

# **Supplemental Material**

**PubMed search**

<b>Keywords</b>	<b>Number of results</b>
<b>(bempedoic acid OR ETC-1002)</b>	<b>54</b>
<b>(bempedoic acid OR ETC-1002) AND (cholesterol)</b>	<b>49</b>
<b>(bempedoic acid OR ETC-1002) AND (cholesterol OR hypercholesterolemia)</b>	<b>49</b>
<b>(bempedoic acid OR ETC-1002) AND (cholesterol OR hypercholesterolemia OR hypercholesterolemic)</b>	<b>49</b>
<b>(bempedoic acid OR ETC-1002) AND (cholesterol OR hypercholesterolemia OR hypercholesterolemic OR lipoprotein)</b>	<b>50</b>
<b>(bempedoic acid OR ETC-1002) AND (cholesterol OR hypercholesterolemia OR hypercholesterolemic OR lipoprotein OR LDL)</b>	<b>50</b>

**Table S1. Assessment of risk of bias in included studies.**

<b>Ballantyne 2016</b>	?	?	?	?	+	+	-
<b>Ballantyne 2018</b>	+	+	+	+	+	+	+
<b>Ballantyne 2019</b>	?	+	?	+	+	+	+
<b>Goldberg 2019</b>	+	+	+	?	+	+	+
<b>Laufs 2019</b>	?	+	?	+	+	+	-
<b>Ray 2019</b>	?	+	?	+	+	+	+
<b>Thompson 2016</b>	+	+	?	+	+	+	+

**Key**

 **Low risk of bias**

 **High risk of bias**

 **Unclear risk of bias**

*Random sequence generation*  
*Allocation concealment*  
*Blinding of participants and personnel*  
*Blinding of outcome assessment*  
*Incomplete outcome data*  
*Selective reporting*  
*Other bias*

**Table S2. Characteristics of included studies.**

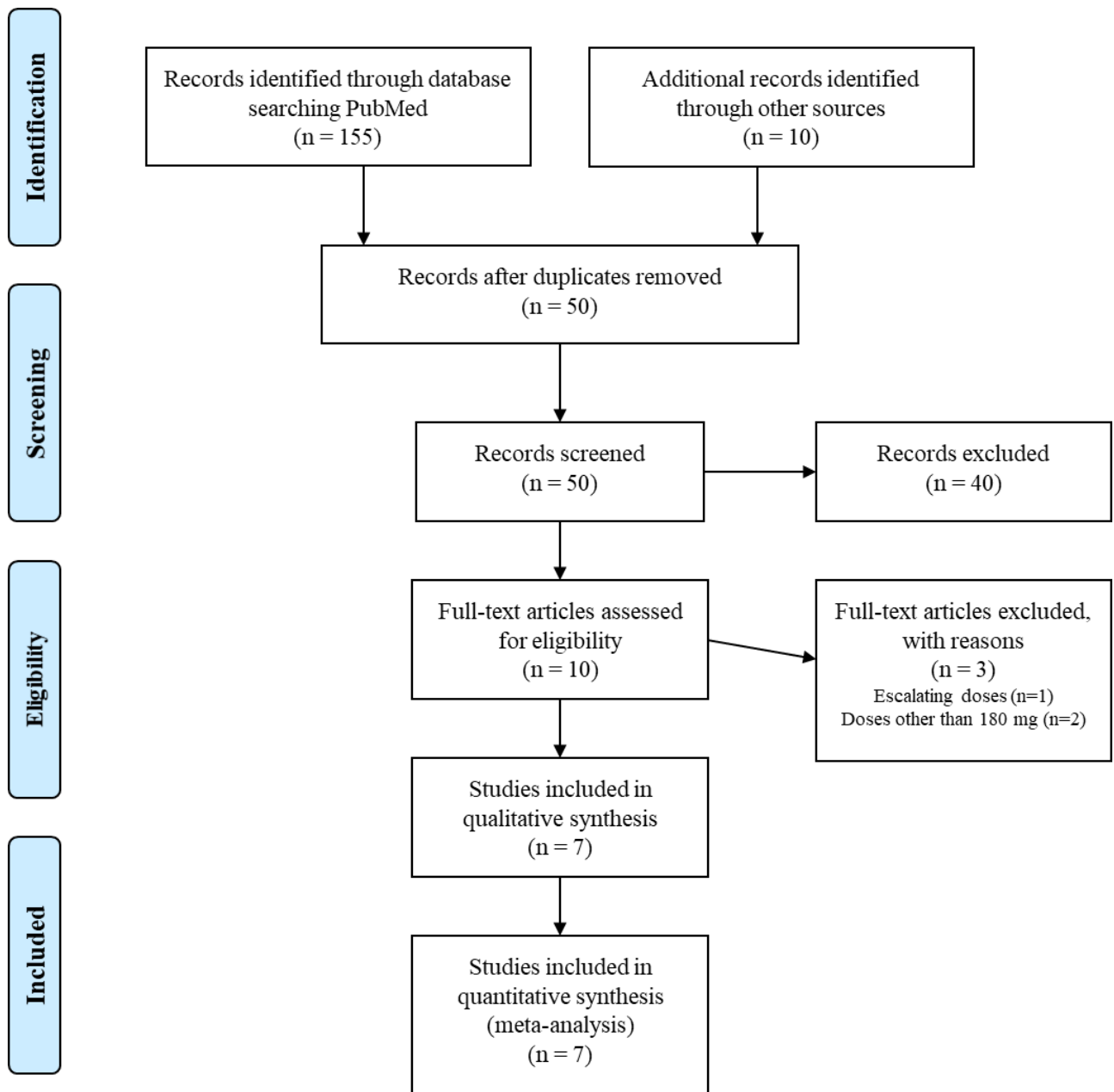
<b>Study</b>	<b>Background lipid lowering therapy</b>	<b>Baseline LDL-c cut-off</b>
Ray 2019 Harmony <sup>26</sup>	Maximally tolerated statin therapy±other LLT	≥ 70 mg/dl
Goldberg 2019 Wisdom <sup>23</sup>	Maximally tolerated statin therapy±other LLT	≥ 100 mg/dl at screening or ≥ 70 mg/dl at randomization
Ballantyne 2019 <sup>24</sup>	Maximally tolerated statin therapy.	≥ 100 mg/dL for CAD/FH ≥130 mg/dL for multiple VRFs
Ballantyne 2016 <sup>29</sup>	Maximally tolerated statin therapy	115-220 mg/dl
Thompson 2016 <sup>28</sup>	Maximally tolerated statin therapy	130-220 mg/dL
Ballantyne 2018 Tranquility <sup>27</sup>	No statin or low-dose statin	≥ 100 mg/dL
Laufs 2019 Serenity <sup>25</sup>	Maximally tolerated statin therapy	≥ 100 mg/dL for CAD/FH ≥130 mg/dL for primary prevention

\*LLT: lipid-lowering therapies

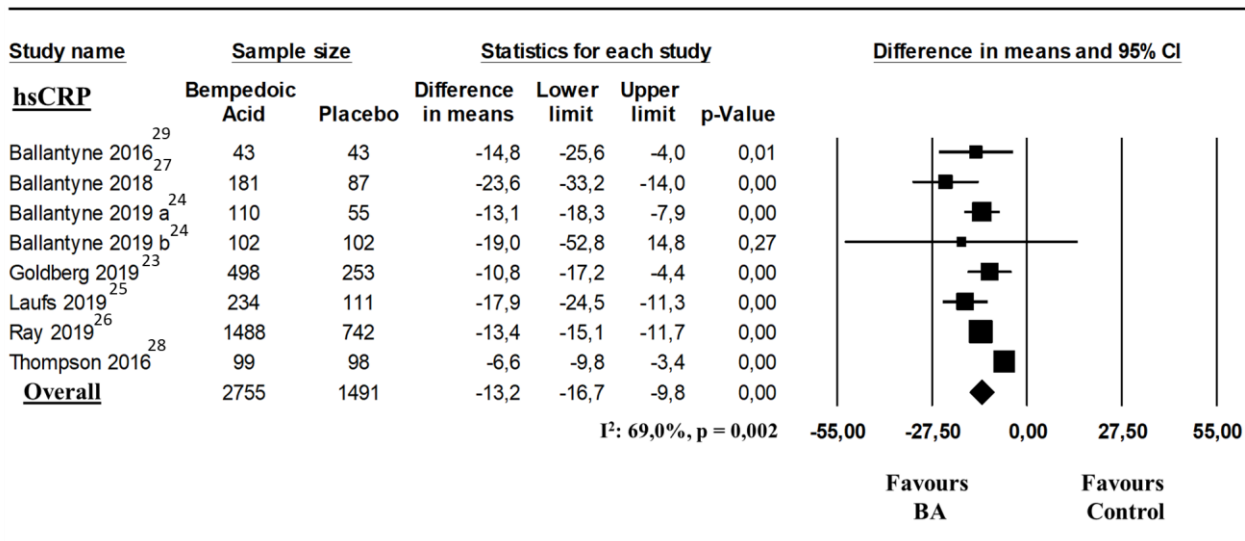
**Table S3. Meta-regression analyses. Impact of Age, male gender, body Mass Index (BMI), diabetes and baseline LDL-C on the difference in the incidence of adverse events, serious adverse events, drug discontinuation, muscle-related side effects and new-onset diabetes, gout flare and changes in uric acid between patients receiving bempedoic acid and control treatment group.**

Outcome		Covariate				
		Age	Male sex	BMI	Diabetes	Baseline LDL
Adverse events	z-value	0.02	-1.43	1.19	1.14	1.65
	p-value	0.983	0.151	0.233	0.251	0.098
Serious adverse events	z-value	0.42	0.17	0.22	-0.42	0.40
	p-value	0.677	0.860	0.824	0.670	0.690
Drug discontinuation	z-value	1.92	1.43	-1.30	-1.31	-0.99
	p-value	0.053	0.153	0.194	0.187	0.322
Muscle-related side effects	z-value	1.84	2.05	-1.00	-0.43	-1.77
	p-value	0.065	0.041	0.315	0.663	0.077
New-onset diabetes	z-value	-1.02	-0.50	1.21	-0.19	0.98
	p-value	0.307	0.618	0.225	0.846	0.328
Gout flare	z-value	0.47	0.64	-0.60	0.20	-0.64
	p-value	0.635	0.518	0.547	0.842	0.522
Uric acid	z-value	3.40	0.70	-0.95	-0.29	-0.31
	p-value	<0.001	0.481	0.343	0.770	0.759

**Figure S1. PRISMA Flow Diagram.**

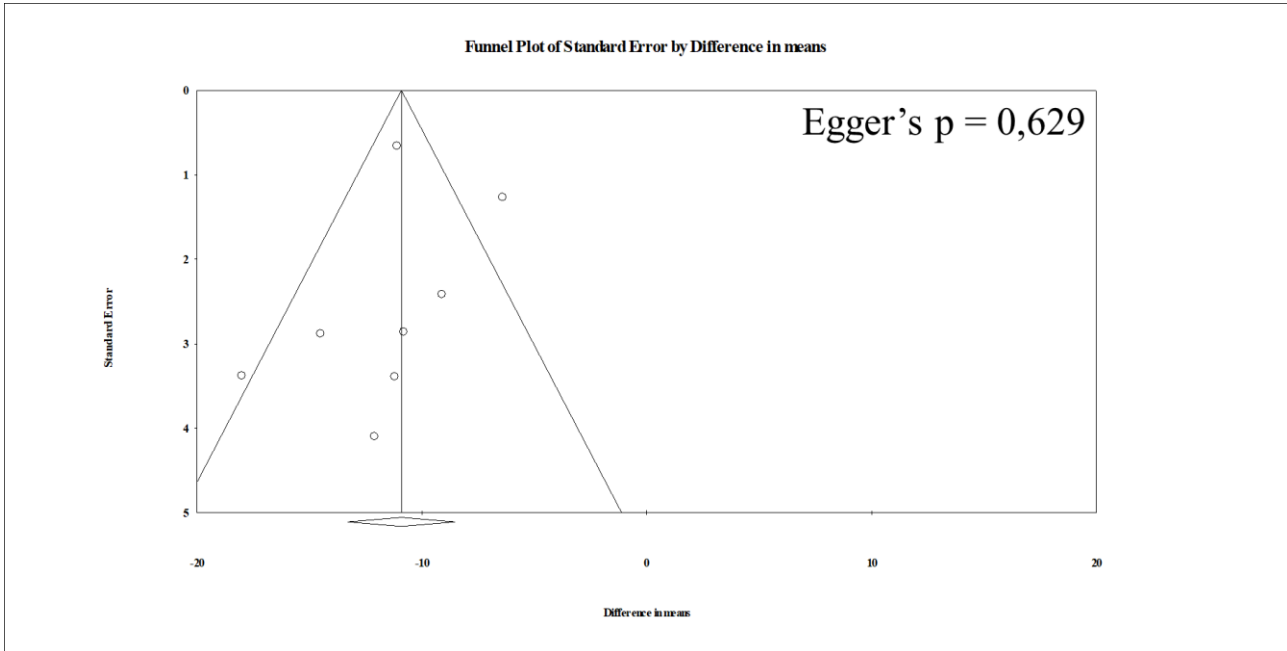


**Figure S2. Changes in high sensitivity C reactive protein (hsCRP) after 12 weeks of treatment with bempedoic acid as compared to control treatment.**

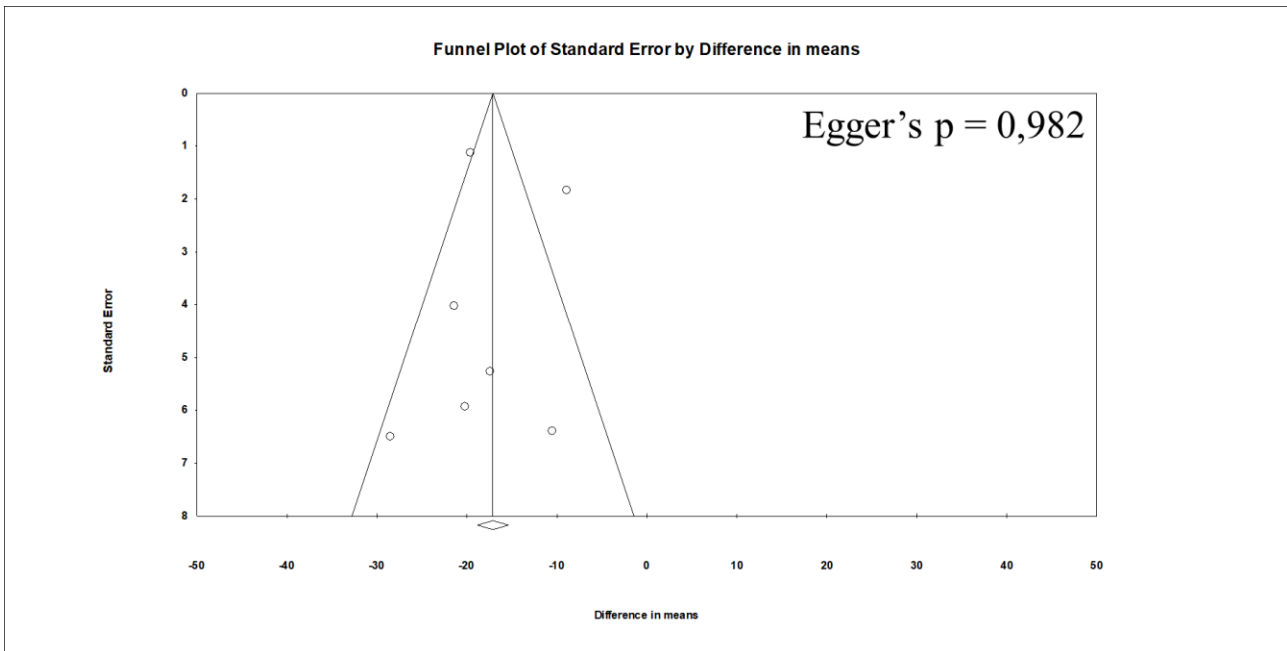


**Figure S3. Funnel plots of effect size versus standard error for studies evaluating the changes in total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), non- high-density lipoprotein-cholesterol (non-HDL-C), Apolipoprotein B (Apo B) and high sensitivity C reactive protein (hsCRP) in subjects receiving bempedoic acid and in control treatment group.**

**Total cholesterol (TC)**

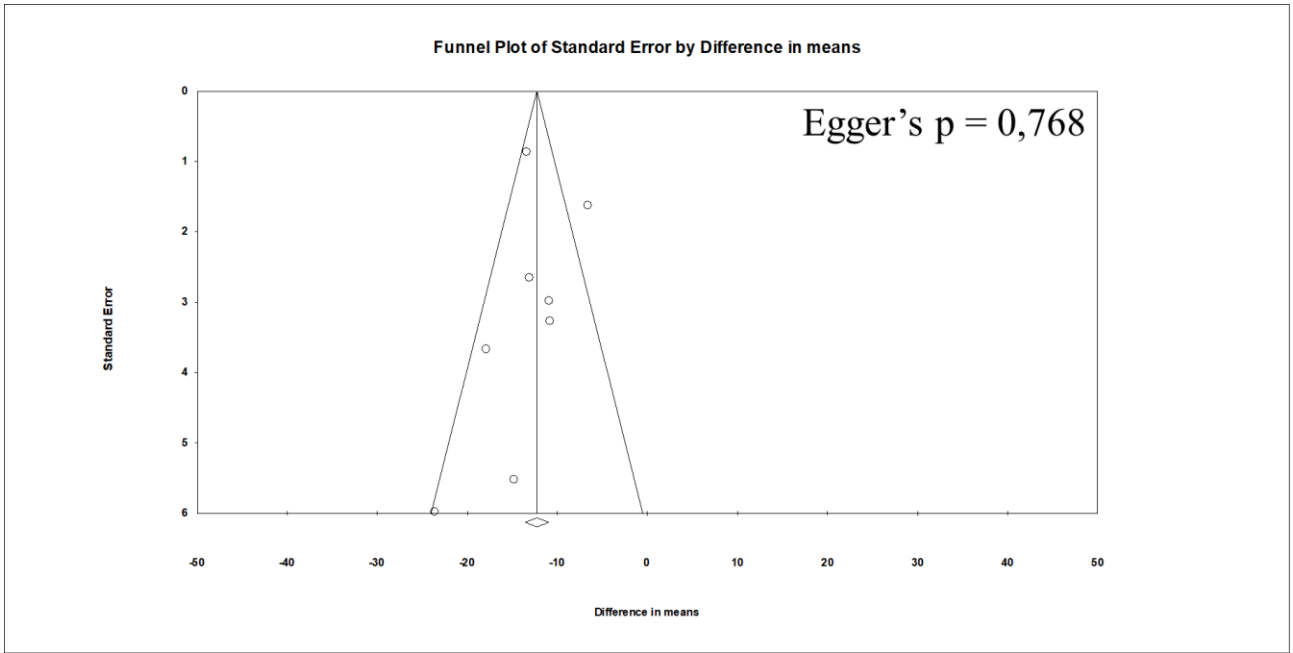


**Low-density lipoprotein-cholesterol (LDL-C)**

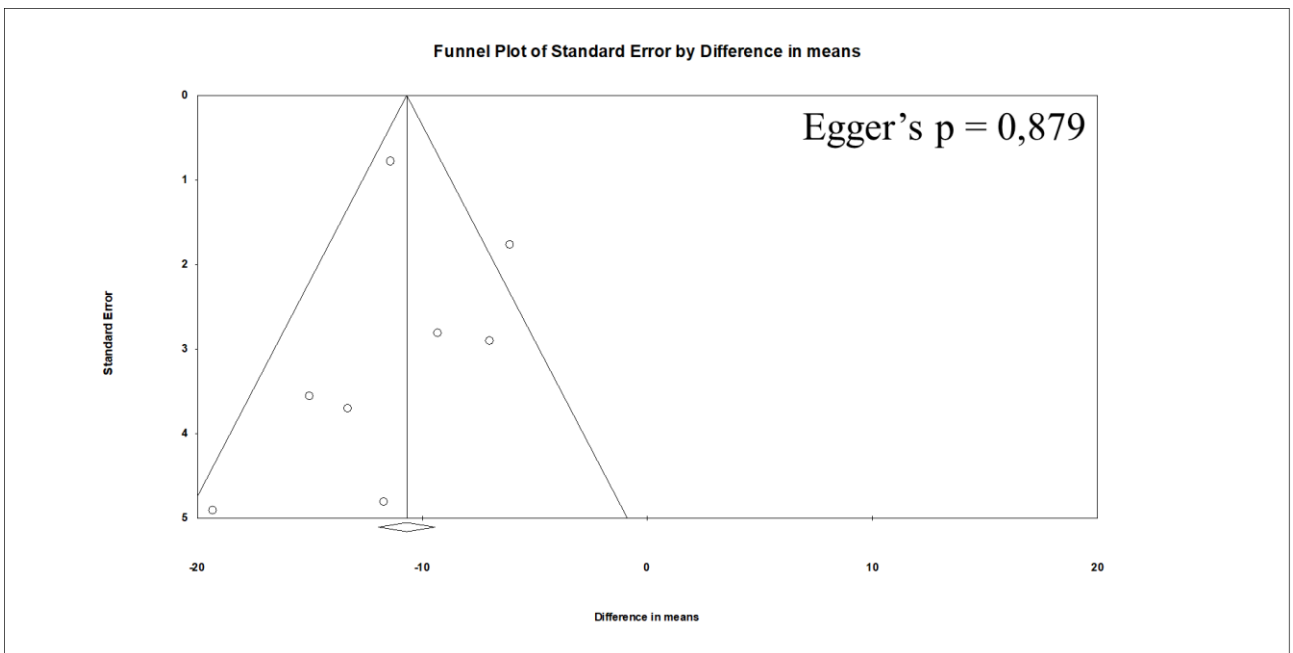


**Non-high-density lipoprotein-cholesterol (HDL-C)**

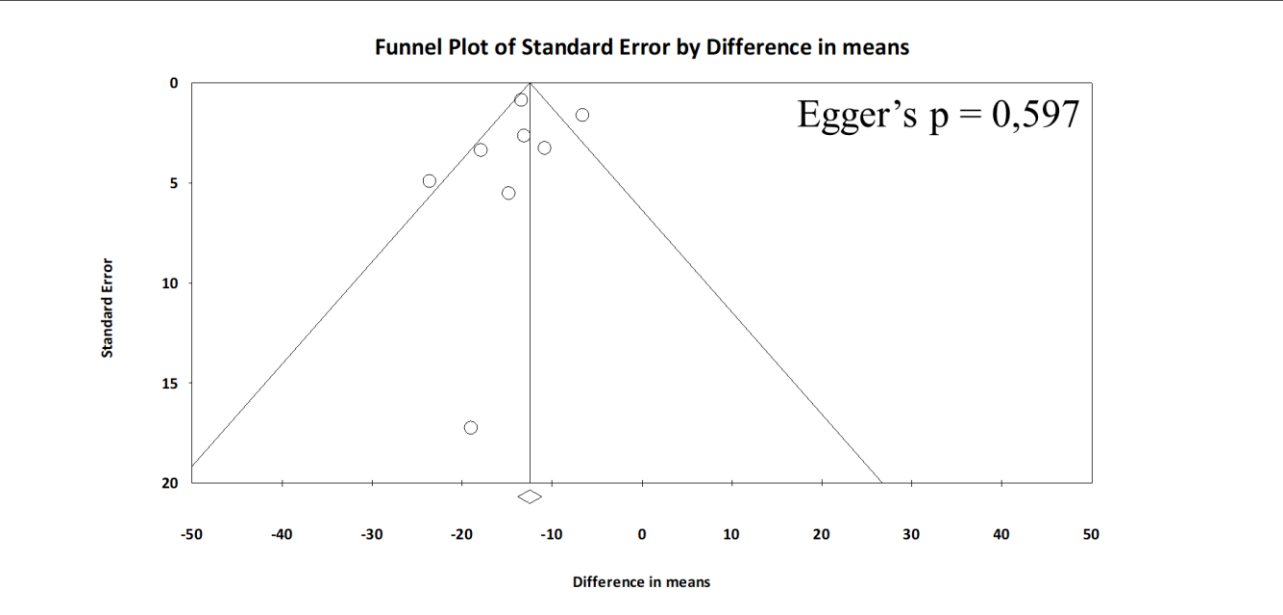




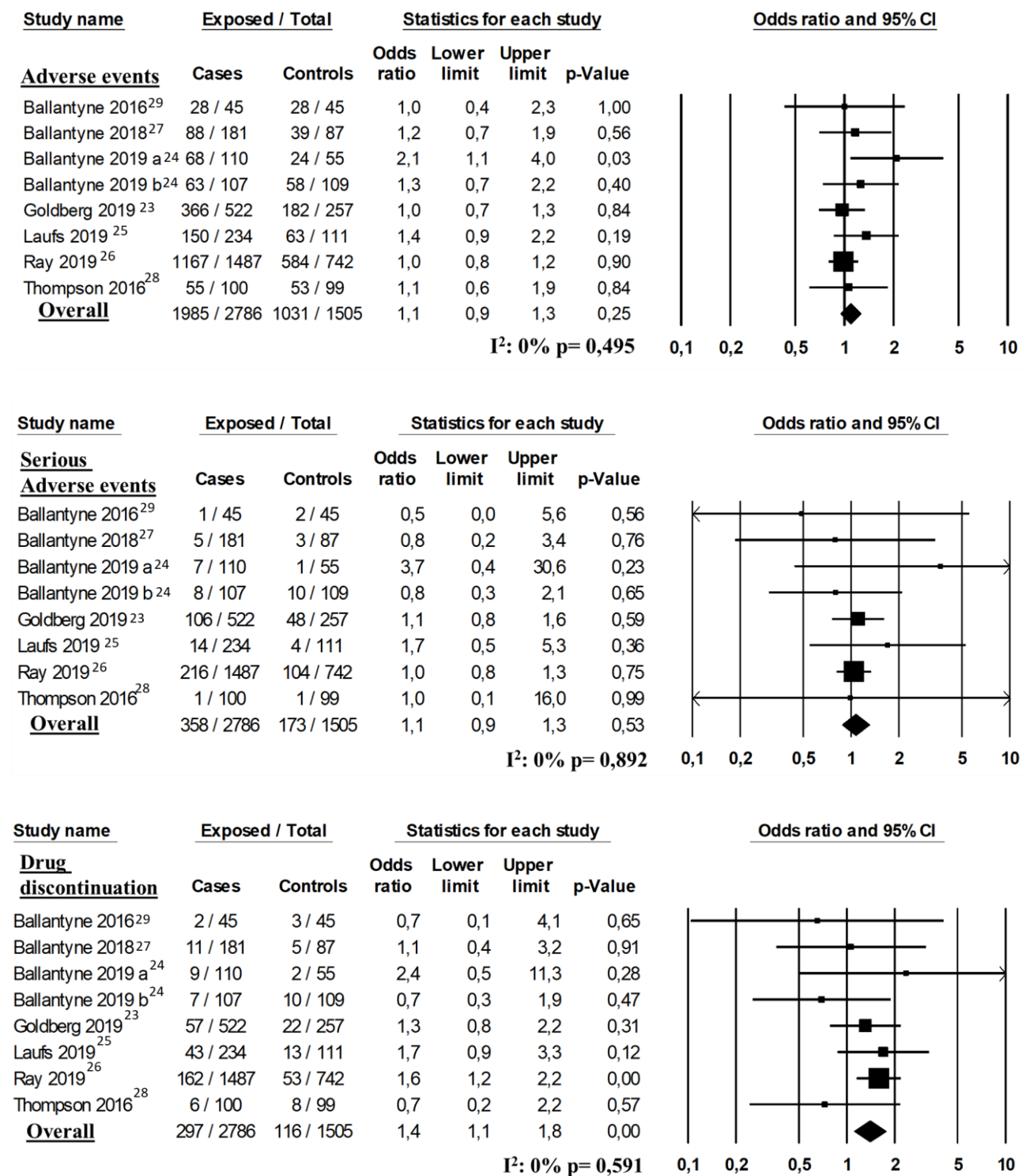
### Apolipoprotein B (Apo B)

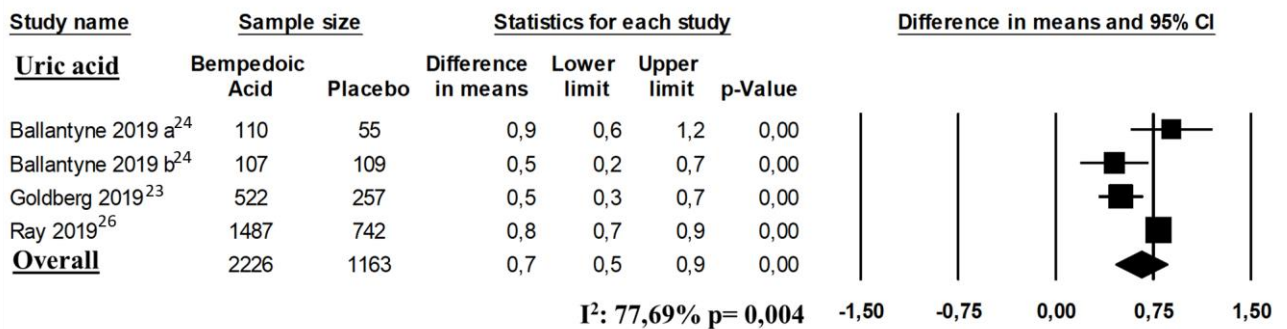
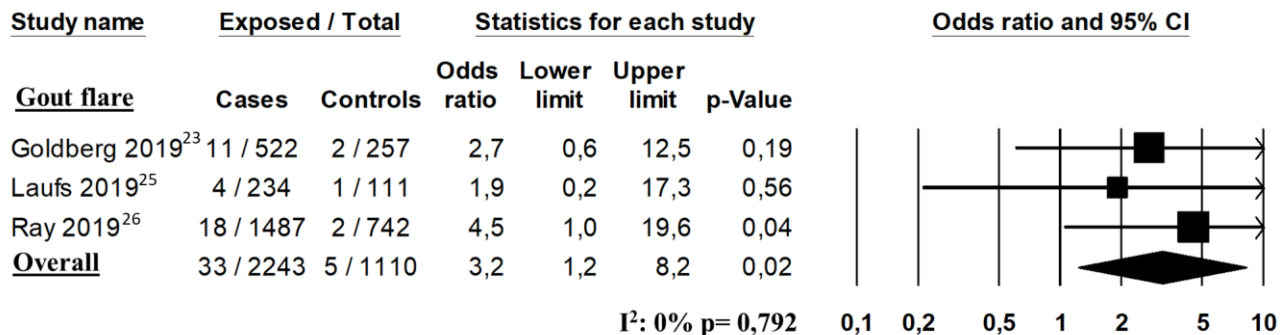
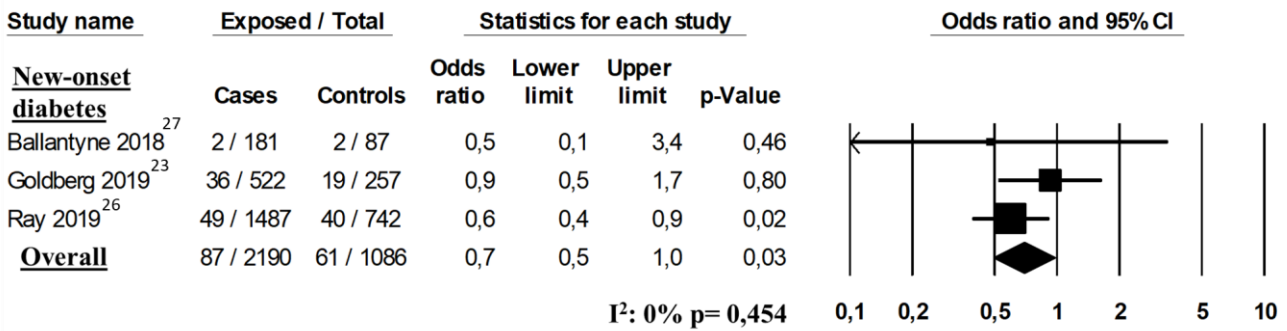
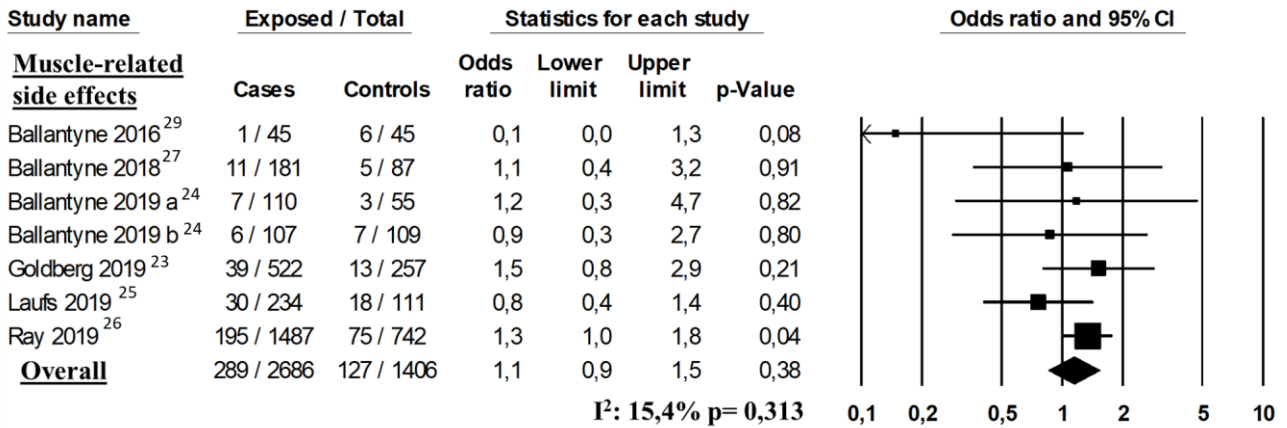


**High sensitivity C reactive protein (hsCRP)**

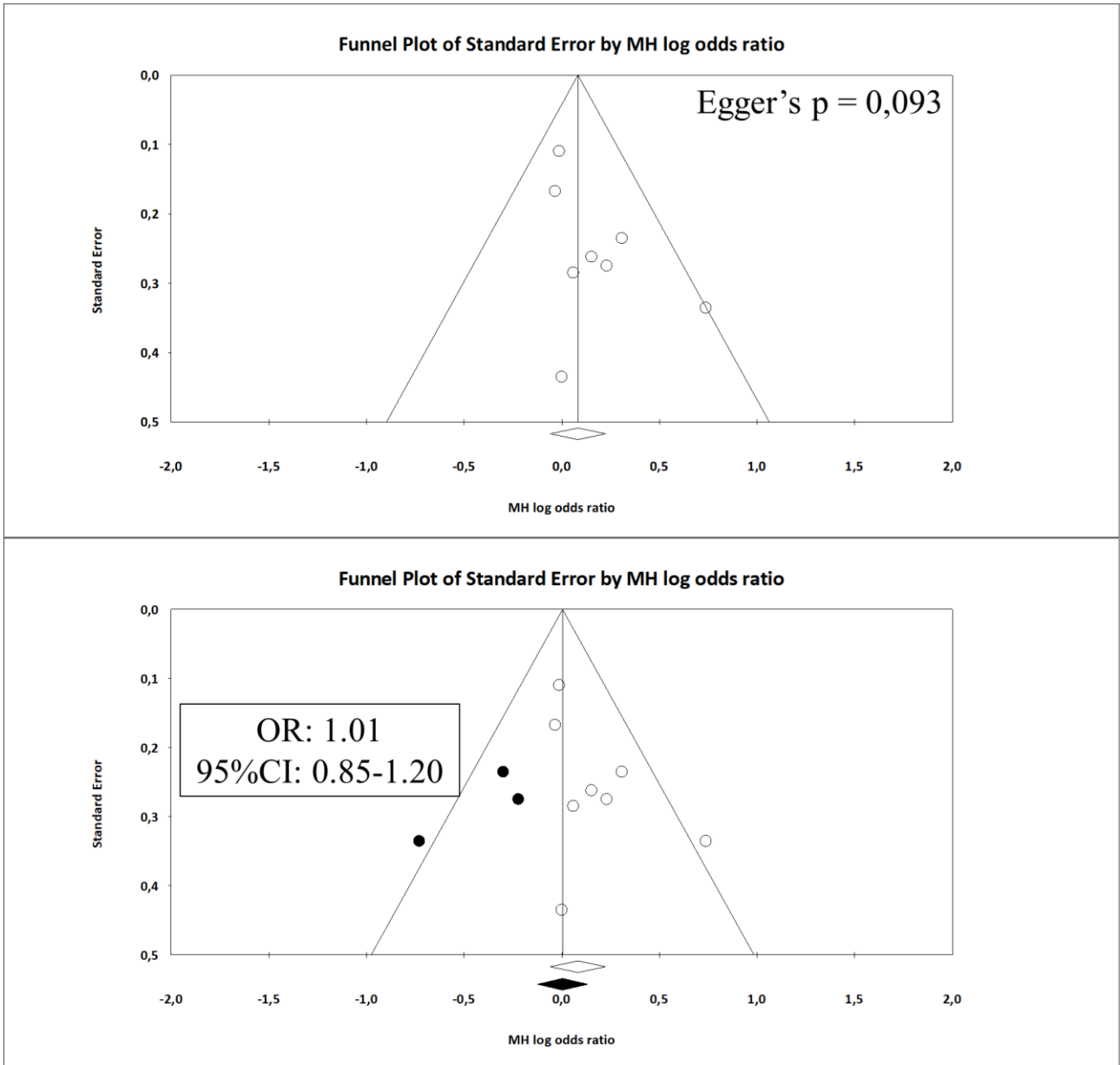


**Figure S4. Incidence of adverse events, serious adverse events, drug discontinuation, muscle-related side effects, new-onset diabetes, gout flare and changes in uric acid during treatment with bempedoic acid as compared to control treatment group.**





**Figure S5. Funnel plots of effect size versus standard error for studies evaluating the incidence of adverse events in subjects receiving bempedoic acid and in control treatment group (upper panel); adjustment of results by means of the Duval and Tweedie's trim and fill method (lower panel)**



**Figure S6. Funnel plots of effect size versus standard error for studies evaluating the incidence of serious adverse events (Panel A), drug discontinuation (Panel B); muscle-related side effects (Panel C); new-onset diabetes (Panel D); gout flare (Panel E); changes in uric acid (Panel F) in subjects receiving bempedoic acid and in control treatment group.**

