- A generation gap was reported in attitudes to sexuality: the new old will be less accepting of abstinence and dissatisfaction.

A Study of Sexuality and Health among Older adults in the US 2007

- Sexual Activity Declines with Age: 73% of 57-64 year olds, 53% of 65-74 year olds, 26% of 75-85 year olds
- Sexual Activity: Men>women
- 50% M and W had a 'bothersome' sexual problem

Cf A US population (all ages) self-identifying as without a sexual problem were in fact found to have a diagnosable sexual difficulty in about 25% of the sample

A Study of Sexuality and Health among Older adults in the US 2007

Amongst the Sexually Active

- Women:
 - desire 43%,
 - vaginal lubrication 39%
 - anorgasmia 34%
- Men: ED 37%

Medication for erection in 14% of all men surveyed.

Global Study of Sexual Attitudes and Behaviour

Cross-national study of sexual well-being in older men and women
Laumann 2006

Sample of 27,000 aged 40-80 (19% response rate) showed gender and cultural differences:

- Men > women reported sexual well-being;
- Men>women effected by smoking, lack of exercise and biological ageing
- Depression was inversely related to sexual satisfaction
- West Europe, US and Australia higher emotional satisfaction and better sexual relationship of Mediterranean, Asia and Brazil
- Highest rated importance of sex in Med, Korea, Malaysia, Philippines and Brazil
- Other Asian countries with 'male-centred' regimes rated reproduction > sexual satisfaction

Maintaining the Relationship



Sexual intercourse in later life equates with factors other than libido and sexual satisfaction alone.

There is evidence that older women may participate in sexual activity primarily in order to maintain their relationship.

Manderson 2005

Sexual Satisfaction/Disatisfaction in women

Frequency of sexual interest, thoughts and SI correlated with satisfaction in preM and PM women

In sexually dissatisfied women frequency of SI did not correlate with being preM or PM

It is suggested women have SI to maintain their relationship

Psychological Factors in Maintaining Sexual Function



Loss of sexual desire in long term relationships:

- 'Brothers and sisters'
- Separation of interests
- Unresolved issues eg 'betrayal'

General health

A review of general health is important in maintaining a couple's sexual function

Hormones and chemical aids to arousal are only part of a complex social/biological system

We should consider:

- Life style factors: nutrition, exercise, 'stress'

- The relationship: communication skills, intimacy and autonomy

- Cultural and socio-economic factors

Maintaining Sexual Function in Later Life

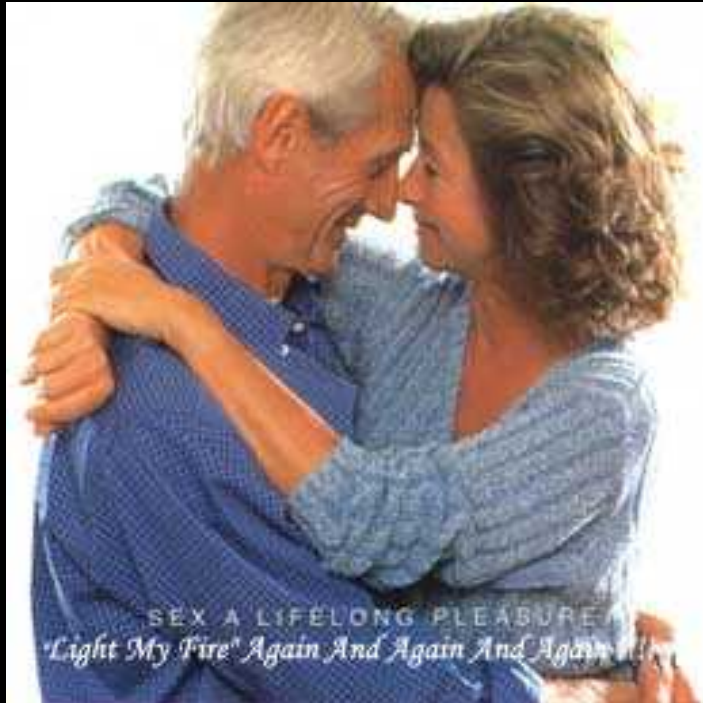


‘The retention of any human function, be it mental, physical, eg cardiac or sexual, is more likely where that function continues to be exercised.’

PS If having sex is good, it does not follow that having no sex is bad!

Demographics

Life expectancy



For every 24 hours of adult life a further 5 hours of additional life may be added to life expectancy.

It will be common place for our children to live into their late 90's.

No ceiling to the increase in life expectancy has been demonstrated.

The 4th Age of Life

In Summary

More of us will live into our 90's and we can do so leading purposeful lives.

We can relate with intimacy, finding its expression through physical closeness, including sexual activity and with, or without, penetrative sex.

The Maintenance of Sexual Function in later Life

Recommended Reading:

1. Our Bodies, Ourselves by the Boston Women's Health Collective (Touchstone Books, £36.50). Health-based classic with large section on women's sexuality.

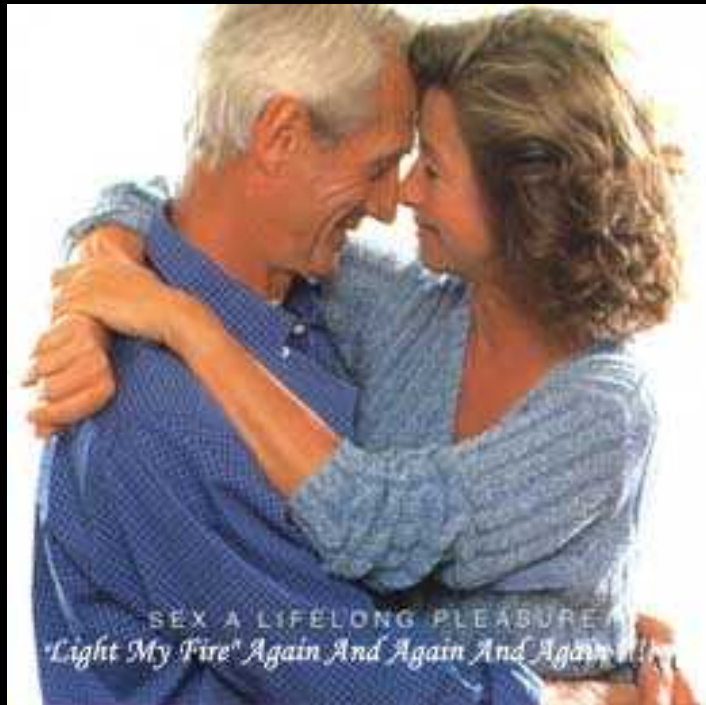
2. Overcoming Sexual Problems by Vicki Ford (Robinson Publishing, £9.99). Information and practical step by step advice on resolving sexual problems like vaginismus

3. The Relate Guide to Sex in Loving Relationships,
by Sarah Litvinoff (Vermilion, £7.99. Relate's guide to sexual fulfillment

4. The New Joy of Sex, by Alex Comfort and Susan Quilliam (Octopus Books, £18.99). Re-invented version of the classic thinking person's guide

5. Hot Sex by Tracey Cox. For fun, for the young.

The Maintenance of Sexual Function in later Life



Thank you!

Maintaining Sexual Function in Later Life



ECAAAM

Dusseldorf, Germany

September 11-14th, 2008

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Maintaining Sexual Function in Later Life



SEMAL VIIth

Anti-Aging Congress

Valencia

October 3-5, 2008

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Maintaining Sexual Function in Later Life – An Overview



There have been major advances in our means to help sexual, and particularly erectile, function in men in the past 15 years

In women advances are less clear: HRT's benefits are limited; the clinical use of Testosterone and oxytocin are being researched.

Other factors influence continuing sexual activity (eg Psychological, physical health)

Maintaining Sexual Function in Later Life



What are the aids that enable men
to maintain better sexual function?

PDE5 Inhibitors

Intracavernosal agents

Non-pharmaceutical aids

Pharmaceutical Aids to Arousal

Sildenafil Citrate (Viagra).

- **Mode of Action:** A phosphodiesterase (PDE5) inhibitor. Its action releases nitric oxide (NO), relaxing endothelial smooth muscle in the corpora cavernosa to fill sinusoidal spaces and give an erection.
- Produces erection with direct stimulation to penis in 60 minutes: duration 12+ hours.
- **Dose:** 25 -100mg, (75% men respond to 50mg dose)
- **Reduced effectiveness:** anxiety, > libido/desire, and >absorption

Pharmaceutical Aids to Arousal

Sildenafil Citrate (Viagra).

Side-effects:

Due to vaso-congestion are mild and dose-related:

Headaches (16%), GI tract (7%), nasal congestion (4%), and visual disturbances (3%).

CV risk is negligible and sildenafil is compatible with drugs for hypertension. (Chetlin 1999)

Contra-indications: Recent myocardial infarction, concurrent use of nitrates.

Pharmaceutical Aids to Arousal

Sildenafil Citrate (Viagra).

- Reported to have 80% efficacy in organic and psychological forms of ED

Levine 1996

- In an older population with arteriosclerosis, hypogonadism, drug interactions, hypertension, and radical prostatectomy overall success rate about 50%

Eidd 2000

Pharmaceutical Aids to Arousal

- Tadalafil (Cialis)
- Mode of action: PDE5 inhibitor.
- Compared to Sildenafil has quicker onset (30 mins).
- $\frac{1}{2}$ life of about 18 hours, and is well-tolerated with similar side-effect profile.
- Efficacy: 80%?
- Dose: 10-20mg
- Contra-indications: CVD (recent MI, unstable angina or angina on SI, arrhythmias and uncontrolled hypertension).

Pharmaceutical Aids to Arousal

Long term use of PDE5 Inhibitors:

- 60% of men using a PDE5 inhibitor were still using it 2 years later.
- 40% required an increased dose to maintain therapeutic efficacy

El-Galley 2001

Pharmaceutical Aids to Arousal

Alprostadyl (Prostaglandin E1) as injection: Caverject

- **Mode of action:** Relaxes penile vasculature, increasing blood flow into the corpora cavernosa to give an erection.
- Produces erection without direct stimulation to penis within 5 minutes lasting an hour.
- **Dose:** 5-20micrograms injected into the corpora cavernosa.
- **Side-effects:** Bruising; rarely priapism.

Non-Pharmaceutical Aids to Arousal

- Penile ring: aids erection
 - Erections graded 1-5
 - Ring converts grade 2 erection to grade 3-4
 - Grade 4 erection is good enough for penetration
- Kegel's exercises: strengthen pelvic floor muscles to aid erection/penetration
- Breathing exercises: aids relaxation
- Sensate Focus training with couple

Erectile Dysfunction (ED)

Definition:

- A persistent inability to attain and maintain an adequate erection to permit satisfactory sexual performance NIHCS 1992

Prevalence:

In a randomised sample of 1290 men:

- Total ED increased from 5-15% between the ages of 40 and 70.
- Some degree of ED occurred in 52%
- In DM prevalence 15% at 30, < 55% aged 60

MMAS, Feldman 1994

Erectile Dysfunction (ED)

Pathogenesis:

- Physical factors primary cause in 75% of cases. (heart disease, hypertension, DM, and medication)
- Psychological factors predominate in 25% (anger, depression and control issues)
- A psychological reaction of anxiety and avoidant behaviour is a common reaction to established ED
- Life-style factors (stress, cigarette smoking) also correlate with ED

Feldman 1994

NB Most men over 60 will obtain better erections, quality of orgasm and enhanced sexual experience from the use of PDE5 inhibitors.

PDE5 Inhibitors plus Testosterone as the Optimal Aids for Arousal

Where there is erectile difficulty the best treatment is a combination of Testosterone with a PDE5 inhibitor (eg Sildenafil, Vardenafil, Tadalafil) or prostaglandin.

There is still a place for traditional remedies: Yohimbine, Ginseng, Tribulis terrestris, Arginine, etc.

The Androgenic Family

- DHEA, DHEA(S)
- Testosterone
- Dehydrotestosterone (DHT)
- Androstenedione
- Androstenediol

The Androgenic Family

Testosterone

Production:

- Leydig cells produce 5-7mg/ 24 hours,
- $\frac{1}{2}$ life 12 hours
- Dependent on LH
- Release is pulsatile, max between 7-9am, reduced 60% at 5-6.00pm

The Androgenic Family

Testosterone

Transport:

- T not stored in testis
- Bound to SHBG (60-70%), albumen (30%), FT (2-3%)

Clearance:

- Aromatisation at target sites (brain, fat, liver, hair follicles)
- Metabolised by 5 alpha-reductase to DHT (prostate, genitals)
- Conjugation to androsterone, which is water soluble, for excretion.

Androgens and Sexual Function in hypogonadal men

Androgens regulate sexual function with central and peripheral effects:

Centrally:

- < libido (interest and motivation)

Alexander 1999

Peripherally:

- Activates nitric oxide synthase which regulates activity in cavernosal smooth muscle to promote erection

Lugg 1996 Shabsigh 2004

Androgens: Other Actions

T has systemic actions other than on sexual function in older men:

- Maintain muscle strength and mass
Melton 2000
- Reduce adipose tissue
Wittert 2003
- Maintain Bone Density
Tenover 1998
- Act on neurones and neuro-transmitters with effects on verbal fluency, memory and energy
Alexander 1999

The above benefits to health and QOL, which are unrelated to sexual function directly, none the less benefit it indirectly.

Androgens and Sexual Function in young (and older?) hypogonadal men

T replacement increases

Sexual activity

Sexual daydreams, thoughts and desires

Spontaneous and nocturnal erections

Alexander 1999

Penile rigidity

Lugg

1996

Penile sensitivity

Orgasm and ejaculation are androgen dependent

Bhasin 1988

Partial Androgen Depletion: Andropause/male menopause

- S/S may be variable, gradual in onset, and subtle in clinical presentation. Gooren 1996
- Lean body mass, loss of muscle volume/strength
- Visceral fat
- Bone mineral density (osteopenia/osteoporosis)
- Fatigue, depression and irritability; mental fluency
- Libido and strength of erection (also spontaneous erections and sexual fantasies)
- Body hair and skin tone/thickness.

Morales 2000

General Health Evaluation:

Sexual activity is a function of health as a whole, including physical and emotional health.

Prior to assessing for HRT evaluate other pathology.

eg: CVD, DM and Cancer: Testosterone impinges on the progression of these conditions.

Actions of Androgens in Clinical Disease:

Ischaemic Heart Disease (IHD)

- T i/v increases coronary artery flow and decreases ischaemic pain (Yue, 1993; Webb, 1999)
- T reduces post-exercise ST segment depression in angina patients (Jaffe, 1977)
- T given for three months to men with chronic stable angina significantly improved tolerance and angina threshold (English, 2000)

Actions of Androgens in Clinical Disease: Diabetes

- T levels are lower in patients with NIDDM compared to controls. (Stellato, 2000)
- Low total and free T are associated with increased risk of type 2 diabetes. (Stellato, 2000)
- Free T inversely related to glucose and insulin sensitivity. (Haffner, 1996)
- Obesity associated with decreased T; T given to obese men increases insulin sensitivity

Endogenous testosterone and mortality:

In a prospective study of men aged 40-79 low testosterone levels were shown to be associated with a reduced life expectancy and an increased risk cardiovascular disease.

Khaw 2007

From age 45 it is suggested testosterone levels be measured routinely when men present at clinic.

Hormone Therapy: Assessment

Blood tests:

- Hormones: Total testosterone
- Sex Hormone Binding Globulin (SHBG)
- FTI
- Dehydrotestosterone (DHT)
- Dihydroepiandrosterone (DHEA)
- Oestradiol (E2)
- Luteinising Hormone (LH)
- Follicle stimulating Hormone (FSH)
- Prolactin.

Hormone Therapy: Assessment

Other Blood Tests: Full Blood Count (FBC) and Liver Function Tests (LFTs)

- Bone Density: Dexascan
- Assess Prostate Function: ? Family History, current urinary symptoms, DRE, prostate specific antigen (PSA)
- If in doubt do rectal u/s.

HT Assessment:

Some Drugs can interfere with T metabolism:

- Alcohol: Promotes T conversion to E2; damages Leydig cells (□ sperm production)
- Aminoglutethamide, Ketoconazole: inhibit steroidogenesis and reduce T levels.
- Cimetidine, spironolactone, cyproterone acetate: androgen receptor antagonists
- Saw Palmetto, finasteride: 5-alpha-reductase inhibitors inhibit DHT production (decrease libido and produce ED).

HT Assessment:

Drugs that interfere with SHBG:

- Barbiturates, anticonvulsants: Hepatic enzyme induction increases SHBG reducing urinary clearance of T and FT, and producing symptoms of andropause.
- Danazol lowers hepatic synthesis of SHBG and displaces T from binding sites on SHBG. Produces increased FT levels and counters andropause symptoms.

Curruthers 2000

Treating with Testosterone

- Orally: Testosterone undecanoate (Restandol): 80mg twice daily; Natural testosterone 100mg/d
- Transdermal Patch: Testosterone (Andropatch) 5mg/d
- I/m testosterone as propionate 30mg, phenylpropionate 60mg, isocaproate 60mg, decanoate 100mg (Sustanon): 250mg every two/three weeks
- I/m testosterone undecanoate (Nebido) 1000mg every 3 months
- Cream/gel: Testosterone (Androgel); DHT (Andractim)
- Implant: Testosterone 600mg every 3 months.

Hormone Therapy (HT):

Review of benefits from HT

Meta-analysis of male HT showed testosterone administration is associated with greater improvement in sexual function compared to placebo treatment in men with sexual dysfunction and low testosterone levels.

Jain 2000

Testosterone may also favorably affect partner interactions and intimacy due to an overall increase in sexual desire and sense of well-being, independent of the change in erectile function.

Bhasin 2001

The Oestrogen Family

- derived as a hormonal cascade from cholesterol to pregnenolone, DHEA, progesterone, E2 and testosterone.



Estradiol E2 (7%)

Derived ovary, strongest action, oral route of admin increases estrone and 16-alpha-hydroxysterone production



Estrone E1 (3%)

After menopause is derived from adrenal and fat tissue, metabolites are 2-hydroxyestrone, 4-hydroxyestrone

and 16-alpha-hydroxyestrone

Low 2:16 ratio relates to Br cancer risk. Phytoestrogens convert 16 to 2-hydroxy estrone

Estriol E3 (90%)

weakest action, occupying E-receptor sites has moderating action,

Oestrogen Depletion

Begins at the perimenopause (35+) and declines rapidly at the menopause (50 years)

Symptoms:

Hot flashes, night sweats, disturbed sleep, fatigue, flatness of affect and anxiety.

Signs:

Physical changes: urinary and vaginal tract atrophy with loss of lubrication and soreness on SI

Cognitive changes: □ memory, concentration, learning capacity

Metabolic effects: altered lipid metabolism

Non systemic HRT management of menopause in women

Symptoms:

- Vaginal and introital dryness, irritation and dysparunia
- Urinary incontinence

Signs

- Atrophy, inflammation
- Poor pelvic muscle tone

Treatment:

- E2 or Estrone as cream, pessary or tablet
- Kegel's exercises
- Treatment of thrush if necessary

Hormone Therapy (HT) for Women

Risks re-evaluated

After 5 years of combined HT (Oestrogen and progestogen) for every 1000 women their will be:

- Deep Vein Thrombosis: 4 extra cases in women over 50
- Ovarian cancer: 1 extra case for every 2500 women
- Strokes: 1 extra case aged 50-59 years
4 extra cases for women 60+ years
- Breast cancer: 2-6 extra cases

Wisdom; Women's Health Initiative; The Million Women Study, Oxford Uni

Hormone Therapy in Women (HT)

Predictors of HT use:

- Socio-economic status: Higher status associated greater use.
- Age: Early menopause
- Surgery (hysterectomy) associated with use of HT 3 times more often

Hormone Therapy for Women

In Summary

- We think HT safer than we did – the number of women taking HT remains lower than before the WHI report
- It's better to start HT early – at the beginning of the menopause for protection against CVD or osteoporosis, as well as for treatment of acute menopausal symptoms such as hot flashes and night sweats
- Some women want to continue HT to age 60+ because of benefits to well-being, libido and sexual function
- They have a choice of replacement therapy with conventional or bio-identical hormones systemically, or topical treatment.

Hormone Therapy for Women

Study: women aged 51-54 years

Adverse effects of HRT less to do with whether women use HRT and more with how it's applied.

- a cyclic combined regimen with application via the skin is associated with a decreased risk of myocardial infarction by more than one third.

Lokkegaard: *European Heart Journal* September 30, 2008

Hormone Therapy for Women

Androgens

Rationale for Treatment

- Pre-menopausal women produce 300 $\mu\text{g}/\text{day}$ of testosterone
 - 50% from the ovaries
 - 50% from the adrenal gland
- Post-menopausal women produce about 150 $\mu\text{g}/\text{day}$ from the adrenal gland.

Despite treatment with E2 many postmenopausal women continue to have \square libido, frequency of SI and sexual satisfaction.

Hormone Therapy for Women

Androgens

- 150-300 µg/day of transdermal testosterone was given to a group of 65 oophorectomised women aged 31-56 years with impaired sexual function.
- The women reported a dose-related increase in sexual thoughts, desires and activities. At the higher dose there was also improvement in mood and well-being

Hormone Therapy (HT): Androgens for Women

Study: 65 women with impaired sexual function (oophorectomised).

- Age: 31-56
- T/d testosterone (Intrinsa): 300 μg – as patch 2- 3 times weekly.

Result:

- Low dose: increase in sexual thoughts, desires and activities.
- High dose: also improvement in mood and well-being

Hormone Therapy for Women

Dehydroepiandrosterone (DHEA)

Hormone replacement?

- Normal Range 0.95 -11.6 mmol/L (women)
2.20 -15.2mmol/L (men)
- Levels are reduced 50% between age 25 and 55

HRT Treatment

Dehydroepiandrosterone (DHEA)

- Replacement doses (DHEA 50mg) were shown to improve energy and well-being in a double-blind cross-over study of a population aged between 40-70 years. Other benefits were reported to sleep and the ability to handle stress

Morales 1994

(This study was with men and women).

HRT Treatment

Dehydroepiandrosterone (DHEA)

DHEA 50mg given for one year to 280 healthy men and women aged 70+ showed (in women only): □ libido, sexual fantasies, activity and satisfaction.

Baulieu1999

Hormone Therapy

Dehydroepiandrosterone (DHEA)

Treatment:

Dose: Oral 50-100mg (men)

10-25mg (women)

S/L 25mg (men)

5-15mg (women)

Side-effects: Changed patterns of hair growth.

NB. Increased levels of testosterone and IGF-1