**Supplementary Materials**

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# Inclusion and exclusion criteria

|  |  |
| --- | --- |
| **Inclusion Criteria**page2image3723888 | page2image3760496page2image2998720**Exclusion Criteria**page2image3762576page2image3762992 |
| * Confirmed diagnosis of anorexia nervosa * Measurement of QTc interval * All genders * All populations in all countries * English language full text available or with English translations * Published in peer-reviewed journal | * Animal studies * Wrong study design (e.g., literature review; case report; RCT; systematic review; meta-analysis) |

# Supplementary Table 1: Quality assessment of studies using the Newcastle-Ottawa scale (NOS)

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Selection** | | | | **Comparability** | **Exposure** | | | **NOS Score /9** |
| Is the case definition adequate? | Representativeness of the cases | Selection of Controls | Definition of Controls | Comparability of cases and controls | Ascertainment of exposure | Same method of assessment for cases and controls | Non-Response rate |  |
| Green et al. 2020 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 5 |
| Janzen et al. 2020 | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 1 | 8 |
| Krantz et al. 2020 | 1 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 7 |
| Janzen et al. 2019 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Frederiksen et al. 2018 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Bomba et al. 2017 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Padfield et al. 2016 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Ertugrul et al. 2015 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Billeci et al. 2015 | 1 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 7 |
| Yahalom et al. 2013 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 6 |
| Nussinovitch et al. 2012 | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 1 | 8 |
| Zulal et al. 2006 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Facchini et al. 2006 | 1 | 0 | 0 | 1 | 2 | 1 | 1 | 1 | 7 |
| Roche et al. 2005 | 1 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 7 |
| Olivares et al. 2005 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Krantz et al. 2005 | 1 | 0 | 0 | 1 | 2 | 1 | 1 | 1 | 7 |
| Takimoto et al. 2004 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Roche et al. 2004 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Vasquez et al. 2003 | 1 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 7 |
| Galetta et al. 2003 | 1 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 7 |
| Galetta et al. 2002 | 1 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 7 |
| Franzoni et al. 2002 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Biadi et al. 2001 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Panagiotopoulos et al. 2000 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Durakovic et al. 1994 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 4 |
| Borgia et al. 2021 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Frederiksen et al. 2021 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Dinardo et al. 2022 | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |

Studies categorized according to NOS as follows: 0-3 = Poor quality, 4-7 = Fair quality, 8-9 = Good quality.

# Supplementary Table 2: Quality assessment of studies using Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach

| **Certainty assessment** | | | | | | | **№ of patients** | | **Effect** | | **Certainty** | **Importance** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **AN** | **Control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Mean QTc (Bazetts)** | | | | | | | | | | | | |
| 26 | observational studies | not serious | very seriousa | not serious | not serious | None | 2084 | 4049 | - | MD **5.55** **higher** (2.38 lower to 13.48 higher) | ⨁◯◯◯ Very low |  | |
| **Mean QTc (Hodges)** | | | | | | | | | | | | |
| 3 | observational studies | not serious | seriousb | not serious | not serious | none | 501 | 194 | - | MD **1.33 higher** (13.90 lower to 19.23 higher) | ⨁◯◯◯ Very low |  | |
| **Mean QTc (Fridericia)** | | | | | | | | | | | | |
| 4 | observational studies | not serious | very seriousc | not serious | not serious | None | 1368 | 3258 | - | MD 2.66 **higher** (21.63 lower to 27.77 higher) | ⨁◯◯◯ Very low |  | |
| **Mean QTc (Framingham)** | | | | | | | | | | | | |
| 2 | observational studies | not serious | seriousd | not serious | not serious | none | 63 | 78 | - | **15.9 higher** (0.03 higher to 31.78 higher) | ⨁◯◯◯ Very low |  | |
| **QT Dispersion** | | | | | | | | | | | | |
| 9 | observational studies | not serious | very seriouse | not serious | not serious | none | 238 | 194 | - | MD **21.32 higher** (10.35 higher to 32.3 higher) | ⨁◯◯◯ Very low |  | |
| **QTc Dispersion** | | | | | | | | | | | | |
| 7 | observational studies | not serious | seriousf | not serious | not serious | none | 254 | 282 | - | MD **16.93 higher** (4.54 higher to 29.32 higher) | ⨁◯◯◯ Very low |  | |

**CI:** confidence interval; **MD:** mean difference

#### Explanations

a. Considerable heterogeneity I2=95%

b. Substantial heterogeneity I2=71%

c. Considerable heterogeneity I2=97%

d. Moderate heterogeneity I2=65%

e. Considerable heterogeneity I2=94%

f. Considerable heterogeneity I2=93%

# Supplementary Figure 1: Meta-regression of age and mean difference in corrected QT interval (QTc) by Bazett formula

A graph with dots and lines

Description automatically generated

Regression co-efficient -0.046; p=0.965

# Supplementary Figure 2: Meta-regression of duration of anorexia nervosa (AN) and mean difference in corrected QT interval (QTc) by Bazett formula

A graph with dots and lines

Description automatically generated

Regression co-efficient 0.135; p=0.426

# Supplementary Figure 3: Meta-regression of body mass index (BMI) and mean difference in corrected QT interval (QTc) by Bazett formula

A graph of dots and numbers

Description automatically generated

Regression co-efficient -4.33; p=0.364

# Supplementary Figure 4: Meta-regression of heart rate (HR) and mean difference in corrected QT interval (QTc) by Bazett formula

A graph of a diagram

Description automatically generated with medium confidence

Regression co-efficient -1.41; p=0.025

# Supplementary Figure 5: Forest plot of the QTc subgroup analysis categorized by AN severity based on BMI (mild: >17kg/m2; moderate: 16-16.9 kg/m2; severe: 15-15.9 kg/m2; extreme <15kg/m2)

A screenshot of a graph

Description automatically generated

Abbreviations: AN – anorexia nervosa; BMI – body mass index; CI – confidence interval; QTc – corrected QT interval

# Supplementary Figure 6: Forest plot of the QTc subgroup analysis categorized by age (above or below mean age of 19.7 years)

A screenshot of a graph

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# Supplementary Figure 7: Forest plot of the QTc subgroup analysis categorized by continent

**A screenshot of a graph

Description automatically generated**

Supplementary Figure 8: Forest plot of the QTc subgroup analysis categorized by antipsychotic use

A screenshot of a math report

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# Supplementary Figure 9: Forest plot of the QTc subgroup analysis categorized by heart rate

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# Supplementary Figure 10: Forest plot of the QTc subgroup analysis categorized by clinical setting

A screenshot of a graph

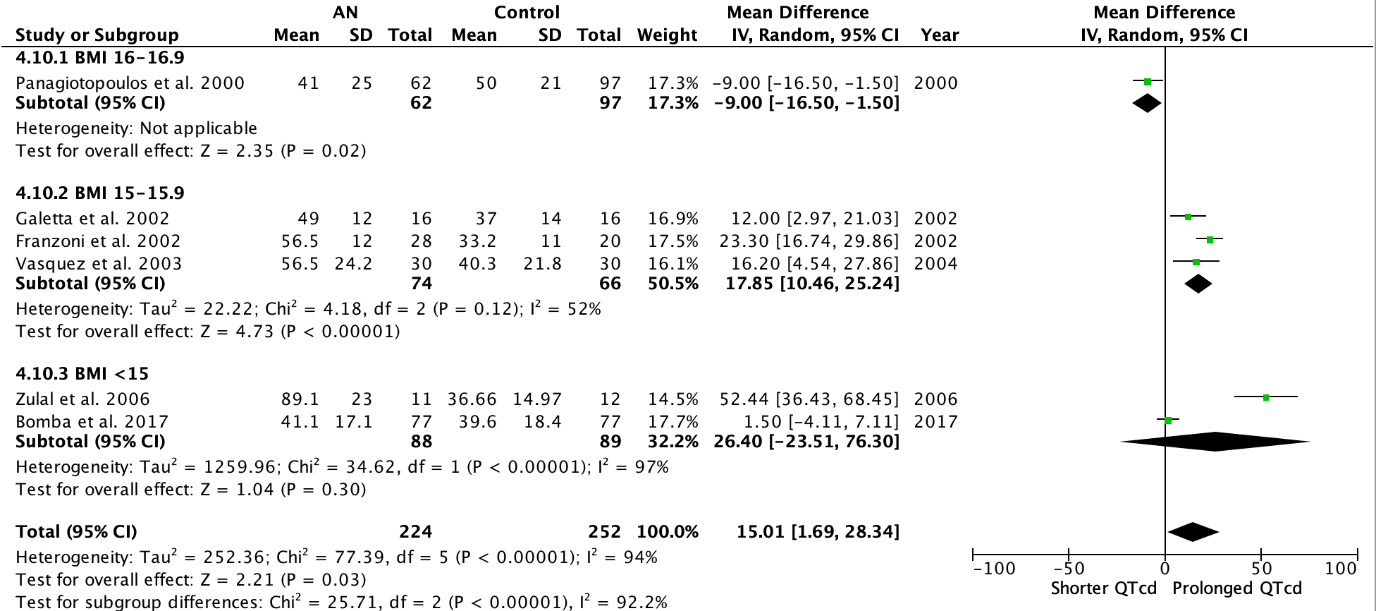
Description automatically generated

# Supplementary Figure 11: Forest plot of the QT dispersion subgroup analysis categorized by body mass index (BMI)

A screenshot of a math document

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# Supplementary Figure 12: Forest plot of the QTc dispersion subgroup analysis categorized by body mass index (BMI)



# Supplementary Figure 13: Funnel plot of the studies comparing corrected QT interval (QTc) calculated by Bazett formula of anorexia nervosa patients and controls

A diagram of a triangle with dots and lines

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