

to the surface [11]. In the urological field, only very limited examples of EVs-based treatment are available, all of those being in vitro models, thus indicating that there is plenty of room for improvement. A few examples include: (1) siRNA-loaded EVs achieved successful knockdown of PLK-1 mRNA and protein in a bladder cancer cell line [12], and (2) EV-mediated drug delivery has been demonstrated to enhance the cytotoxicity of the antimetabolic cancer therapeutic paclitaxel in autologous prostate cancer cells [13].

Overall, the road is still very long; however, a few promising advances clearly show that that path is likely to be fruitful. In that scenario, we may see two roads and two velocities: on one hand, a clinical translation in its embryonic stage for EV-based therapeutic interventions, with a great potential in terms of anticancer therapy, thus confirming Shah et al when they wrote that we are beginning to recognize EVs as potential drug delivery vectors in a whole new class of therapeutic agents; on the other hand, a faster path for potential biomarkers discovery, thanks to the liquid tissues availability in institutional biobanks (thus including urine and semen). However, translational science has to climb quite high mountains since only a few biomarkers achieved high sensitivity and negative predicting values. Prior to clinical adoption, an external validation in a prospective observational setting is certainly compulsory, but only the future will tell us whether an effective role could be found even in the urological field (preferably if broadly considered, from non-oncological to oncological disorders).

**Conflicts of interest:** The authors have nothing to disclose.

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## Re: Paternal Lifestyle Factors in Relation to Semen Quality and In Vitro Reproductive Outcomes

Borges E Jr, Braga DPAF, Provenza RR, Figueira RCS, Iaconelli A Jr, Setti AS

*Andrologia* 2018;50:e13090

### Experts' summary:

Borges and colleagues analyzed the effect of paternal lifestyle habits on semen quality and on intracytoplasmic sperm injection (ICSI) outcomes. Semen from 965 Brazilian men was meticulously assessed, of whom 233 received an

estimation of their ICSI outcomes. While sperm count and DNA fragmentation were negatively influenced by cigarette smoking and alcohol consumption, other semen parameters such as semen volume, concentration, total sperm count, and total motile sperm count were negatively influenced only by cigarette smoking. Furthermore, smoking and drinking negatively influenced fertilization and blastocyst formation rates.

### Experts' comments:

The theory of the early origin of diseases considers that

alterations in the intrauterine environment can lead to permanent changes in the number, structure, and even function of different types of cells, tissues, and organs, increasing susceptibility to any diseases throughout the course of a person's life [1]. There is evidence indicating that some deleterious maternal conditions could be the trigger for programming mechanisms that explain the development of some diseases during the life of offspring [2–4].

However, there is increasing focus on the role of fathers as new evidence highlights the paternal contribution to the health of the next generation. In this context, Borges et al. [5] demonstrate that the men with poor lifestyle habits such as cigarette smoking and drinking have poor reproductive outcomes (ie, ability to fertilize). Soubry [6] coined the term *Paternal Origins of Health and Disease* to make the point that obesity, poor exercise, smoking, and excessive drinking habits of fathers can negatively impact the development of the paternal germline. In the same vein, our group has demonstrated the positive effect of a father's diet rich in antioxidants on pregnancy outcomes for women who have suffered recurrent gestational loss [7,8].

Information like this is of great relevance because the number of individuals suffering from noncommunicable diseases is increasing worldwide, and lifestyle can influence the occurrence of these types of illness. The World Health Organization [9] reported an average intake of 6.2 l of pure alcohol by individuals aged >15 yr, which equates to a daily intake of approximately 13.5 g/d of pure alcohol. On a global basis, 23% of adults are physically inactive and 11% of adult men are obese.

Therefore, it is not illogical to assume that individuals with excessive alcohol intake or weight, or those who smoke and do not exercise frequently enough could experience fertility problems in the future, or could have negative consequences for their children's health. It is time to act, and this evidence provides further motivation to change unhealthy lifestyle habits.

**Conflict of interest:** The authors have nothing to disclose.

**Re: A Prospective Randomised Placebo-controlled Study of the Impact of Dutasteride/Tamsulosin Combination Therapy on Sexual Function Domains in Sexually Active Men with Lower Urinary Tract Symptoms (LUTS) Secondary to Benign Prostatic Hyperplasia (BPH)**

Roehrborn CG, Manyak MJ, Palacios-Moreno JM, et al

BJU Int 2018;121:647–58

**Experts' summary:**

This is the first randomised clinical trial (double-blind and placebo-controlled) to prospectively assess the effects of dutasteride and tamsulosin (DUT-TAM) combination therapy on subdomains of sexual function in men with benign prostatic hyperplasia (BPH) having lower urinary

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tract symptoms (LUTS) and prostate volume of  $\geq 30$  cm<sup>3</sup>. The authors used the Male Sexual Health Questionnaire (MSHQ) to assess three core domains (erection, ejaculation and satisfaction) of male sexual function at baseline and 1, 3, 6, 9, and 12 mo; higher scores indicate better sexual function.

The intent-to-treat population included 489 patients (243 DUT-TAM and 246 placebo). A significant decrease (worsening) was observed with DUT-TAM therapy versus placebo on the total MSHQ score (–8.7 vs –0.7; SE: 0.81, 0.78;  $p < 0.001$ ) and the ejaculation and satisfaction domains, but not the erection domain (–1.0 vs –0.5; SE: 0.19, 0.19;  $p = 0.091$ ).

The most common drug-related adverse events (AEs) were those in the reproductive system and breast disorder