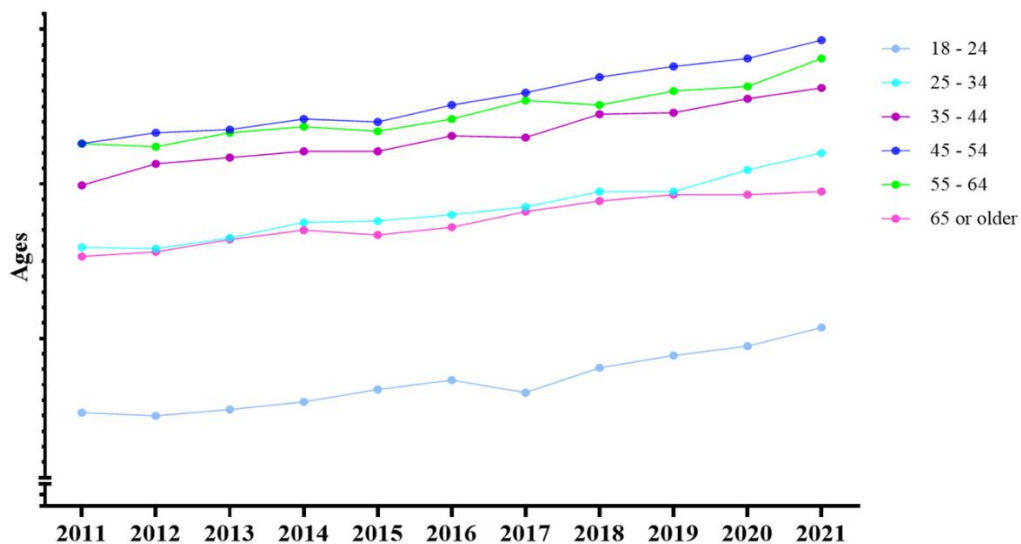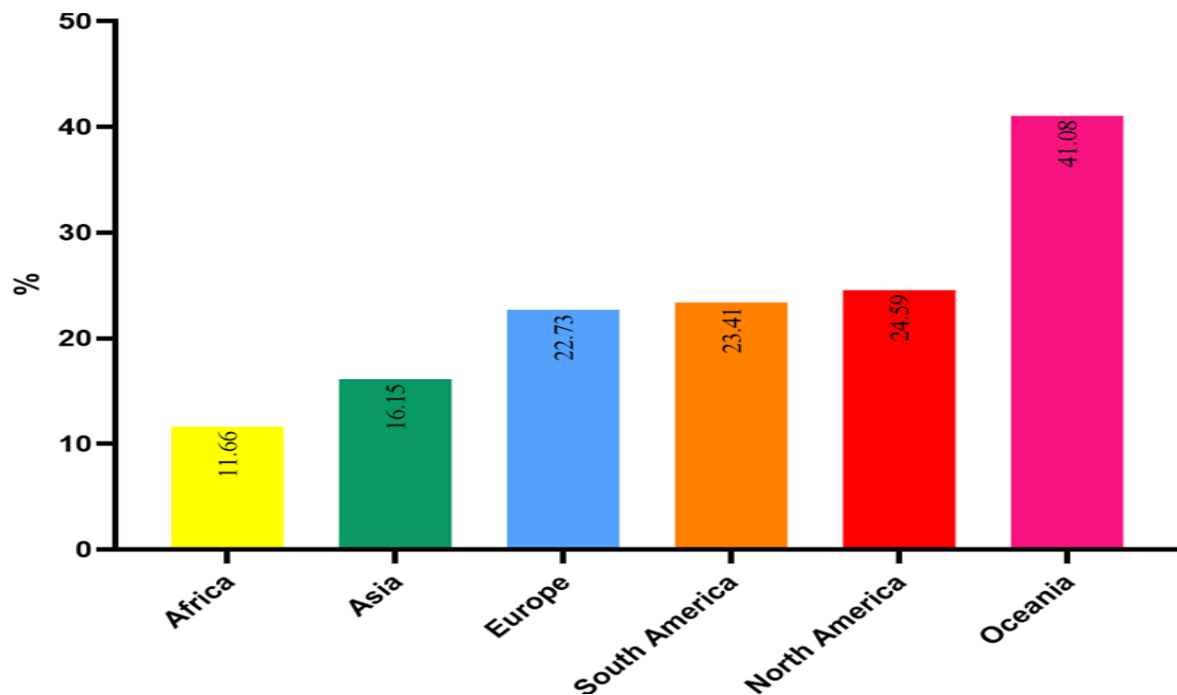**STRING network linking POMC, FTO, and MC4R.**

Protein-protein association network highlighting melanocortin-pathway connectivity; edge confidence and scores as reported by STRING. This mechanistic view is provided for biological context and is not part of the evidence grading. Source: STRING Consortium (accessed 2023) (accessed 12 Aug 2025)
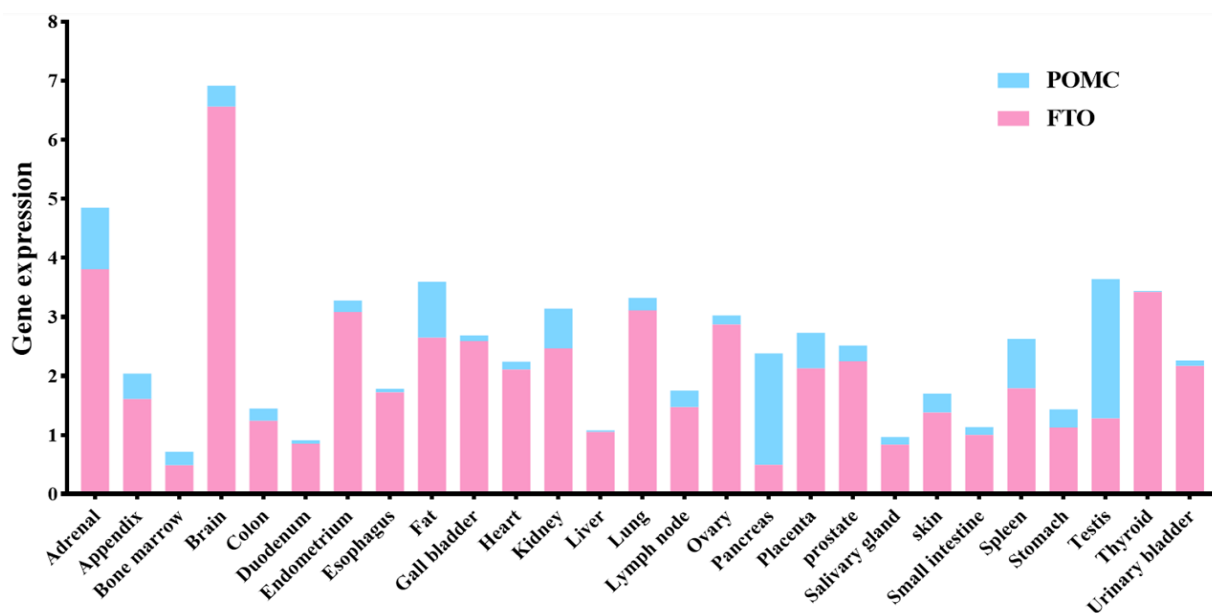


**United States: percentage of adults (≥18 years) with obesity by age group, 2011-2021.**

Age-stratified trends based on CDC surveillance; descriptive context only. Source: CDC, National (accessed 12 Aug 2025) estimates
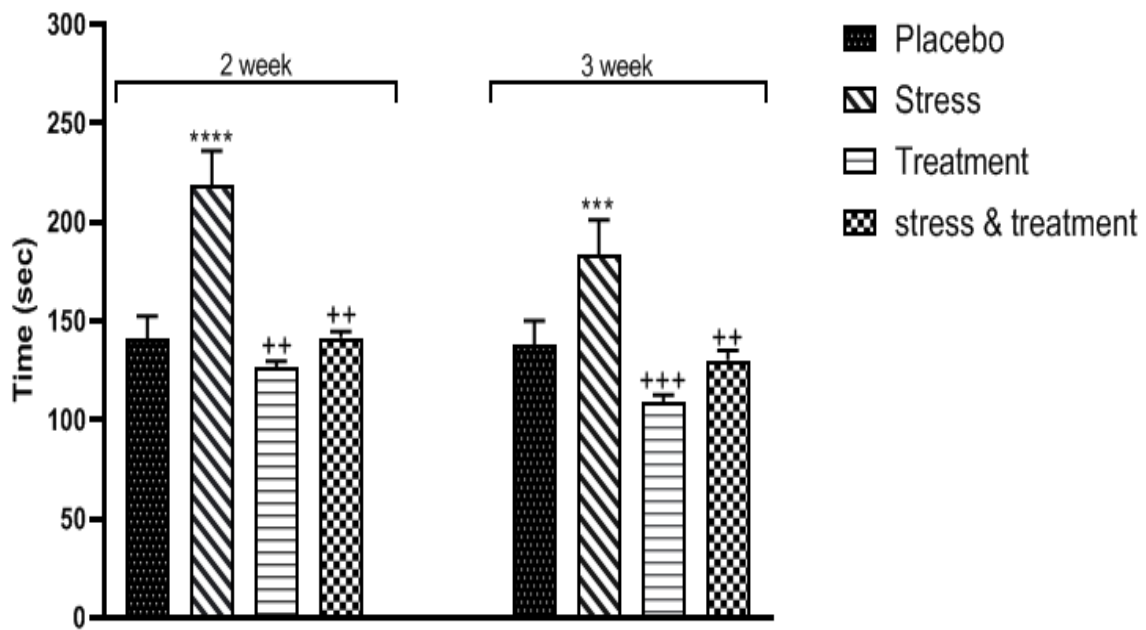
**Obesity rates by world region, 2023 (mean of country estimates).**

Regional comparison derived from WHO/World Obesity/Global Obesity Levels reports; illustrative context only (not analyzed in the review). Sources: WHO & World Obesity Federation compendium (accessed 12 Aug 2025)



**Tissue expression of FTO and POMC in humans.**

Relative expression across selected tissues compiled from public portals (e.g., GTEx as catalogued on NCBI Gene); provided for context and not included in synthesis. Source: NCBI Gene entries for POMC and FTO (accessed 2023) (accessed 12 Aug 2025)
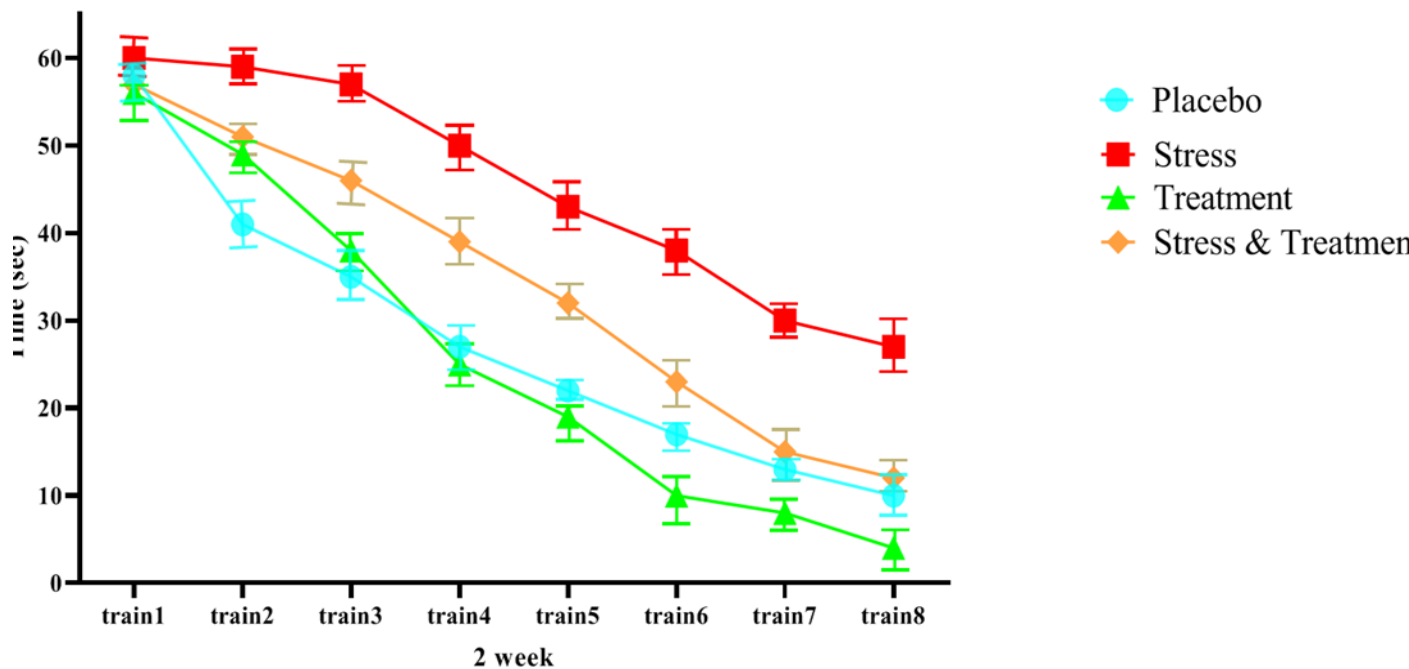
**Locomotion (2 vs 3 weeks)**
Locomotion outcomes in the 2-week and 3-week groups across four experimental conditions (Control, Stress, Treatment, Stress+Treatment) in the rodent model.
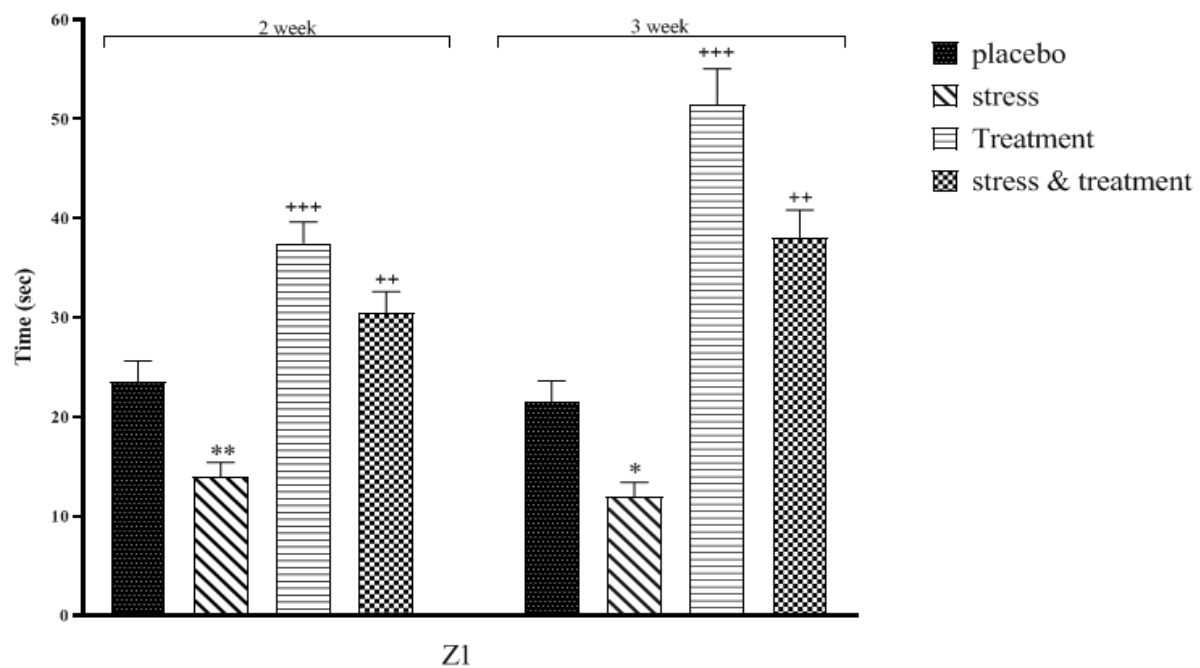\* Significant vs. Control; + Significant vs. Stress.
\*\*\* $p < 0.0001$; \*\*\*\* $p < 0.00001$; ++ $p < 0.001$; +++ $p < 0.0001$.
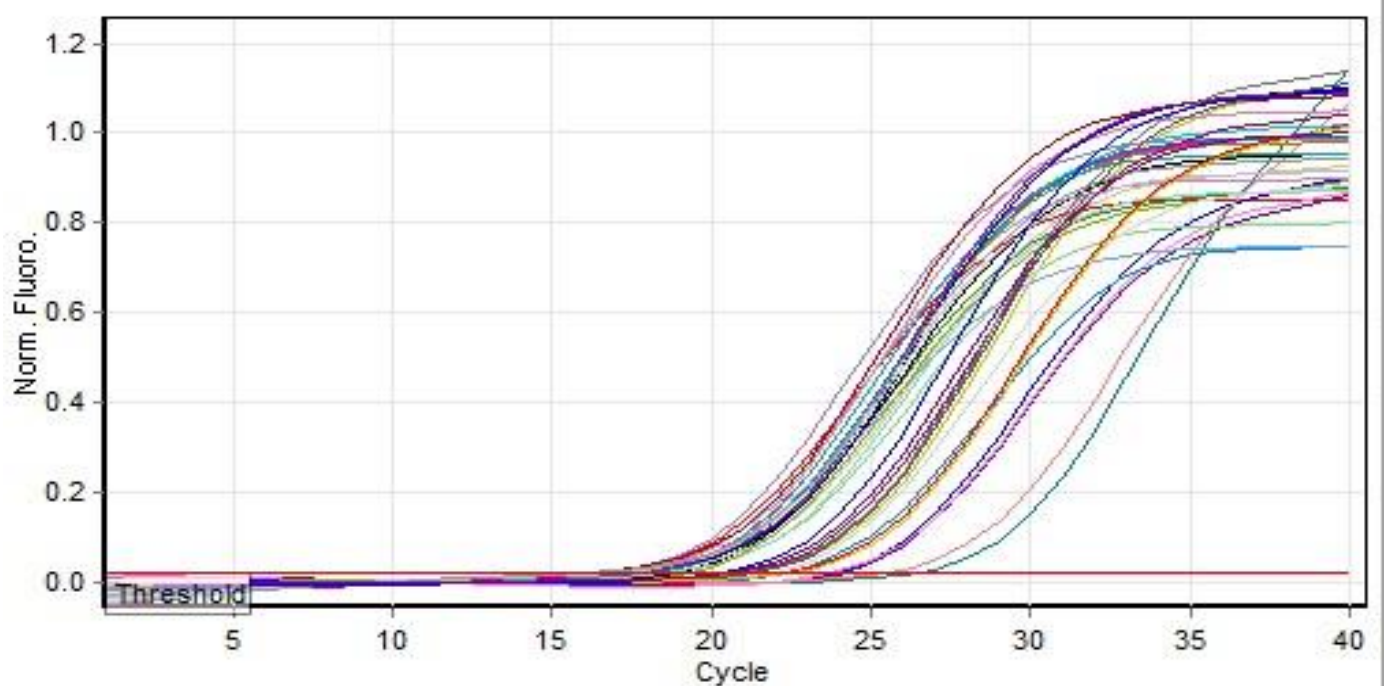


**Morris Water Maze – Training (2-week)**

Figure 4-4. Morris Water Maze (MWM) training performance: time/latency across training trials in the 2-week groups (Control, Stress, Treatment, Stress+Treatment) in the rodent model.
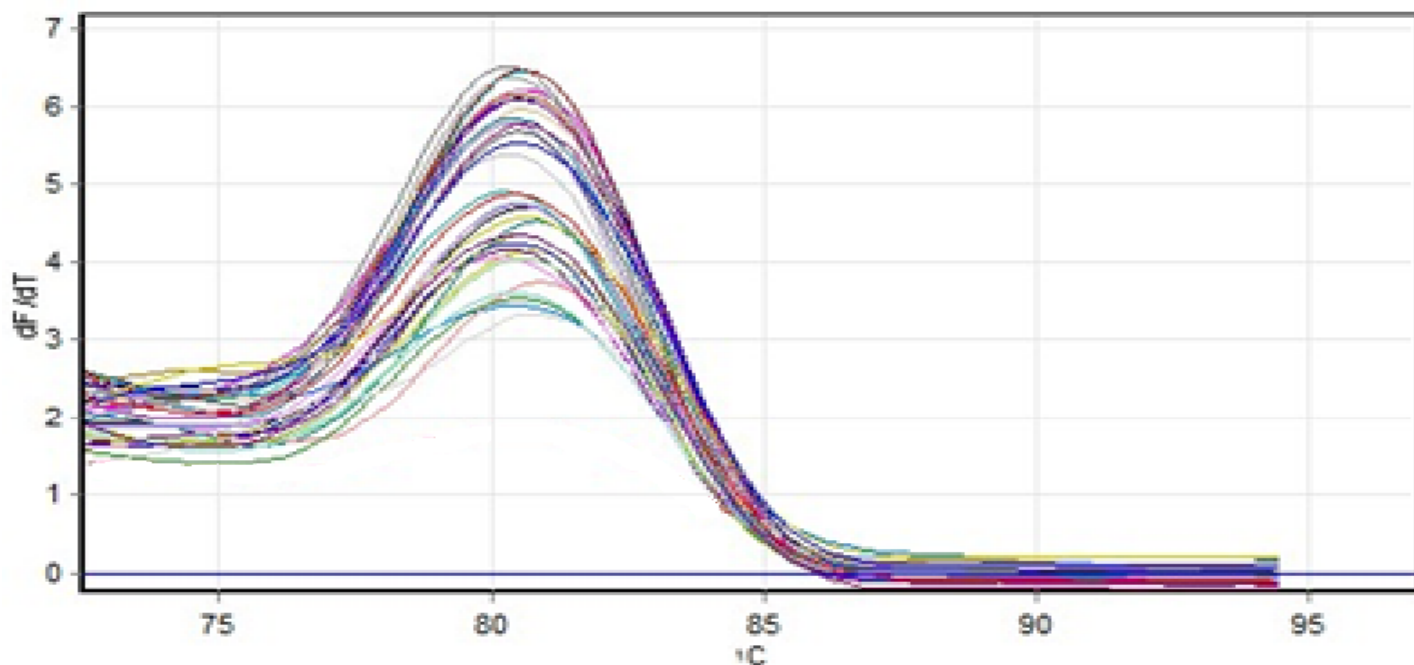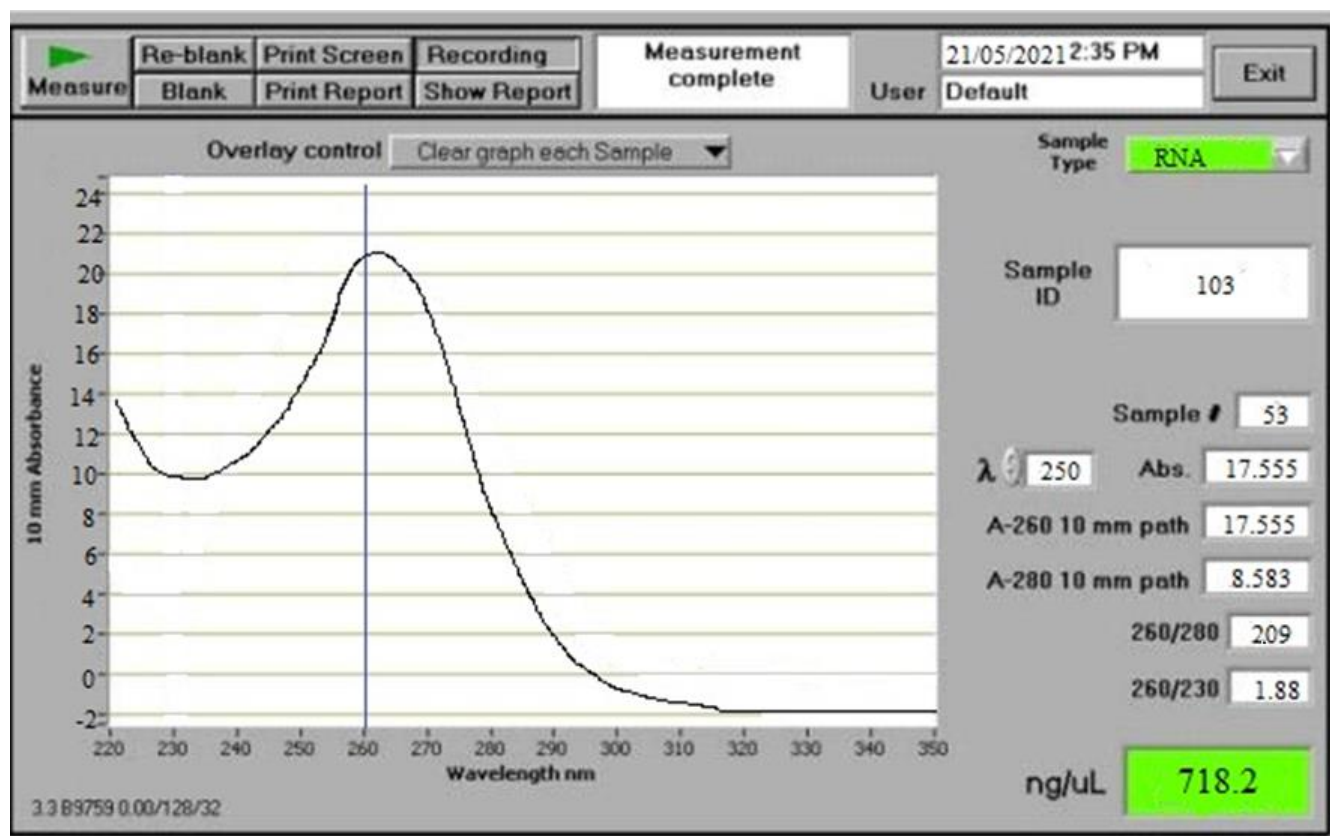
**Morris Water Maze – Test day (2 & 3 weeks)**

Figure 4-8. Morris Water Maze (MWM) probe/test-day performance: time/latency in the 2-week and 3-week groups (Control, Stress, Treatment, Stress+Treatment) in the rodent model. Z1 indicates the target quadrant.
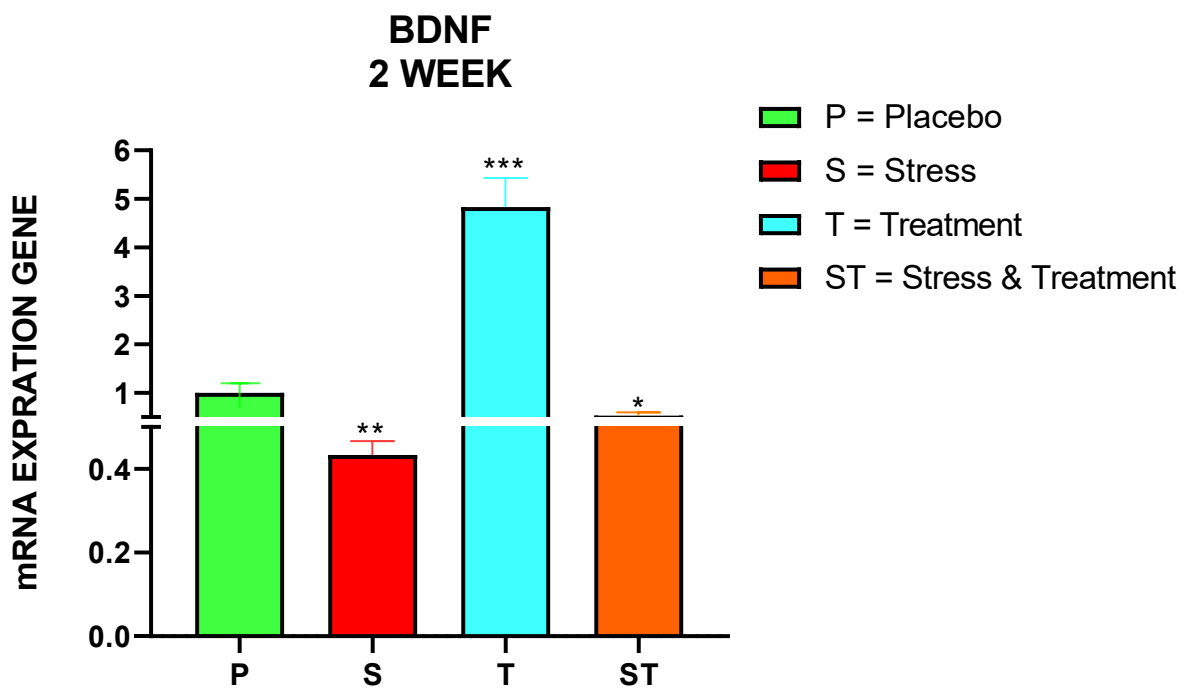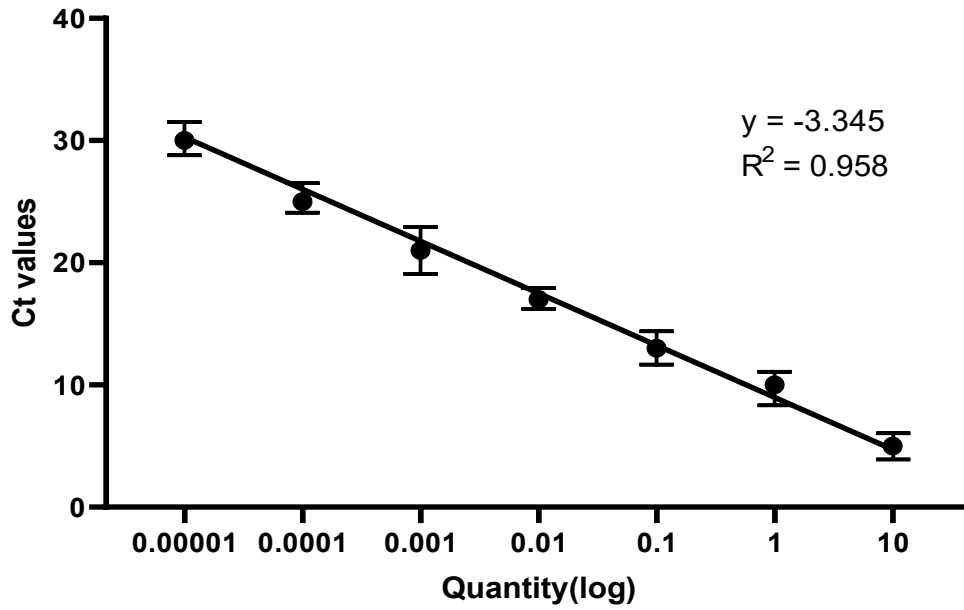


**qPCR amplification curve for the BDNF gene.**
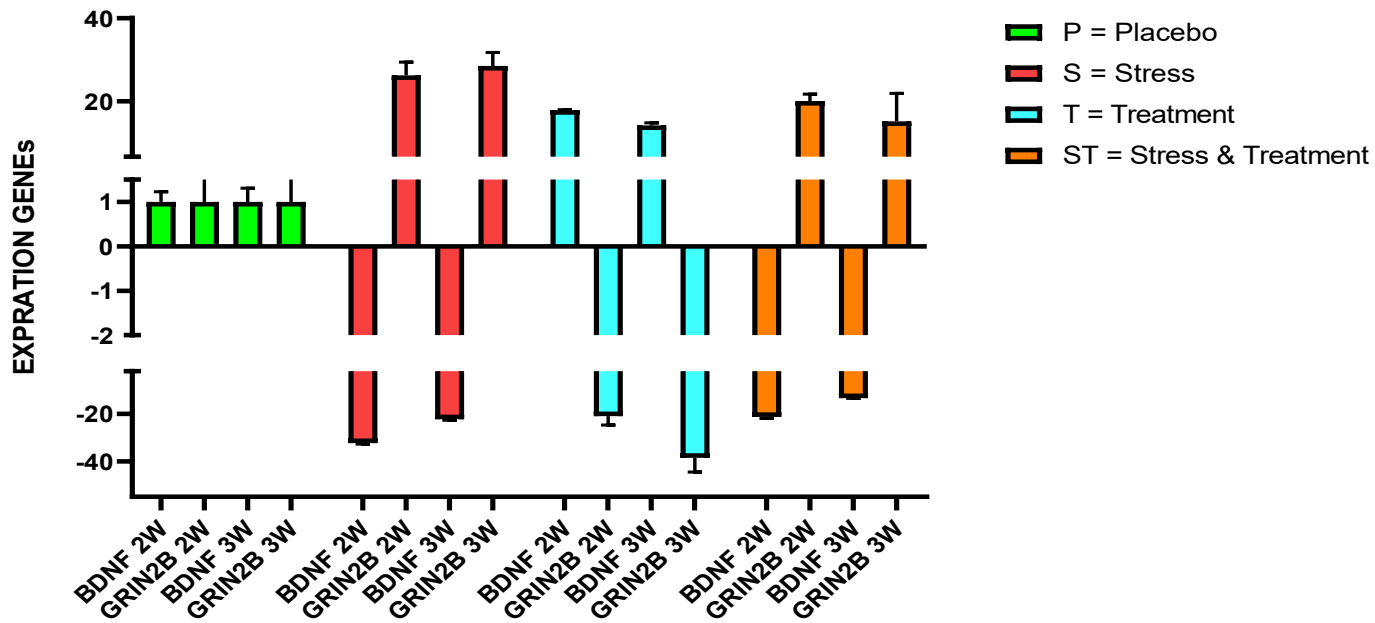
**qPCR melt curve for the BDNF gene.**



**NanoDrop measurements for RNA concentration determination.**

**Primer optimization curve for the BDNF gene.**

$y = -3.345$
$R^2 = 0.958$
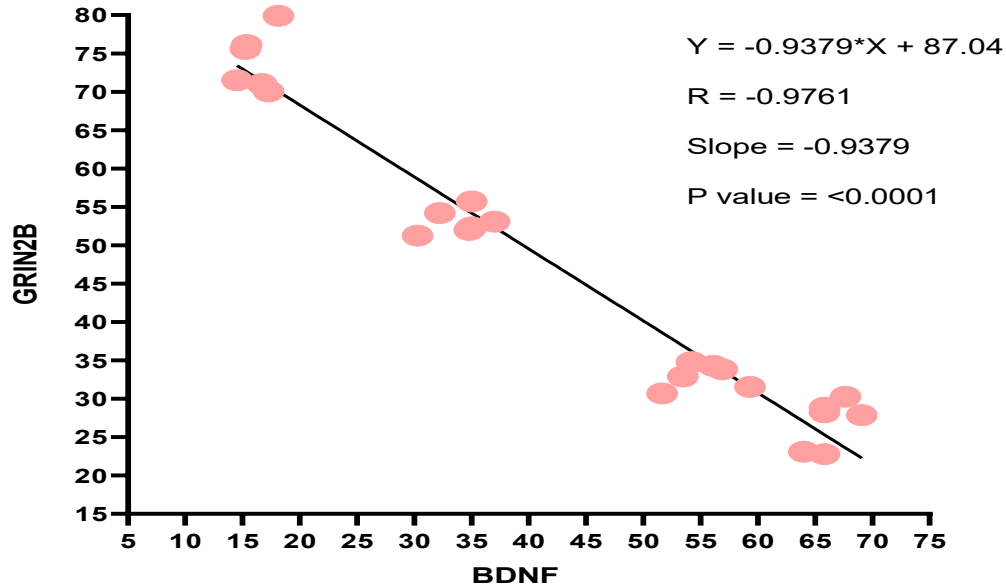


**BDNF expression – 2-week group**

Figure 4-21. Relative BDNF gene expression in the 2-week groups (Control, Stress, Treatment, Stress+Treatment).
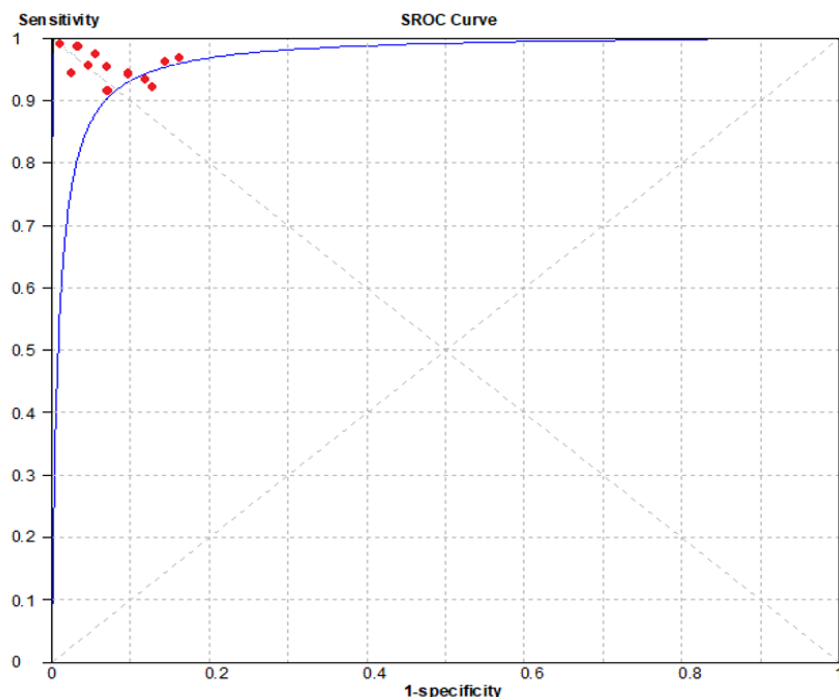
**BDNF & GRIN2B expression – 2 & 3 weeks**
Relative expression of GRIN2B and BDNF in the 2-week and 3-week groups (Control, Stress, Treatment, Stress+Treatment).

## 2 WEEK



$Y = -0.9379*X + 87.04$
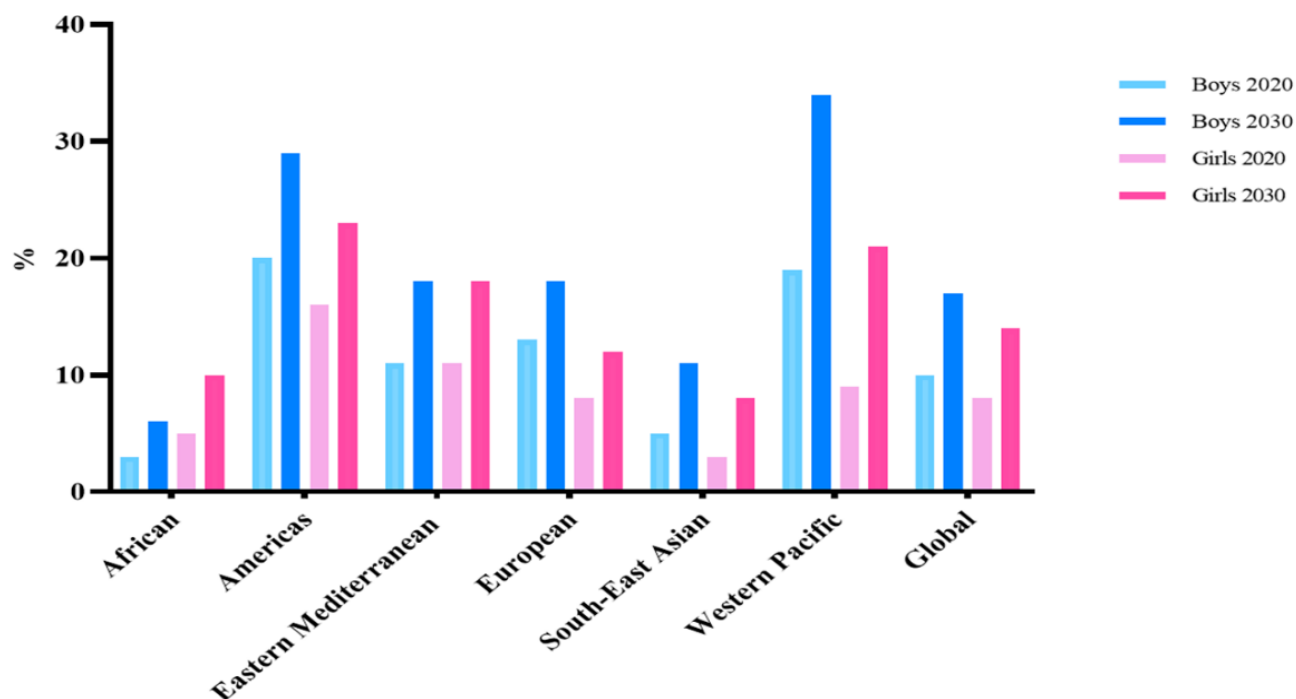
$R = -0.9761$

Slope = -0.9379

P value = <0.0001

**Correlation (2-week)**

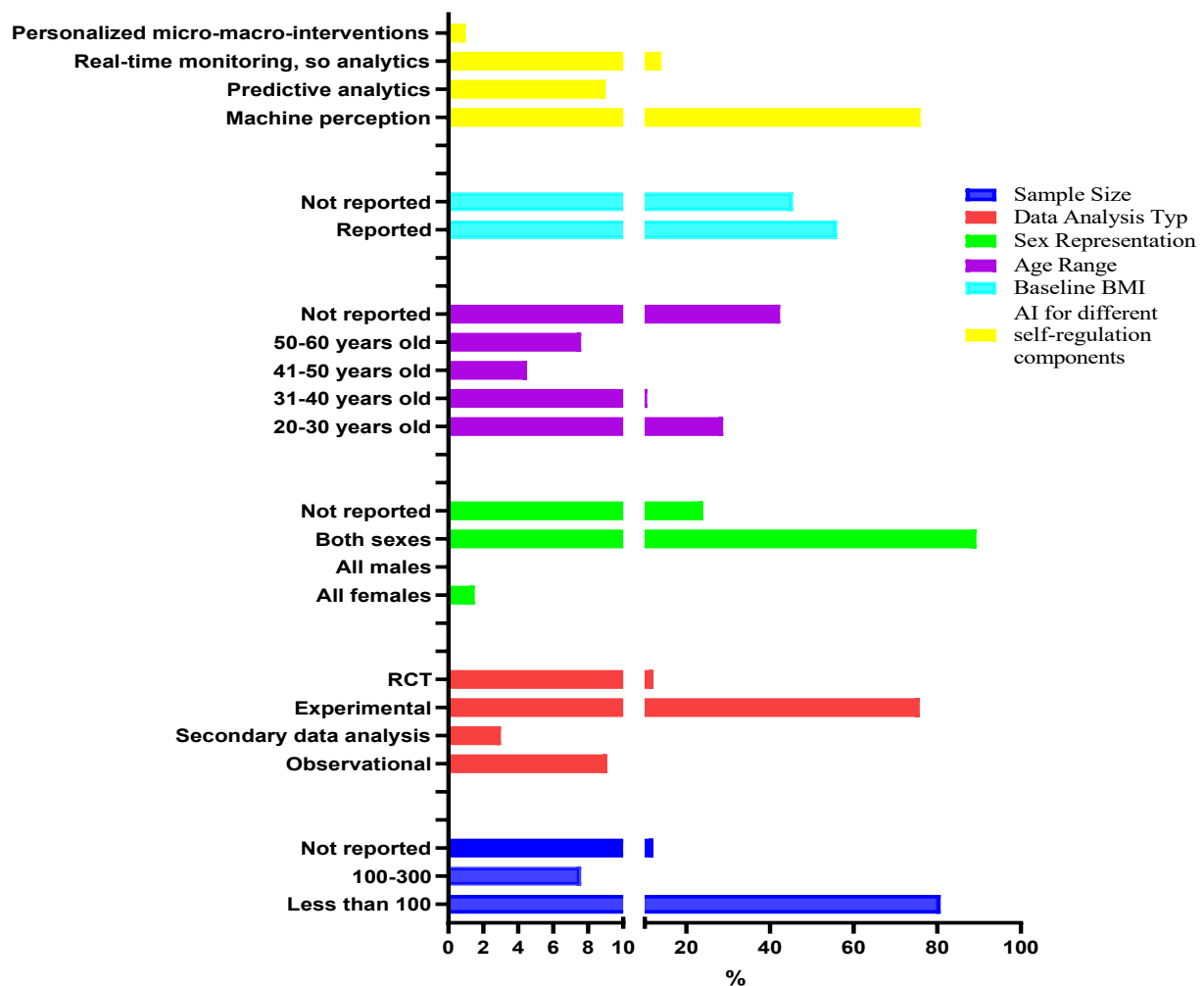Correlation between GRIN2B and BDNF gene expression in the 2-week group.

**ROC – BDNF**

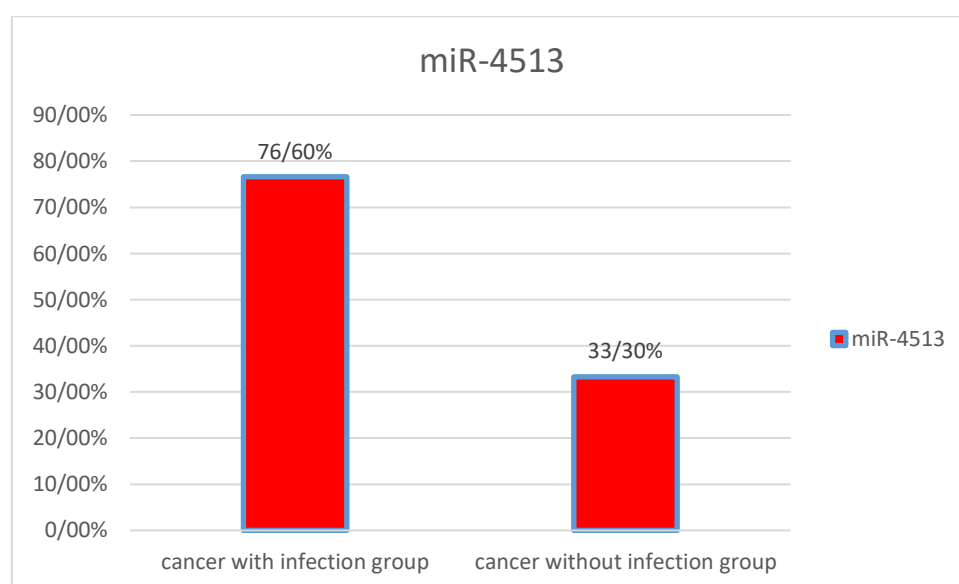Receiver operating characteristic (ROC) curve for the BDNF gene.



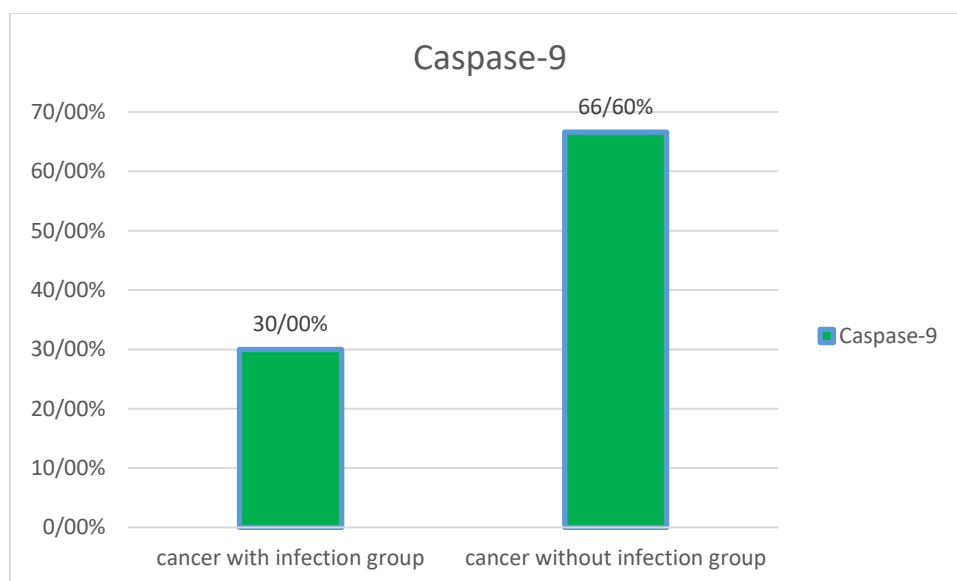**Global obesity trends in children and adolescents (aged 5-19 years) by sex, 2020-2030.**

Regional prevalence trajectories for boys and girls; projections are provided for context and are not part of the genotype-phenotype synthesis. Source: World Obesity Atlas 2023 (accessed 12 Aug 2025)
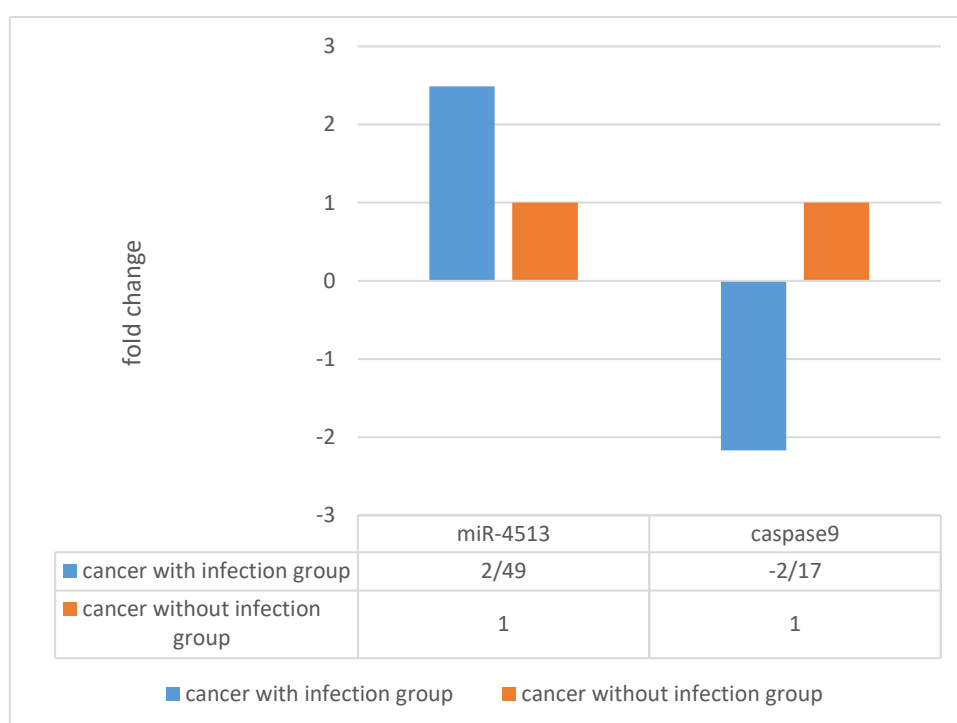
**Distribution of Study Characteristics by Percentage and Sample Size in Health Research**



**Positivity rate of miR-4513 in peripheral blood of patients with and without oral infection.** The positivity rate of the miR-4513 biomarker is higher in the patient group with oral infection.

**Positivity rate of Caspase-9 mRNA in peripheral blood of patients with and without oral infection.** The positivity rate of the Caspase-9 mRNA biomarker is higher in patients **without** oral infection.



|  | miR-4513 | caspase9 |
|---|---|---|
| cancer with infection group | 2/49 | -2/17 |
| cancer without infection group | 1 | 1 |

■ cancer with infection group　■ cancer without infection group

**Differential expression of miR-4513 and Caspase-9 in patients with and without oral infection.** miR-4513 expression is 2.49-fold higher in patients with oral infection compared to patients without oral infection. In contrast, Caspase-8 mRNA expression is 2.17-fold lower in patients with oral infection than in patients without oral infection.