

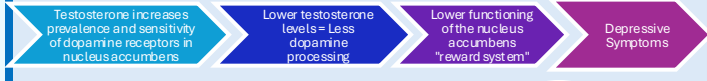
A Systematic Review Exploring the Role of Testosterone Replacement Therapy (TRT) in Improving Depression in Men Following the Male Menopause

Molly Gibson BSc (4th Year Medical Student - University of Manchester)
 Supervisor: Dr James Ricketts MBChB (Hons), MRCGP, PGCert Med Ed (GP & Lecturer - University of Manchester)

INTRODUCTION:

- Male menopause refers to testosterone levels dropping below the therapeutic range (300-1000ng/dL) [1] due to an age-related decline, therefore resulting in symptoms – *hot flushes, mood changes, insomnia, fatigue and low self-esteem* [2].
- Free testosterone levels peak in the third decade of life and reduce by 1% per year thereafter [3] – this can be accounted for by an increase in sex hormone binding protein [4] and a decrease in gonadotrophin releasing hormone [5].
- Current literature supports a **causative bidirectional relationship** between low testosterone levels and depressive symptoms, but this is not unanimous. Thought to do this by acting on the nucleus accumbens [6]. Addition of exogenous testosterone can help to prevent this process.

Figure 1



- Exogenous testosterone via TRT can be administered through IM, PO or topical preparations. For IM, TRT can take **up to 6mths** to become effective [7]. Typically, symptoms resolve in the order demonstrated in *Figure 2*.
- One study suggested that **TRT could trigger depression**. [8]

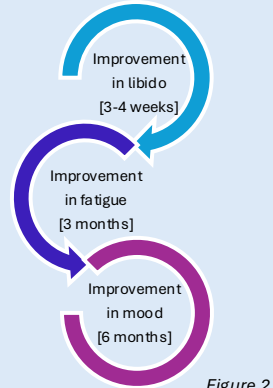


Figure 2

AIMS:

- This systematic review **aims to explore the potential positive effect of TRT on depression** in men secondary to the “male menopause” and, secondarily, whether this outcome is influenced by formulation, route or frequency of administration
- Hypothesised that TRT would improve depressive symptoms** of this demographic, but this outcome would not be influenced by administrative techniques

RELEVANCE:

- 22% of males aged 65yrs+ experience depression** [9], therefore there is a requirement to understand reasoning for this alongside preventative and curative measures.
- Improved knowledge base surrounding the female menopause has allowed for HRT and subsequently **minimal impact of the menopause on quality of life**.

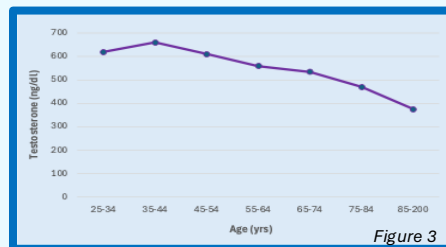


Figure 3

METHOD:

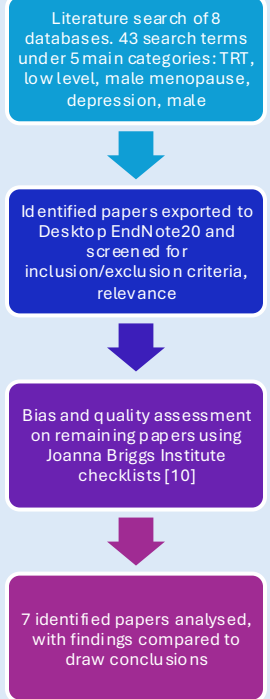


Figure 4

RESULTS AND DISCUSSION:

FORMULATION	FREQUENCY	ROUTE
<ul style="list-style-type: none"> <u>Testosterone Undecanoate (TU) more effective</u> [p=0.027] than Testosterone Enanthate (TE) [p>0.05] in reducing depressive symptoms <u>Fewer side effects associated with TU</u> compared to TE, decreased mood more likely if side effects impact quality of life 	<ul style="list-style-type: none"> Discontinuity between studies in prescribing in accordance NICE recommended dose, <u>TE prescribed at too low a dose</u> in some studies [11] - could account for reduced efficacy TE requires more regular intramuscular (IM) injections than TU - could contribute to more pain and therefore more depressive symptoms 	<ul style="list-style-type: none"> TU administered orally / intramuscularly, TE administered intramuscularly only <u>TE levels in the body more variable</u>, hence more regular injections required so mood should be expected to vary more also due to regimen not being correctly followed in all studies TU administered orally is effective in reducing depressive symptoms, side effects not likely to exhibit psychological distress <u>Topical route only effective in those with severe depression</u>, and not in those with mild / moderate depression. Variation in efficacy of topical preparations dependent on location to which they are applied – not specified within studies

CONCLUSION:

- No unanimous consensus from literature base on efficacy of TRT in reducing depressive symptoms following the male menopause
- Combining all findings from this review, hypothetically, an **IM injection of TU is the most effective method to administer TRT to alleviate depression following the male menopause**
- Pivotal to understand the potential for harmful effects following TRT, as suggested by a paper in this review, before TRT can be suggested as a therapeutic pharmacological option for improving depressive symptoms in post-menopausal males

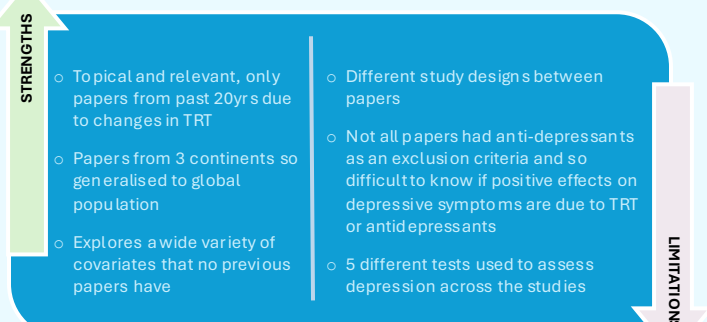


Figure 5

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