Impact of Biologics on Health-Related Quality of Life Outcomes (HRQoL) in Patients with Ankylosing Spondylitis: A Systematic Review and Meta-Analysis

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BACKGROUND

- Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that affects mainly the sacroiliac joints and the spine[1].
  - The disease can progress to involve peripheral joints and extra-articular structures including eyes, intestine, lungs, heart, skin, bone, and kidneys.[1, 2]
  - AS starts before their 40s in most patients causing chronic pain, stiffness and fatigue[1], resulting in reduced physical function and quality of life.[3, 4]
- The first line of treatment for AS is nonsteroidal anti-inflammatory drugs (NSAIDs); however, potential intolerance and safety issues are concerning.[5]
- The second line of treatment for AS is novel biologics.
  - Seven biologics, including five tumor necrosis factor (TNF) inhibitors (*infliximab, etanercept, adalimumab, certolizumab pegol,* and *golimumab*) and two Interleukin-17A (IL-17A) antibody agents (*secukinumab* and *ixekizumab*), have been approved for the treatment of AS in the United States.[6]
  - They are well-tolerated and effective,[7, 8] but their impact on patients' quality of life is not collectively well-reported.

OBJECTIVE

- The current meta-analysis examines the impact on health-related quality of life (HRQoL) outcomes of novel biologic therapy with TNF inhibitors or IL-17A antibody agents in patients with AS.

METHODOLOGY

- A literature search on PubMed, Embase, and Clinicaltrials.gov databases was performed through September 2021 to identify qualified randomized, controlled trials (RCTs).
- The inclusion criteria were the following:
  1. A placebo-controlled RCT;
  2. Patients were diagnosed with AS according to the 1984 modified New York diagnostic criteria;[9]
  3. Intervention was a TNF inhibitor or an IL-17A antibody agent;
  4. HRQoL outcome was reported.
- Data extraction was performed independently by three authors. Cochrane Collaboration's tool was used to assess the quality of included RCTs.[10] Data analysis done using Review Manager version 5.4.[11]
- I^2 value of 25%, 50%, and 75% were set as low, moderate, and high heterogeneity, respectively. A p-value < 0.05 was considered statistically significant.
- This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.[12] Data and information were from published clinical trials; thus, Ethics Committee and Institutional Review Board (IRB) were not required.

RESULTS

Figure 1: Flow diagram for study inclusion

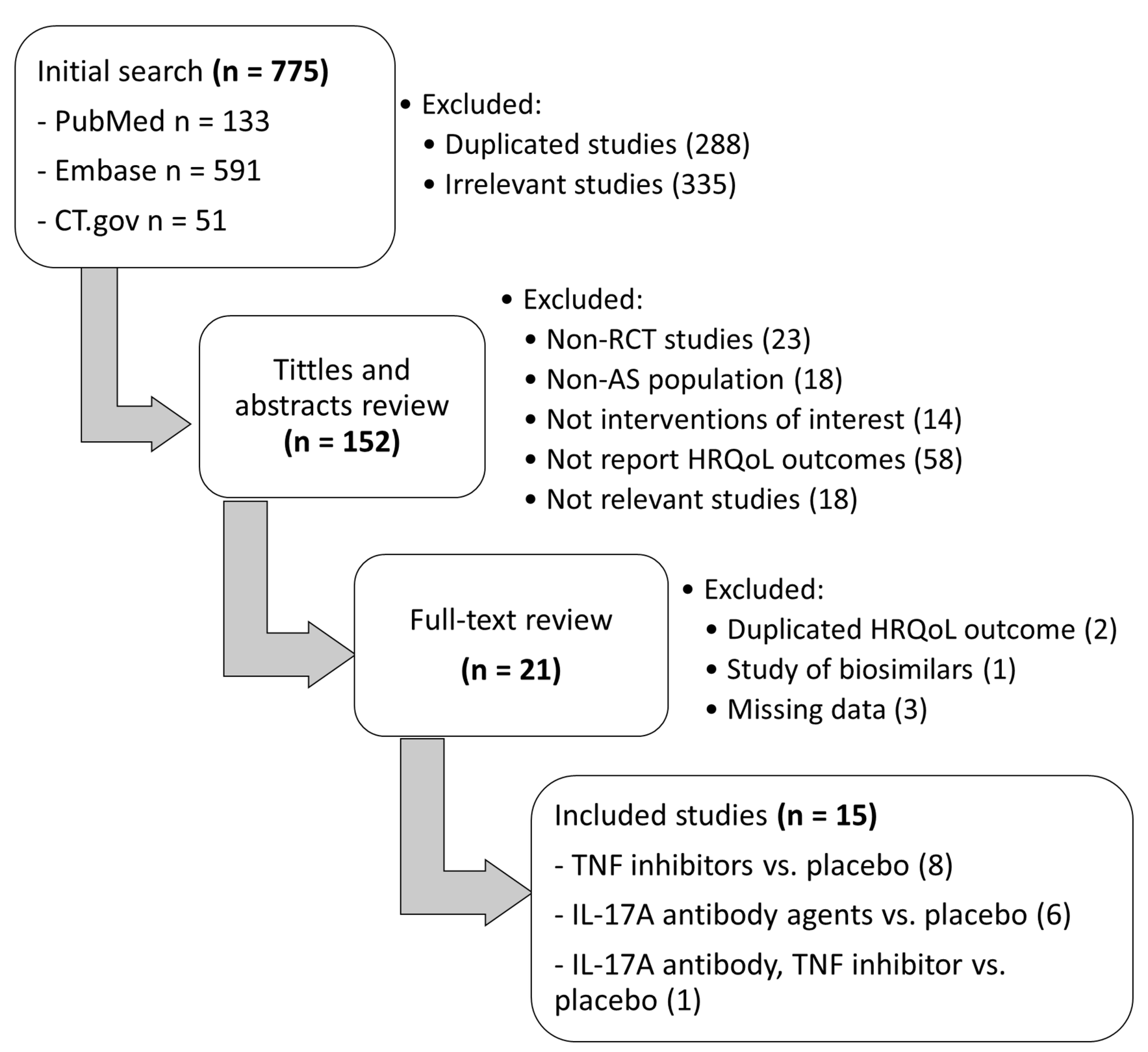


Table 1: Study characteristics[13-27]

Study/ Reference	Biologics	Size No	Duration Week	Male %	Mean age Year (SD)	HRQoL outcome reported: SF-36 PCS	SF-36 MCS	EQ-5D	ASQoL	Overall risk of bias
MEASURE 1 (Beaten 2015 & Deodhar 2016)	SEC	371	16	69.3	41.8 (12.4)	●	●	●	●	green
MEASURE 2 (Beaten 2015 & Marzo-Ortega 2017)	SEC	219	16	70.0	43.3 (12.9)	●			●	green
MEASURE 4 (Kivitz 2018)	SEC	350	16	77.6	43.0 (11.8)	●			●	green
COAST – W (Deodhar 2019)	IXE	316	16	80.0	46.1 (12.4)	●	●			green
COAST – V (van der Heijde 2018)	IXE; ADA	341	16	81.3	41.7 (11.6)	●	●			green
GO-ALIVE (Deodhar 2018 & Reveille 2020)	GOL IV	208	16	78.4	38.8 (10.4)	●	●	●	●	yellow
Bao 2014	GOL	213	20	83.1	30.5 (9.46)	●	●			green
GO-RAISE (Inman 2008)	GOL	278	24	71.5	37.2 (16.5)	●	●			green
Huang 2014	ADA	344	12	81.7	29.9 (8.3)	●	●			green
ATLAS (van der Heijde 2006 & Davis 2007)	ADA	315	24	74.7	42.3 (11.6)	●	●		●	yellow
RAPID-axSpA (Landewe 2014)	CZP	178	12	72.5	41.5 (11.6)	●	●			yellow
ASSERT (van der Heijde 2005)	IFX	279	24	82.7	39.9 (10.8)	●	●			yellow

- SF-36 PCS = 36-Item Short Form Survey Physical Score Component; SF-36 MCS = 36-Item Short Form Survey Mental Score Component; EQ-5D = European Quality of Life – 5 Dimensions; ASQoL = Ankylosing Spondylitis Quality of Life.
- SEC = secukinumab; IXE = ixekizumab; ADA = adalimumab; GOL = golimumab; CZP = certolizumab; IFX = infliximab.
- Green circle indicates low risk of bias; yellow circle indicates unclear risk of bias.

Figure 2: Risk of bias graph

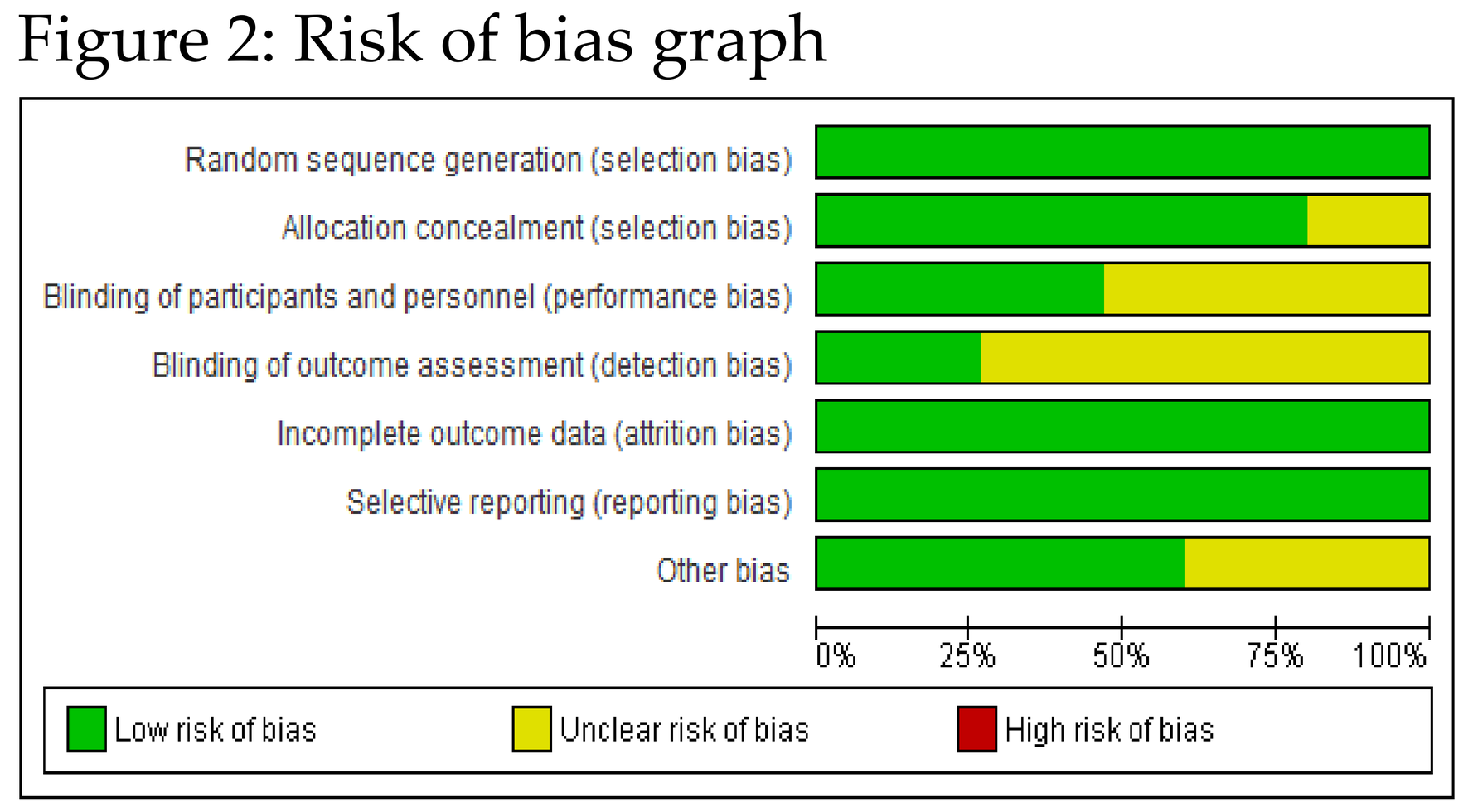


Figure 3.1: Mean difference in SF-36 PCS between biologics vs. placebo

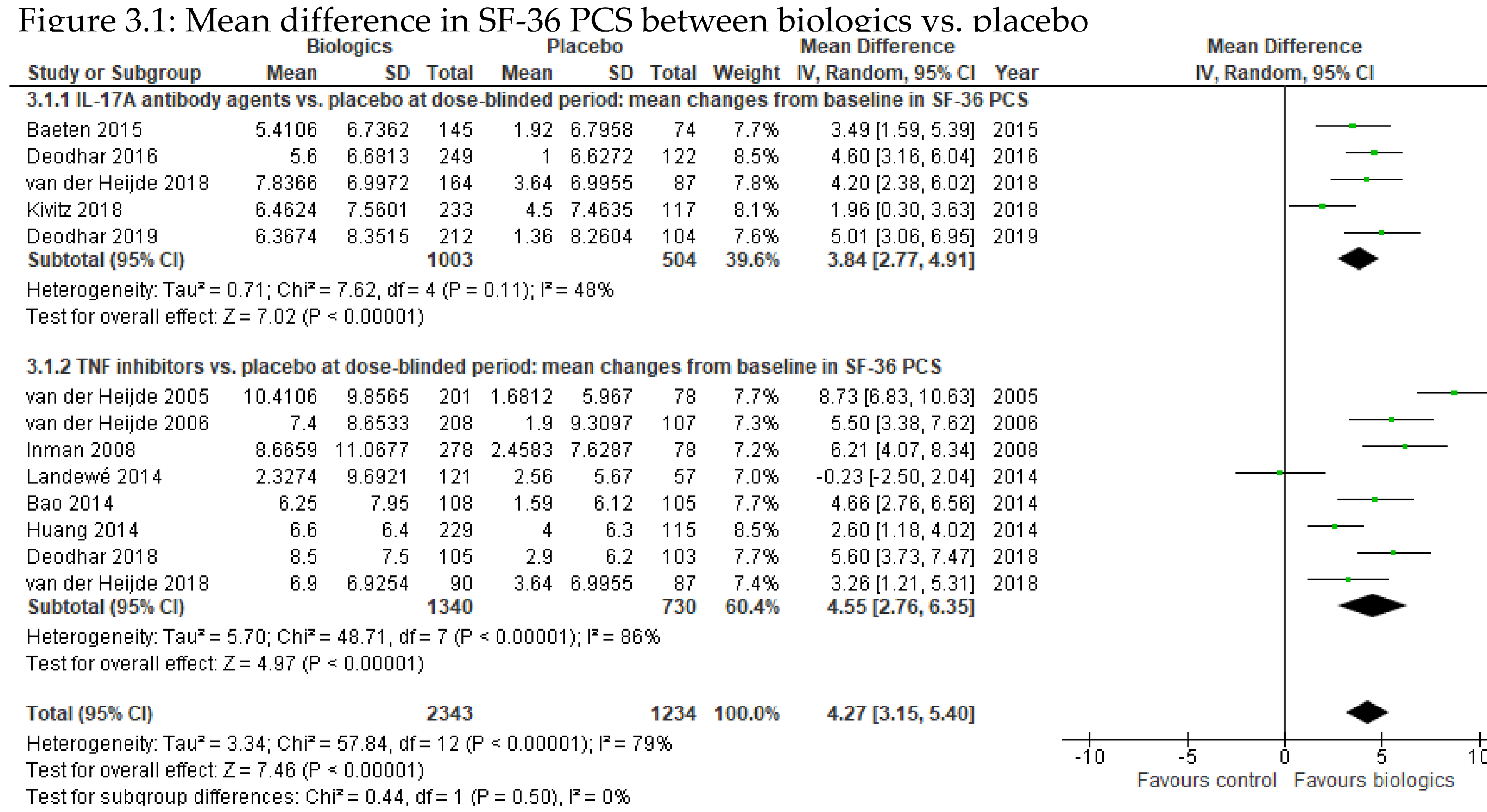


Figure 3.2: Mean difference in SF-36 MCS between biologics vs. placebo

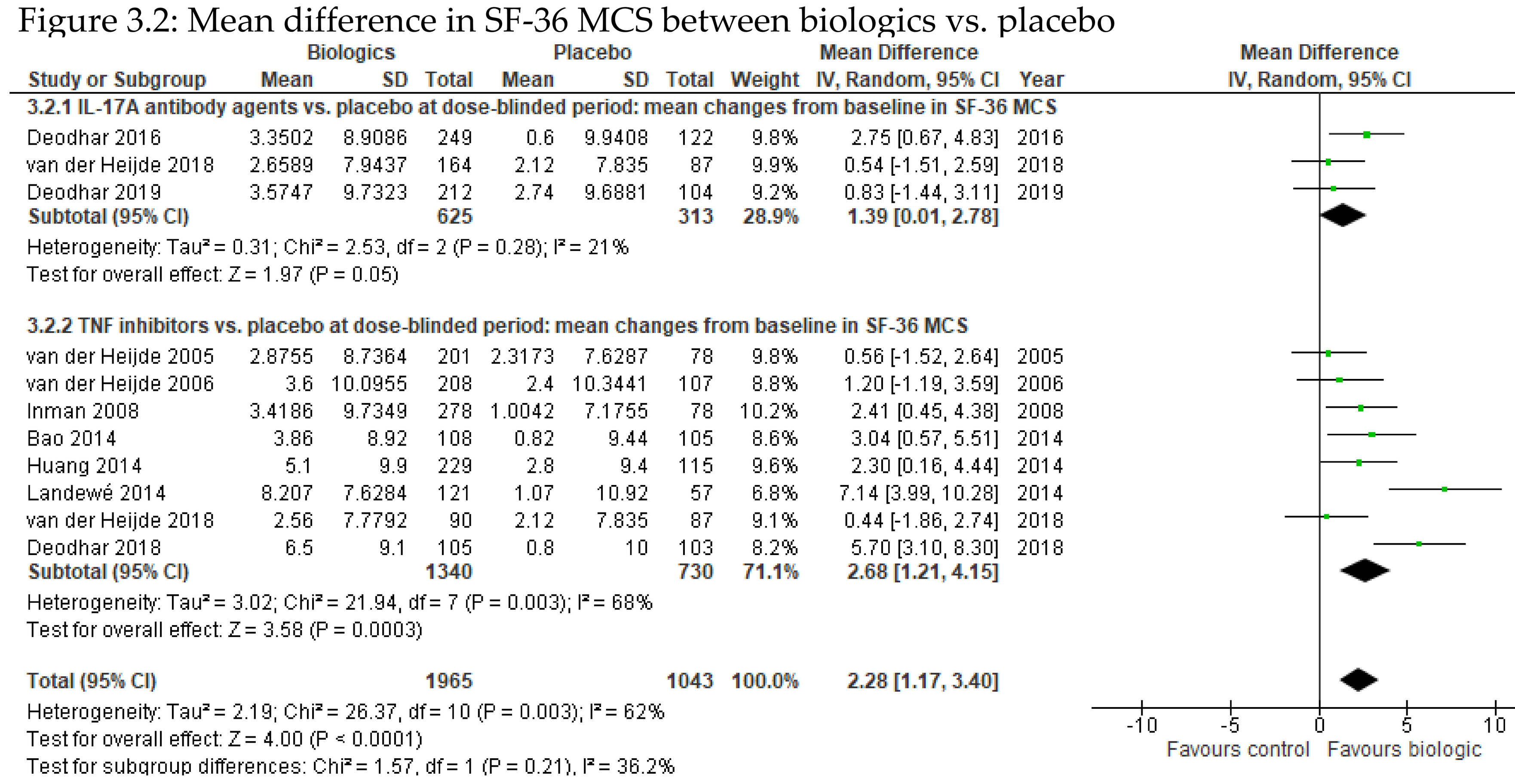


Figure 3.3: Mean difference in EQ-5D between biologics vs. placebo

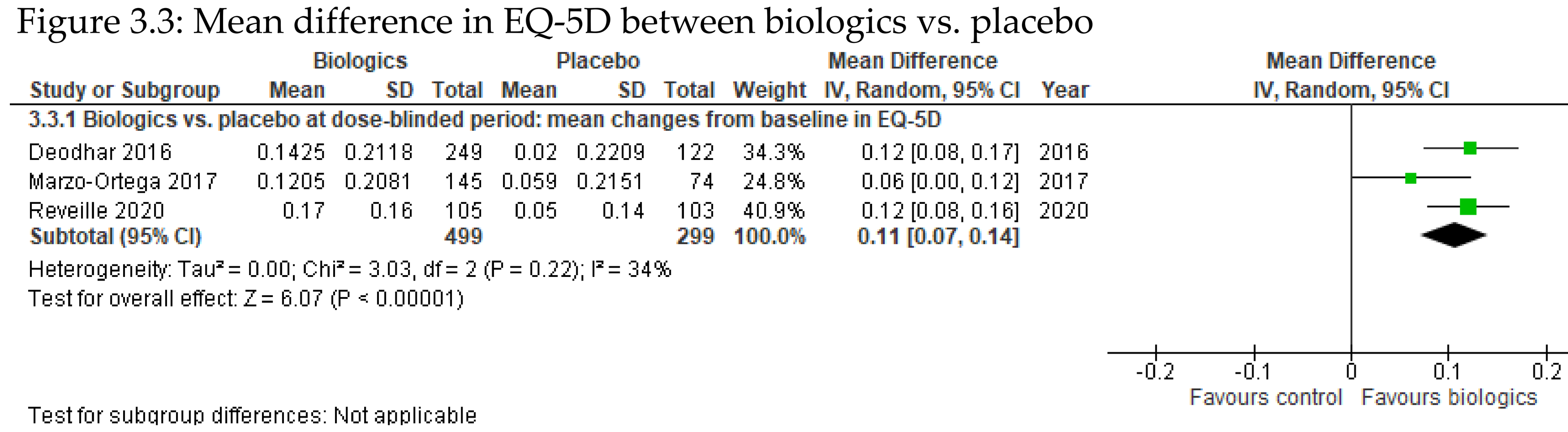
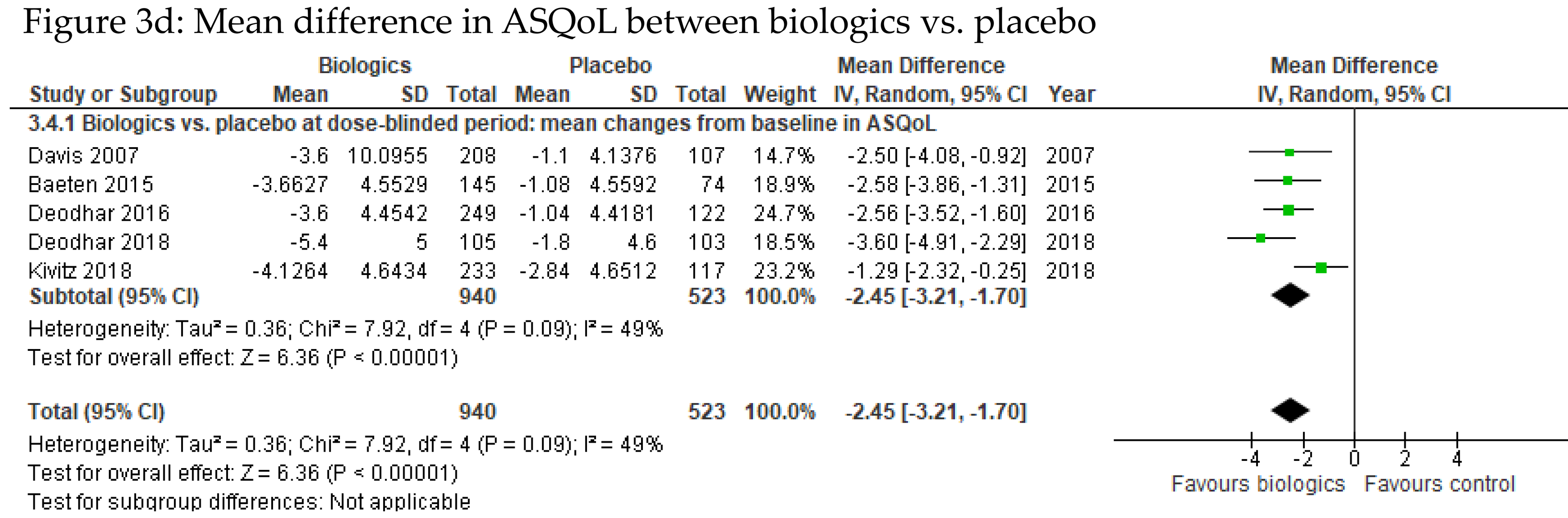


Figure 3d: Mean difference in ASQoL between biologics vs. placebo



RESULTS

- Fifteen RCTs, involving 3,412 participants, were included:
  - Low risk of bias was observed in 9 studies, and unclear risk of bias was observed in 6 studies (Table 1); detection bias was the most observed type of bias (Figure 2).
- Three HRQoL outcomes measures were reported (Table 1):
  - 36-Item Short Form Survey (SF-36), measuring general health status with summarized physical component score (PCS) and mental component score (MCS)[28], were reported in 12 studies.
  - European Quality of Life – 5 Dimensions (EQ-5D), measuring preference-based health utility,[29] were reported in 3 studies.
  - Ankylosing Spondylitis Quality of Life (ASQoL), a disease-specific instrument measuring quality of life in patients with AS,[30] were reported in 5 studies.
- The differences of the mean changes in HRQoL outcomes from baseline between the novel biologic therapy and placebo were as followed (Figure 3):
  - SF-36 PCS: 4.27 (95%-CI: 3.15 to 5.40, p < 0.001),
  - SF-36 MCS: 2.28 (95%-CI: 1.17 to 3.40, p < 0.001,
  - EQ-5D: 0.11 (95%-CI: 0.07 to 0.14, p < 0.001);
  - and ASQoL: -2.45 (95%-CI: -3.21 to -1.70, p < 0.001).
- Heterogeneity was high (I^2 = 79%) among studies reporting SF-36 PCS, and moderate (I^2 = 62%, 34%, and 49%) among studies reporting SF-36 MCS, EQ-5D, and ASQoL, respectively (Figure 3).

DISCUSSION

- The high heterogeneity among studies reporting SF-36 PCS could be explained by the variations in study design, methodology, duration of treatment, treatment drug, and baseline characteristics of the sample population.
- Data on HRQoL outcomes reported from clinical trials were limited (the HRQoL outcome most reported was SF-36).
- The differences of mean changes from baseline between the novel biologic therapy and placebo on HRQoL SF-36 PCS, EQ-5D, and ASQoL outcomes, but SF-36 MCS, were clinically important improvement based on their established minimal clinical important difference (MCID) values.[31]
- This study accessed the short-term (12 – 24 weeks) impacts of biologics, limited by the availability of data.
- Future clinical trials on AS should include HRQoL outcomes assessment in their study designs.

CONCLUSION

- The novel biologic therapy was associated with significant improvement in HRQoL measures with the SF-36, EQ-5D, and ASQoL compared to placebo.

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