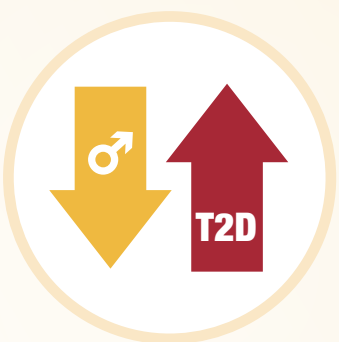
EXPLAINING THE T4DM STUDY

The T4DM (Testosterone for Diabetes Mellitus) Phase 3 study[1] is the world's first large-scale, placebo-controlled randomized trial assessing testosterone treatment for preventing or reversing type 2 diabetes (T2D) in overweight or obese men with low testosterone levels.

WHY IS THIS STUDY IMPORTANT?

Globally, diabetes is among the top 10 causes of death.[2] T2D is the most common type of diabetes, accounting for around 90% of all diabetes cases.[2]



Low testosterone levels commonly seen in overweight or obese men are associated with an increased risk of T2D.[3]

While there is evidence that weight loss can prevent or reverse T2D,[4-10] **it was not previously known whether testosterone treatment increases the benefits of lifestyle intervention.**

THE STUDY[1]

The objective was to determine whether testosterone treatment prevents progression to or reverses early type 2 diabetes, beyond the effects of a community-based lifestyle program.

Men at high risk of T2D (pre-diabetes) or with newly-diagnosed T2D and low testosterone levels were enrolled in a community-based lifestyle program and were randomized into two groups:

TESTOSTERONE GROUP: 504 MEN

Testosterone injection every 3 months for 2 years

Testosterone undecanoate intramuscular injection (1000 mg/4 mL) was supplied by Bayer (Reandron®) which is marketed in most countries as Nebido®.

PLACEBO GROUP: 503 MEN

Placebo injection every 3 months for 2 years

THE RESULTS

Testosterone treatment for two years combined with lifestyle intervention significantly reduced the presence of T2D compared to lifestyle intervention alone in men with low testosterone levels.*

The study had two primary outcomes:

12.4% (55/443) of the testosterone group had T2D after 2 years

VS

21.1% (87/413) of the placebo group had T2D after 2 years

There was also a greater mean change from baseline in 2-hour glucose level in men treated with testosterone compared to placebo.*

-1.70 mmol/L

-0.95 mmol/L

-0.75 mmol/L, p<0.0001
Mean difference

Of the secondary endpoints, men in the testosterone group had:

2.7 kg mean decrease in total fat mass

1.7 kg mean increase in total muscle mass

Both mean decrease in total fat mass and mean increase in total muscle mass were statistically significantly greater than in the placebo group.

A SUB-GROUP ANALYSIS SHOWED THAT, AFTER TWO YEARS*

PREVENTING T2D
Of the men at high risk (pre-diabetes) at baseline:

7.6% (27/355) of the testosterone group had T2D

14.9% (49/329) of the placebo group had T2D

REVERSING T2D
Of the men with newly-diagnosed T2D at baseline:

31.8% (28/88) of the testosterone group had T2D

45.2% (38/84) of the placebo group had T2D

ADDITIONAL INFORMATION ABOUT THE T4DM STUDY

The safety profile of the study was reassuring, with 41 serious adverse events recorded in the placebo group and 55 in the testosterone group, and no difference in incident cardiovascular events or prostate cancer.[1]

The data from this study provide some reassurance regarding 2-year cardiovascular safety and are in accordance with a recent meta-analysis indicating the cardiovascular safety of testosterone treatment.[11]

A treatment-limiting increase in haematocrit to 54% or higher, a prespecified safety trigger, was flagged in 106 (22%) of 491 participants treated with testosterone.[1] This proportion is within the range of treatment-limiting increases in haematocrit (2·5 – 40%) in other studies of testosterone treatment.[12,13] This trigger led to the cessation of treatment for 26 participants (25 in the testosterone group).[1]

As for all patients with obesity, reduction of weight by lifestyle modifications should be emphasized along with any pharmacologic therapy.[14]

The T4DM study, *Testosterone treatment to prevent or revert type 2 diabetes in men enrolled in a lifestyle programme (T4DM): a randomised, double-blind, placebo-controlled, 2-year, phase 3b trial*, was a national Australian study led by the University of Adelaide.

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* T2D for outcomes was defined as glucose ≥11 mmol/L, measured through a 2-hour oral glucose tolerance test

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