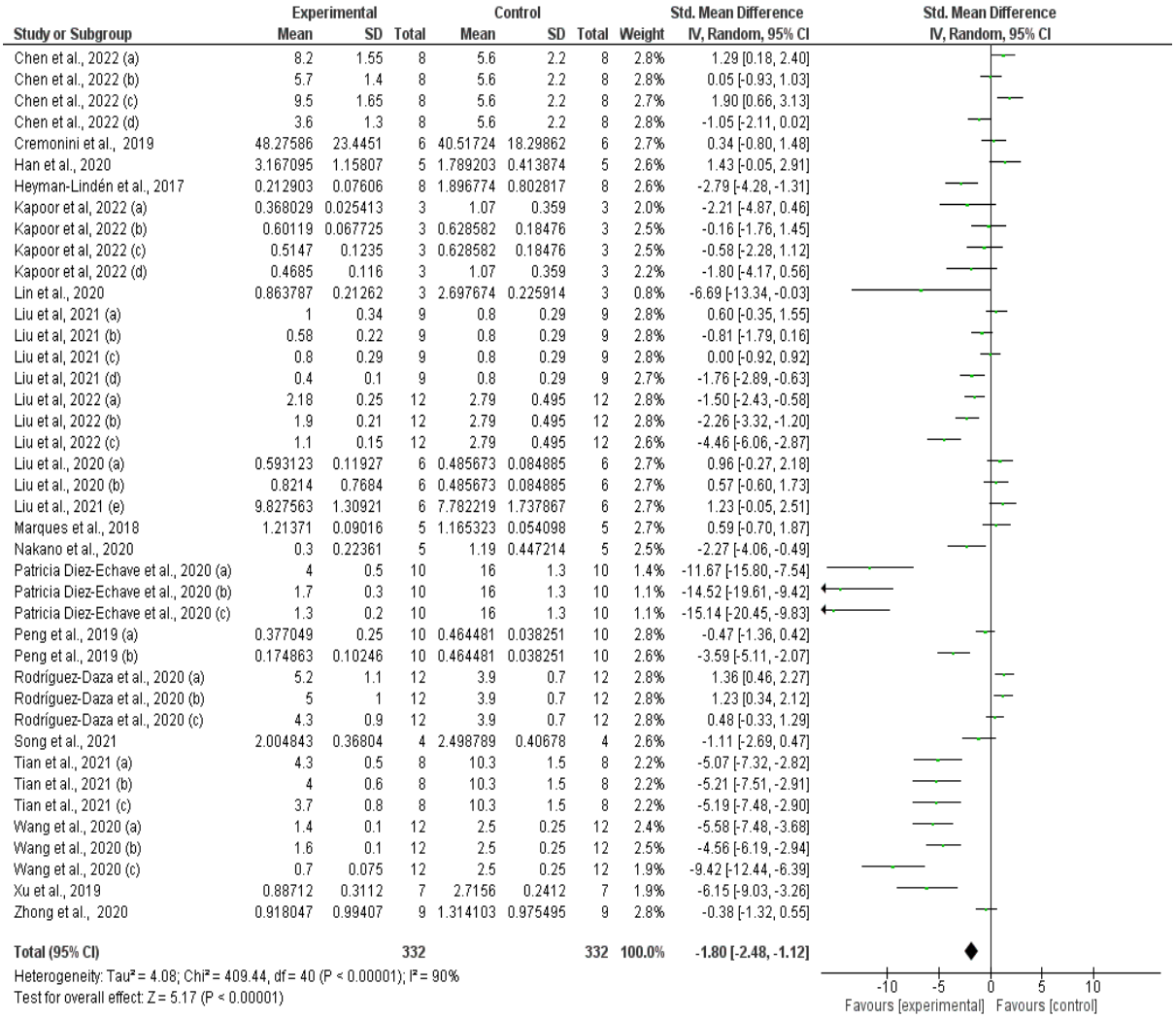
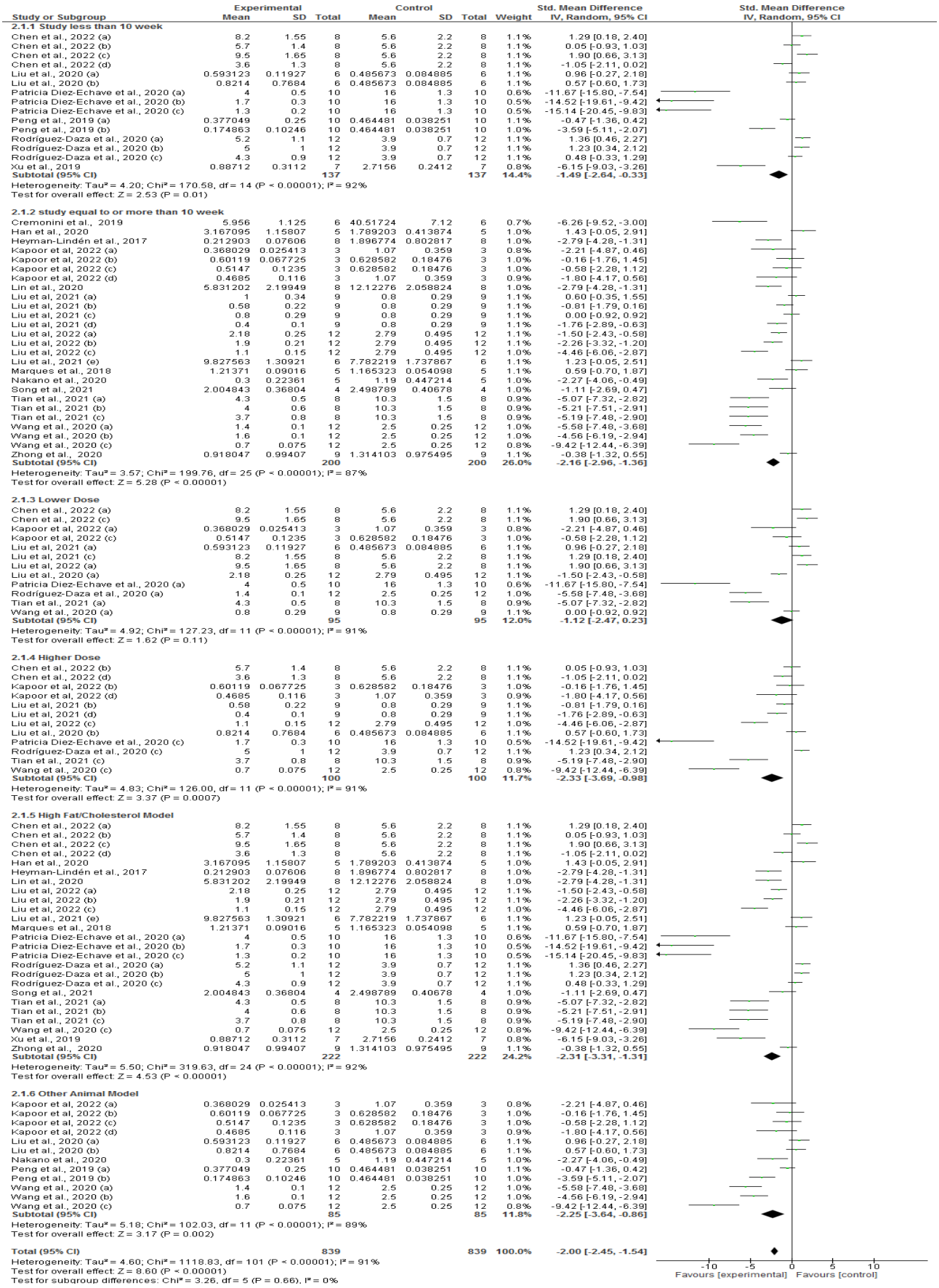
Effect of anthocyanins on gut health markers, *Firmicutes-Bacteroidetes* ratio and short-chain fatty acids: A systematic review via meta-analysis

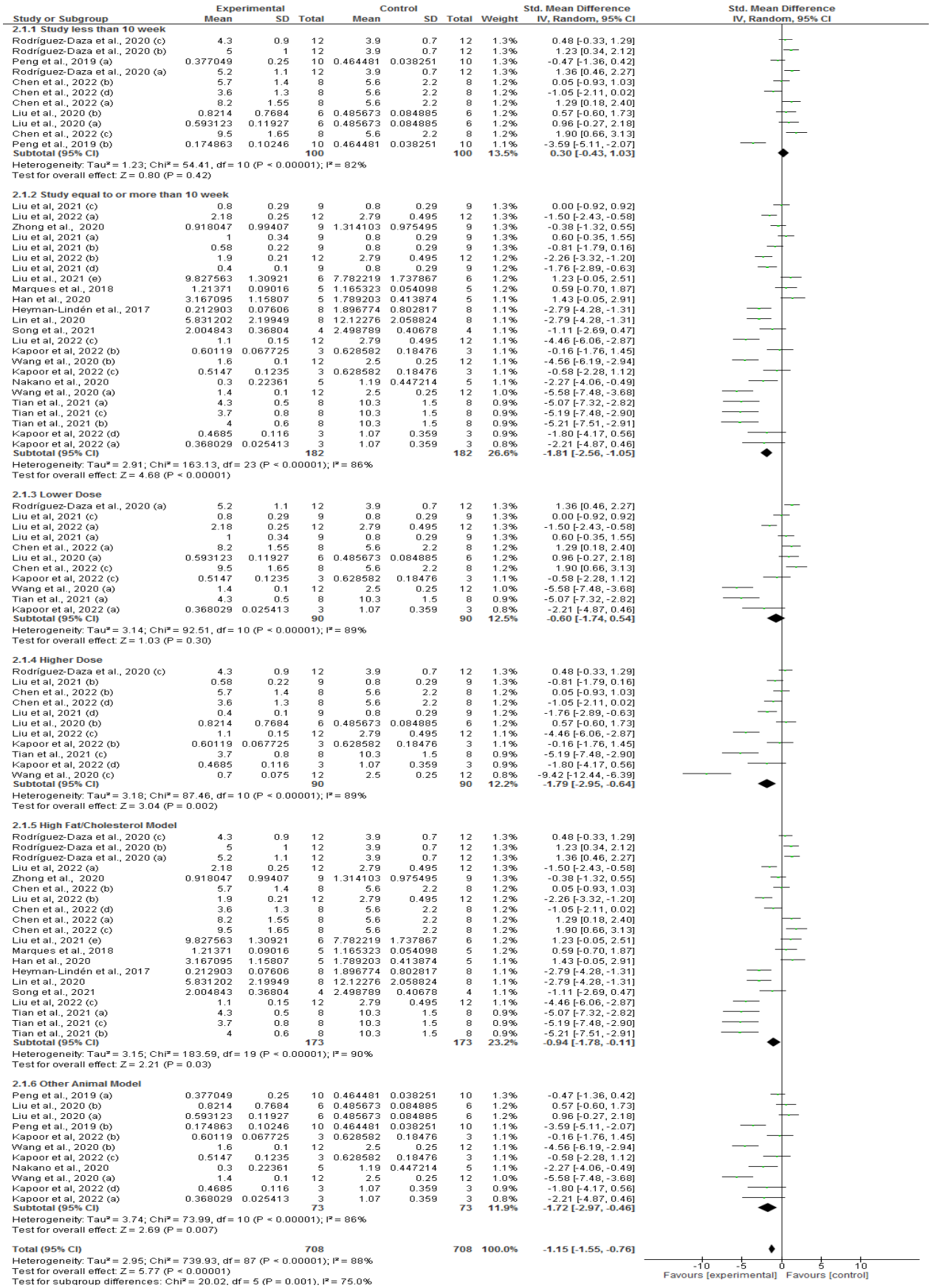
Payal Kapoor



S Figure 1: Forest plot of studies investigating the effect of anthocyanin supplementation on the *Firmicutes* to *Bacteroidetes* ratio (Fir/Bac). Pooled effect estimates (diamonds) for Fir/Bac are shown. Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



S Figure 2: Forest plot of the sub-group analysis to study effect of anthocyanin supplementation on the *Firmicutes* to *Bacteroidetes* ratio (Fir/Bac). Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Pooled effect estimates (diamonds) for Fir/Bac are shown. Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



S Figure 3: Forest plot of the sub-group analysis after elimination of high-influencer studies, for understanding the effect of anthocyanin supplementation on the *Firmicutes* to *Bacteroidetes* ratio (Fir/Bac). Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Pooled effect estimates (diamonds) for Fir/Bac are shown. Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).

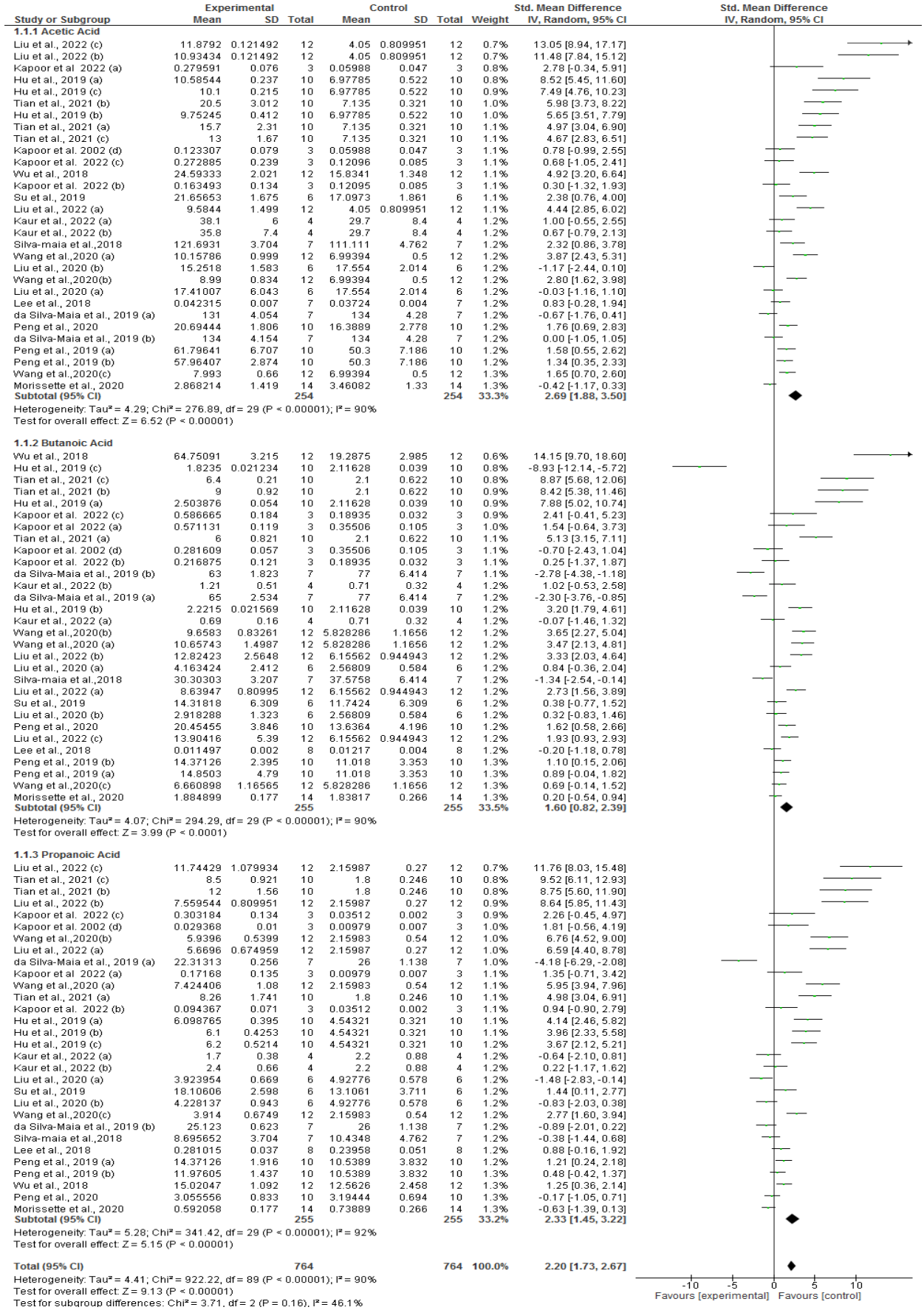
Question: Should Anthocyanin Rich vs Normal Diet be used for Fir/Bac?

Bibliography: . [Intervention] for [health problem]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

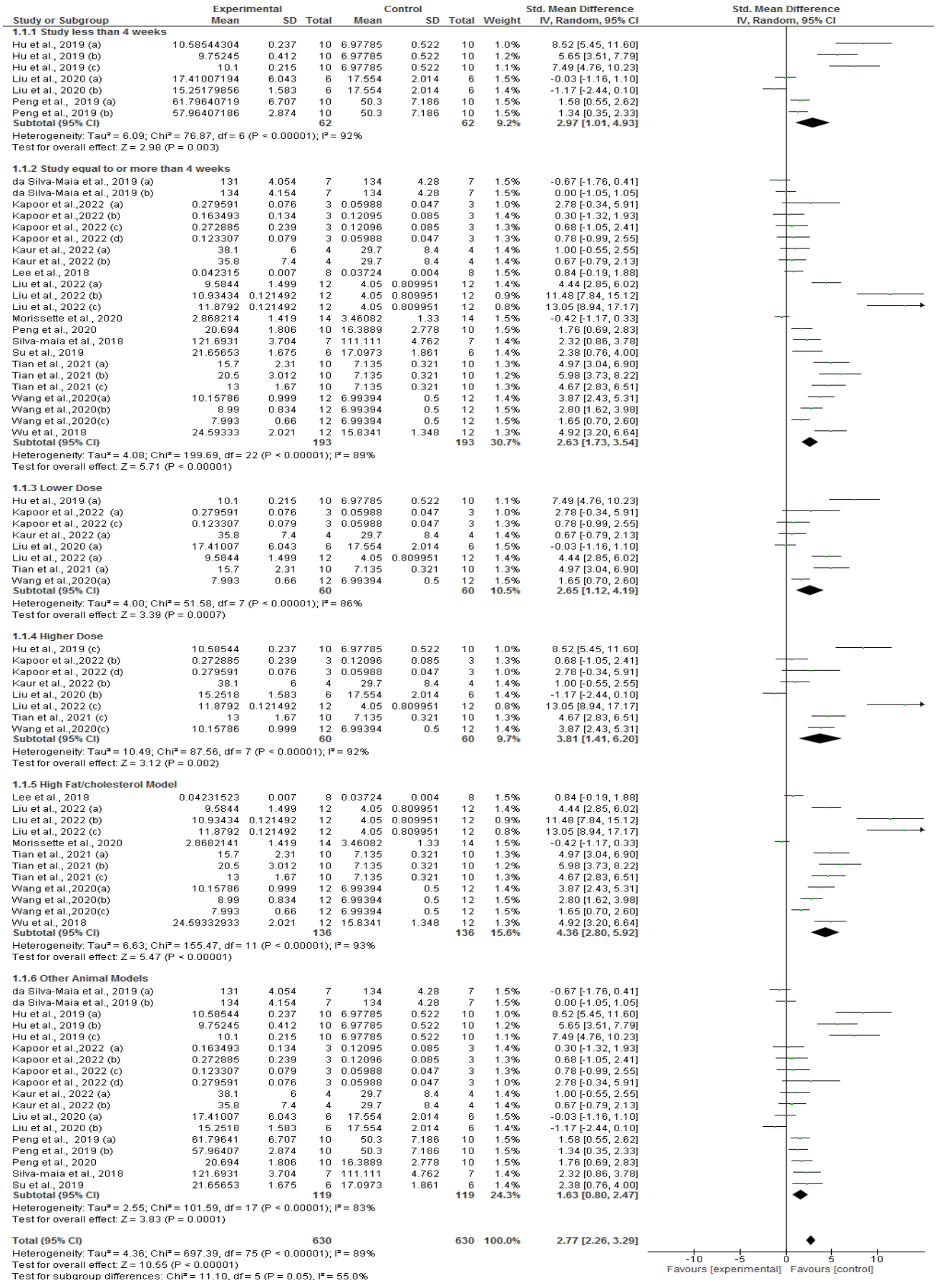
Quality assessment							Summary of Findings			
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Normal Diet	With Anthocyanin Rich		Risk with Normal Diet	Risk difference with Anthocyanin Rich (95% CI)
Fir/Bac (Better indicated by higher values)											
536 (34 studies)	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊕ **HIGH**[1] due to inconsistency, large effect	268	268	-		The mean fir/bac in the intervention groups was **0.89 standard deviations lower** (1.47 to 0.31 lower)

[1] High heterogeneity

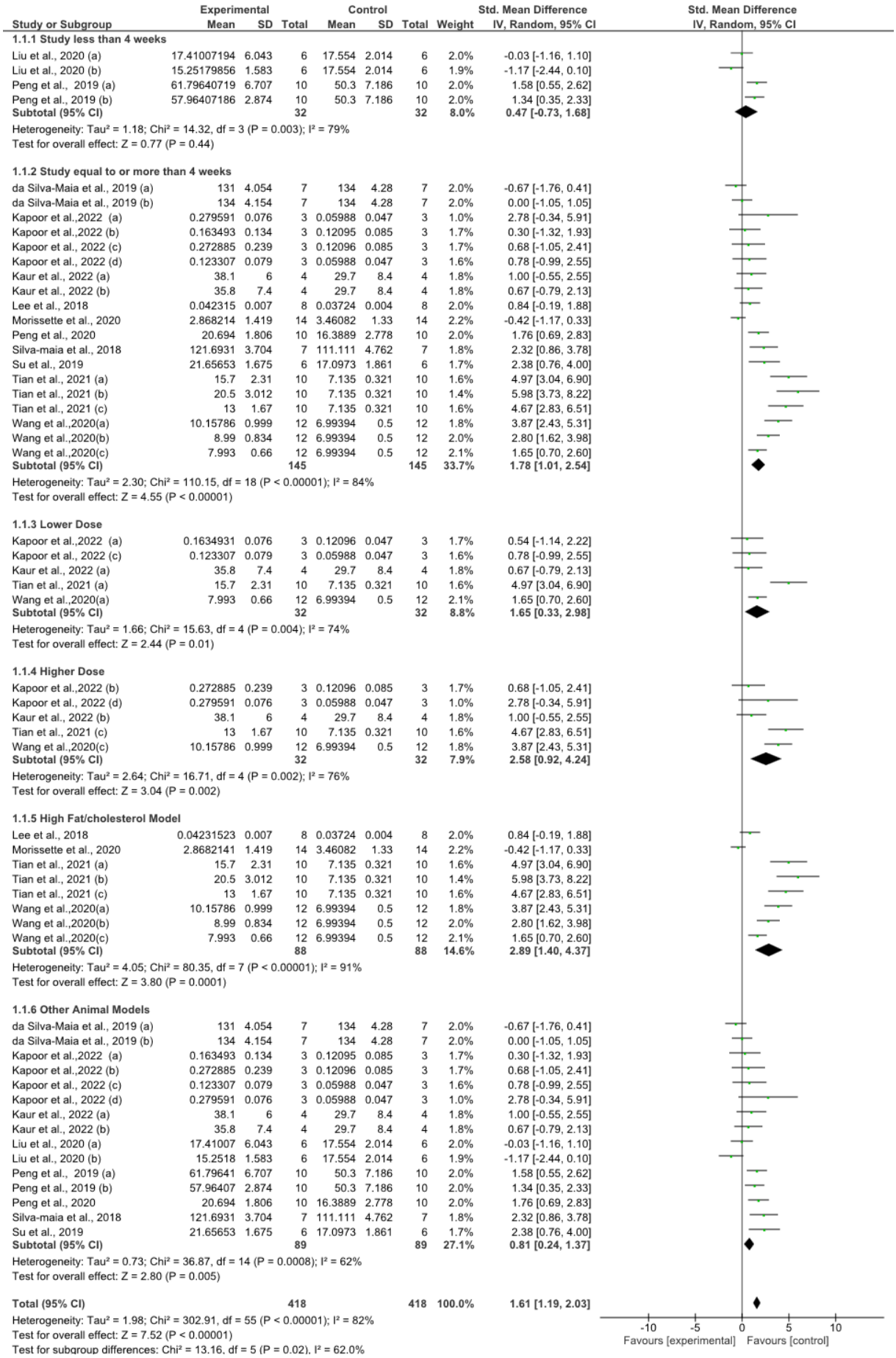
S Figure 4: Fir/Bac data quality assessment using GRADE tool.



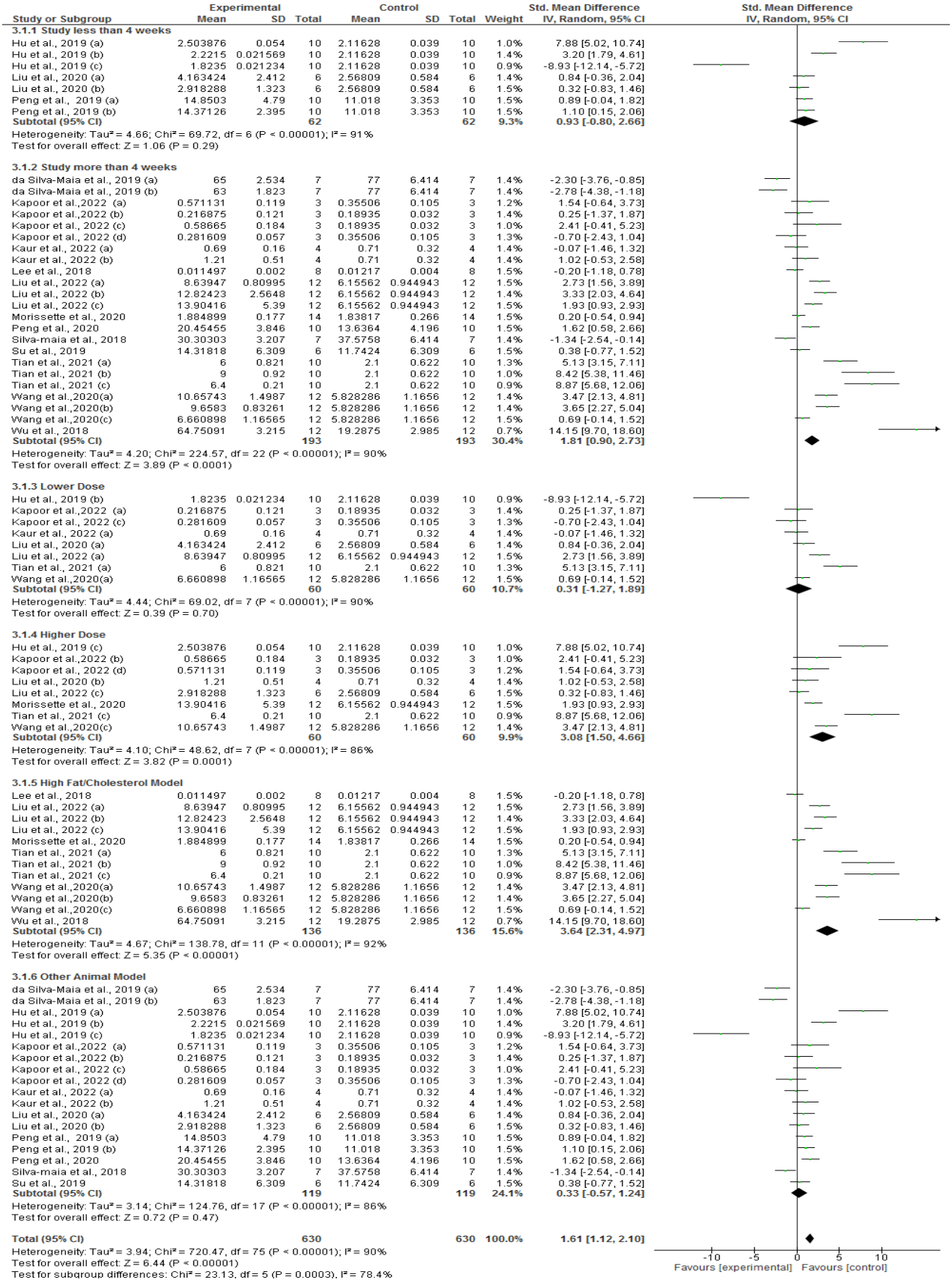
S Figure 5: Forest plot of studies investigating the sub-grouped based effect of anthocyanin supplementation on the SCFA profile. Sub-grouping was on the basis of proportion of acetic acid, butanoic acid and propionic acid. Pooled effect estimates are shown by diamonds. Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



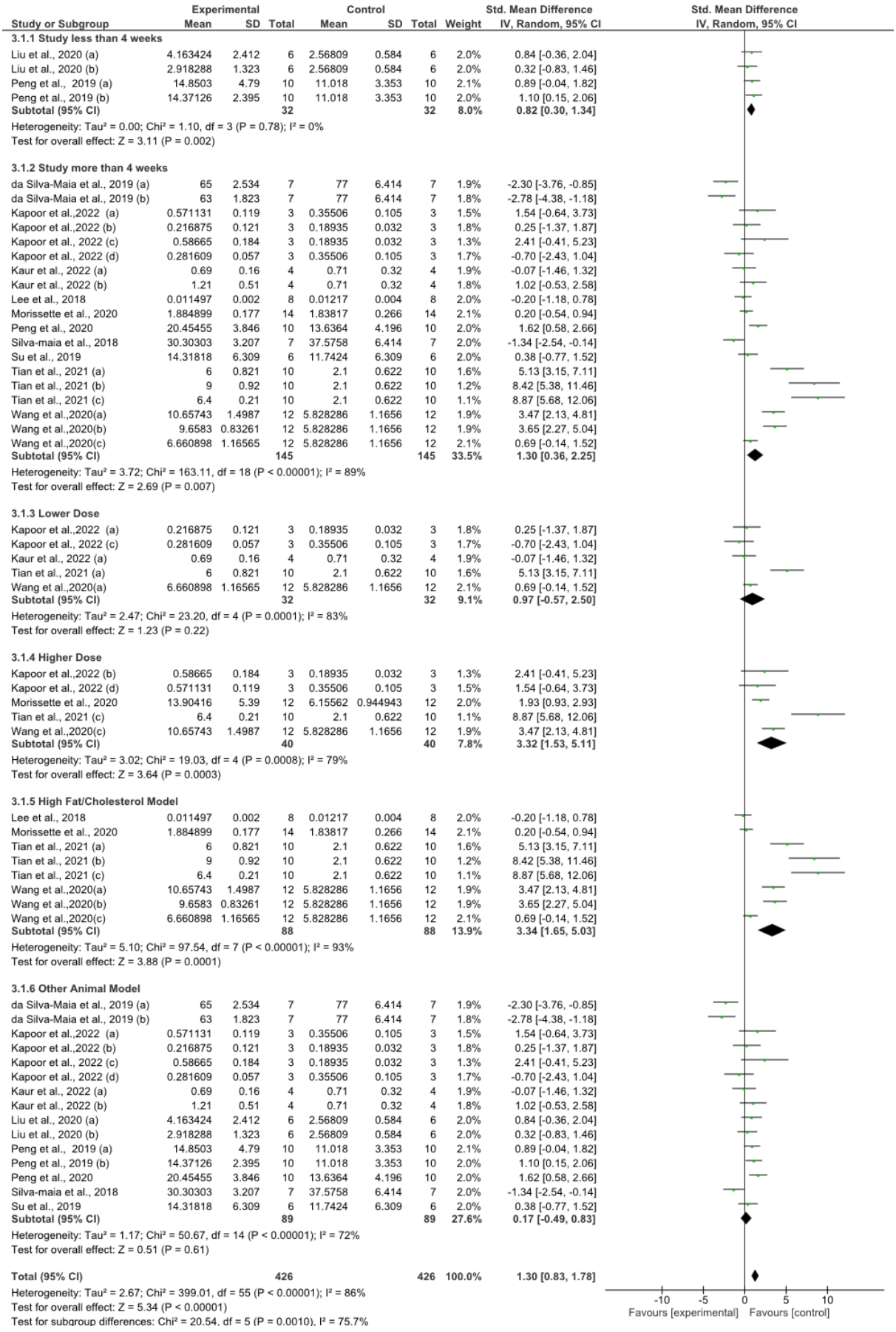
S Figure 6: Forest plot of the sub-group analysis to study effect of anthocyanin supplementation on the acetic acid, SCFA. Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



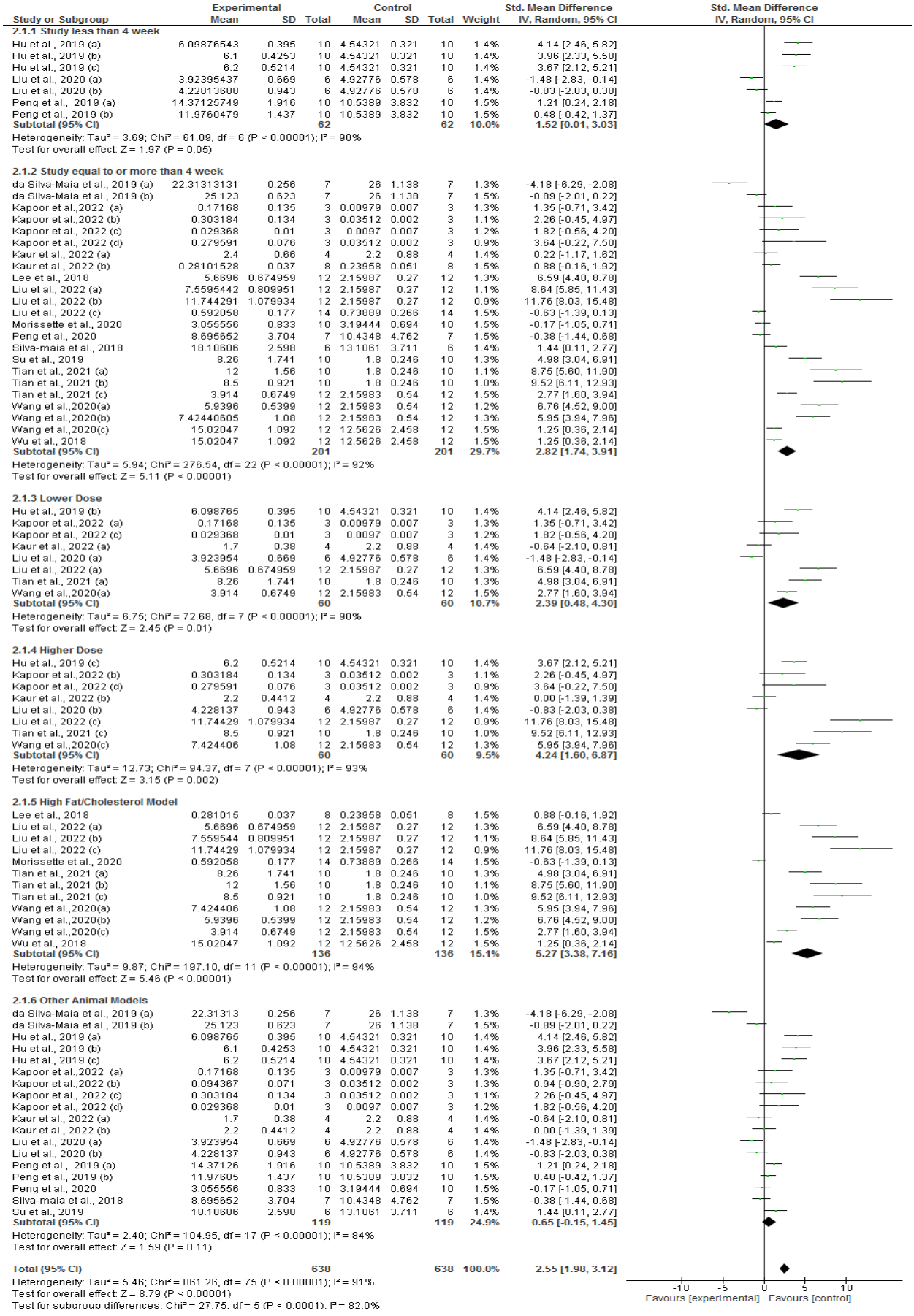
S Figure 7: Forest plot of the sub-group analysis after elimination of high-influencer studies, for understanding the effect of anthocyanin supplementation on the acetic acid, SCFA type. Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



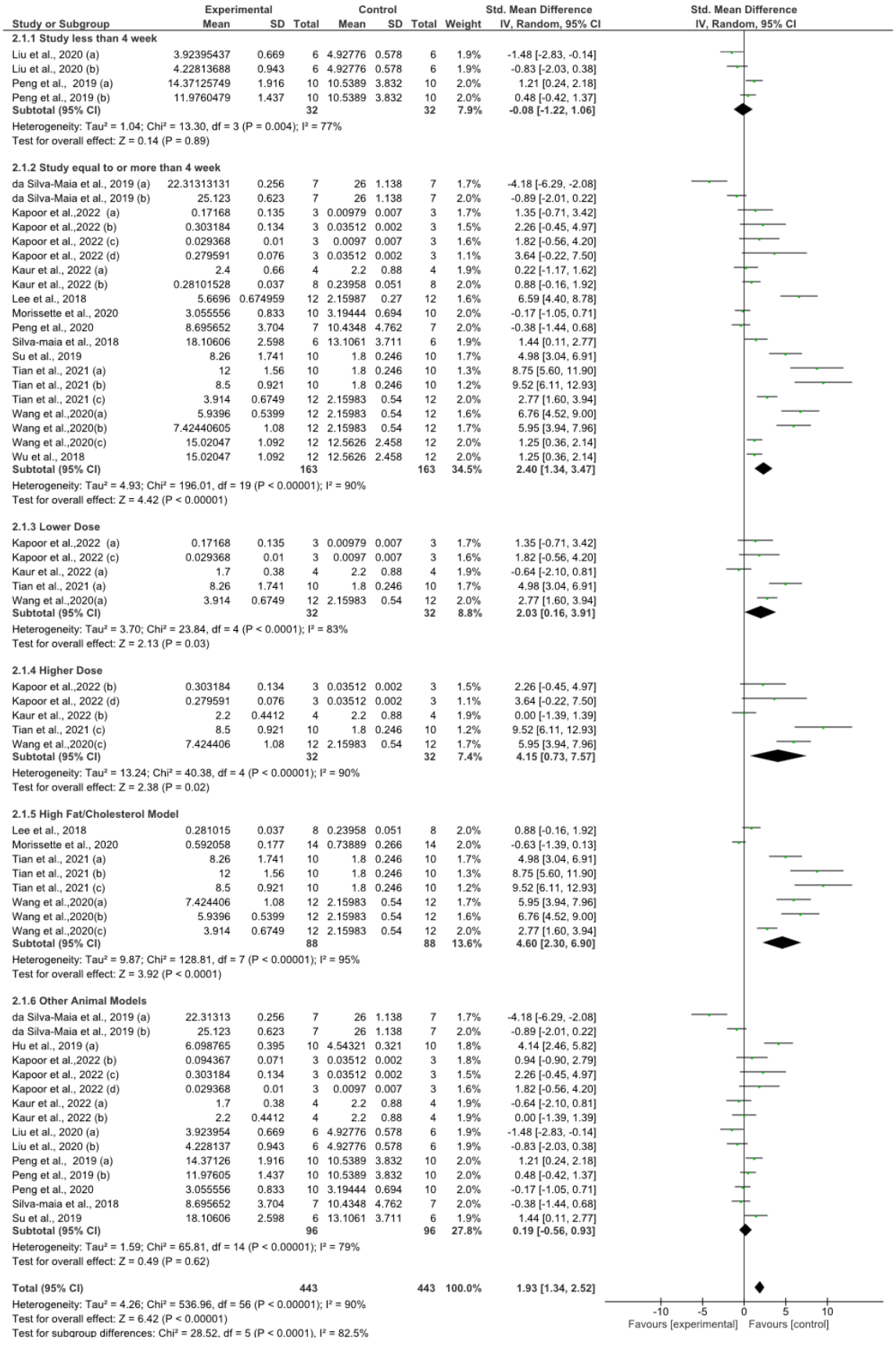
S Figure 8: Forest plot of the sub-group analysis to study effect of anthocyanin supplementation on the butanoic acid, SCFA type. Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



S Figure 9: Forest plot of the sub-group analysis after elimination of high-influencer studies, for understanding the effect of anthocyanin supplementation on the butanoic acid, SCFA type. Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



S Figure 10: Forest plot of the sub-group analysis to study effect of anthocyanin supplementation on the propionic acid, SCFA type. Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).



S Figure 11: Forest plot of the sub-group analysis after elimination of high-influencer studies, for understanding the effect of anthocyanin supplementation on the propionic acid, SCFA type. Sub-grouping was on the basis of duration of the study, dose of the anthocyanin given and disease status of the subjects (animal models). Values are standardized mean differences with 95% CIs determined with the use of random-effects models. Heterogeneity was quantified by I^2, inverse variance and standardised mean difference (SMD).

Question: Should Anthocyanin Rich vs Normal Diet be used for SCFA (Acetic Acid)?

Bibliography: . [Intervention] for. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							Summary of Findings			
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects
							With Normal Diet	With Anthocyanin Rich		Risk with Normal Diet / Risk difference with Anthocyanin Rich (95% CI)
Acetic Acid (Better indicated by lower values)										
1060 (23 studies)	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊕ **HIGH**[1] due to inconsistency, large effect	530	530	-	The mean acetic acid in the intervention groups was **1.52 standard deviations higher** (0.86 to 2.17 higher)

[1] High heterogeneity

Question: Should Anthocyanin Rich vs Normal Diet be used for SCFA (Propoinic Acid)?

Bibliography: . [Intervention] for. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							Summary of Findings			
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects
							With Normal Diet	With Anthocyanin Rich		Risk with Normal Diet / Risk difference with Anthocyanin Rich (95% CI)
Propoinic Acid (Better indicated by lower values)										
1048 (25 studies)	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊕ **HIGH**[1] due to inconsistency, large effect	524	524	-	The mean propoinic acid in the intervention groups was **1.44 standard deviations higher** (0.56 to 2.23 higher)

[1] High heterogeneity

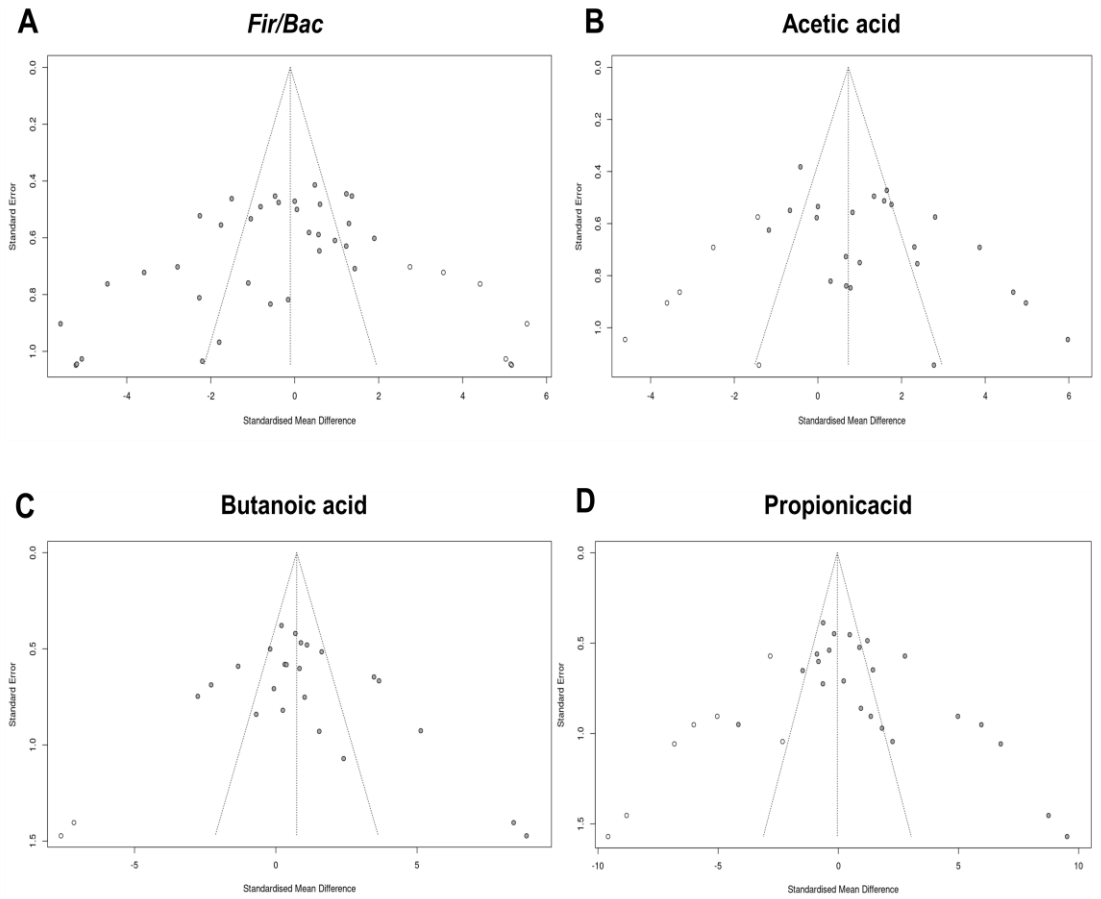
Question: Should Anthocyanin Rich vs Normal Diet be used for SCFA (Butanoic Acid)?

Bibliography: . [Intervention] for. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Quality assessment							Summary of Findings			
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects
							With Normal Diet	With Anthocyanin Rich		Risk with Normal Diet / Risk difference with Anthocyanin Rich (95% CI)
Butanoic Acid (Better indicated by lower values)										
1048 (23 studies)	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊕ **HIGH**[1] due to inconsistency, large effect	524	524	-	The mean butanoic acid in the intervention groups was **1.15 standard deviations higher** (0.41 to 1.9 higher)

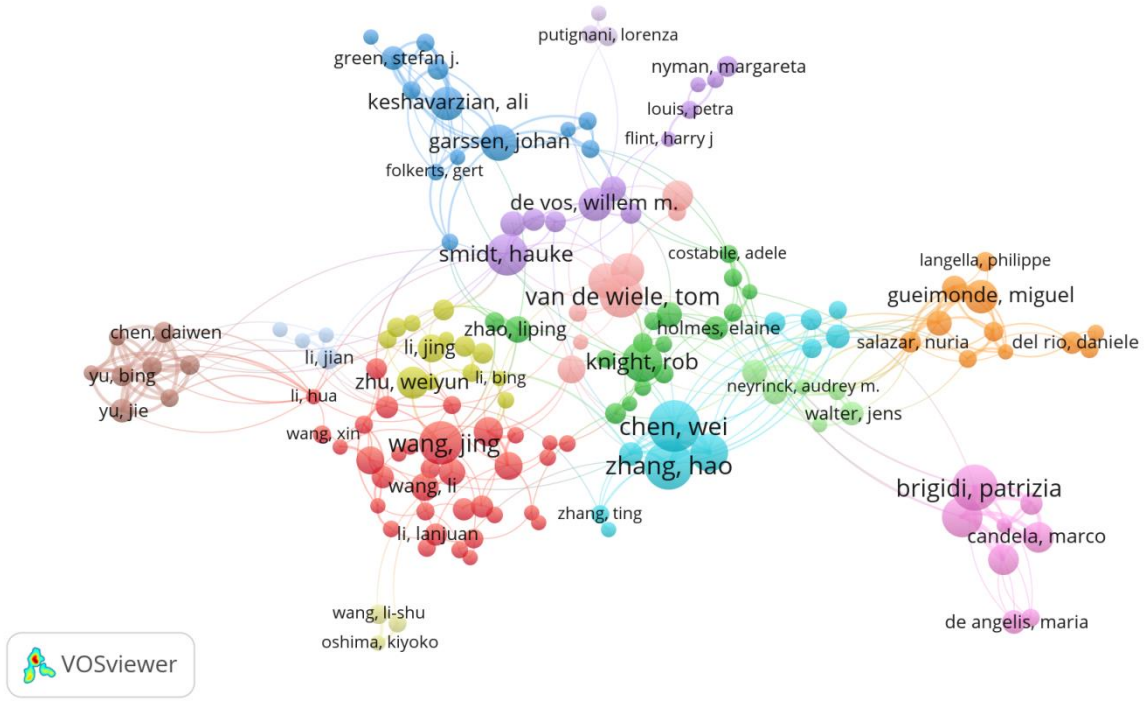
[1] High heterogeneity

S Figure 12: SCFA data quality assessment using GRADE tool.

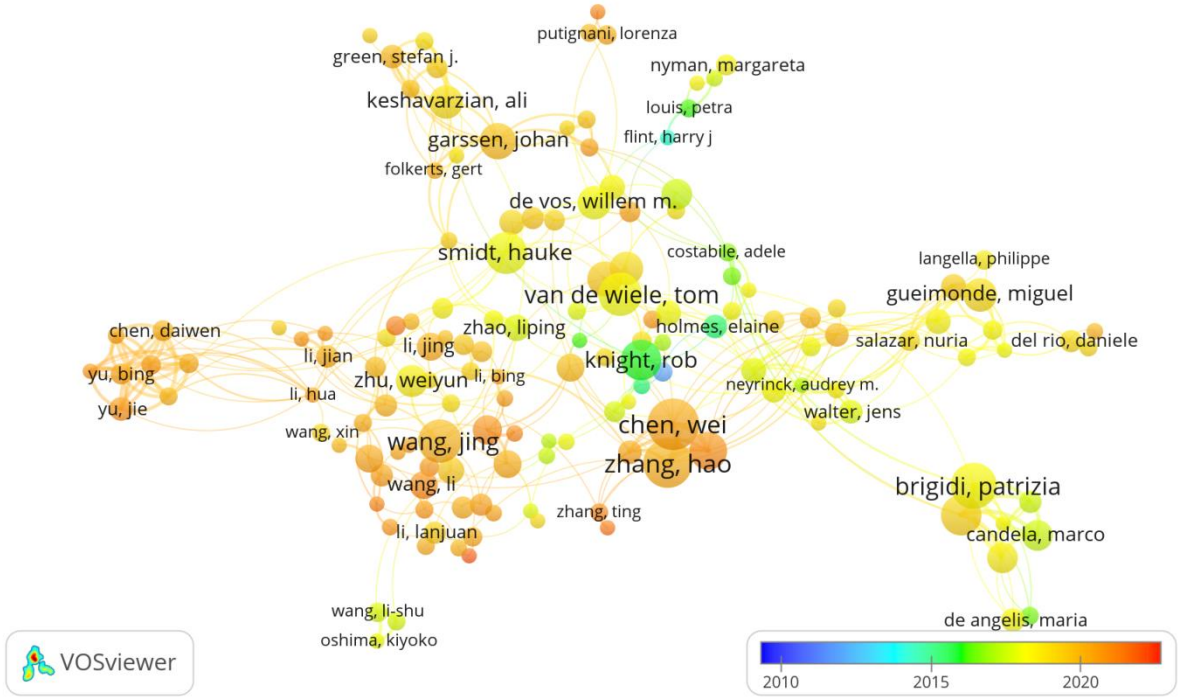


S Figure 13: **Funnel plots for publication bias assessment(A)** For *Fir/Bac*using data from 41 studies. **(B)**For Acetic acid using data from 29 studies. **(C)** For Butanoic acid using data from 25 studies. **(D)**For Propionic acid using data from 30 studies.
The plot was created by putting the standard error on the y-axis and SMD on the x-axis

A

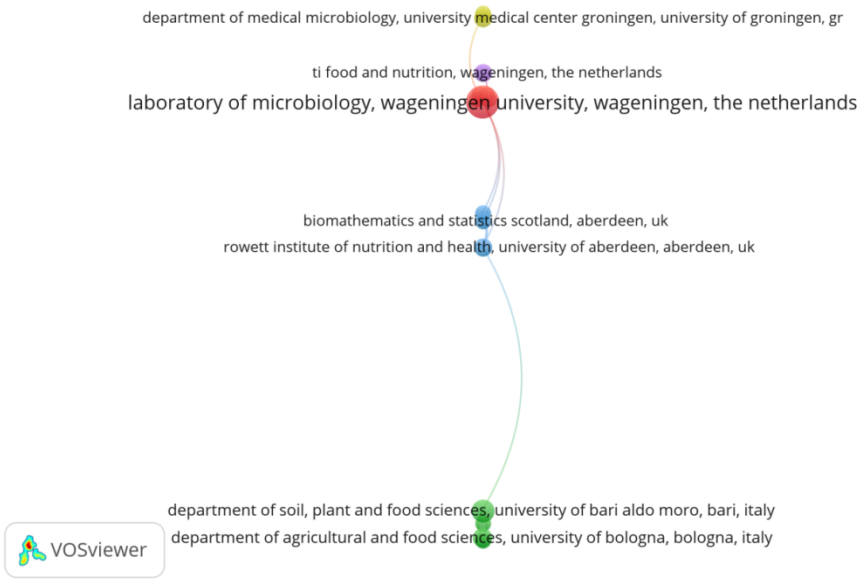


B

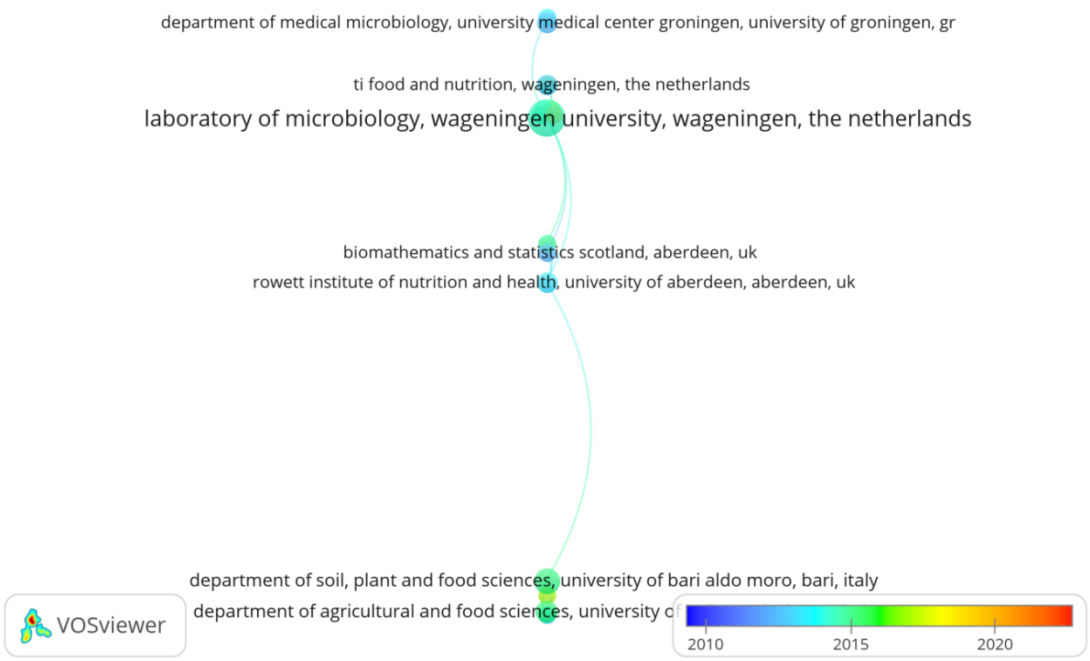


S Figure 14: Bibliographic coupling of leading researchers in anthocyanin, gut microbiota and SCFA research (A) Network visualization **(B)** Overlay visualization (year wise)

A

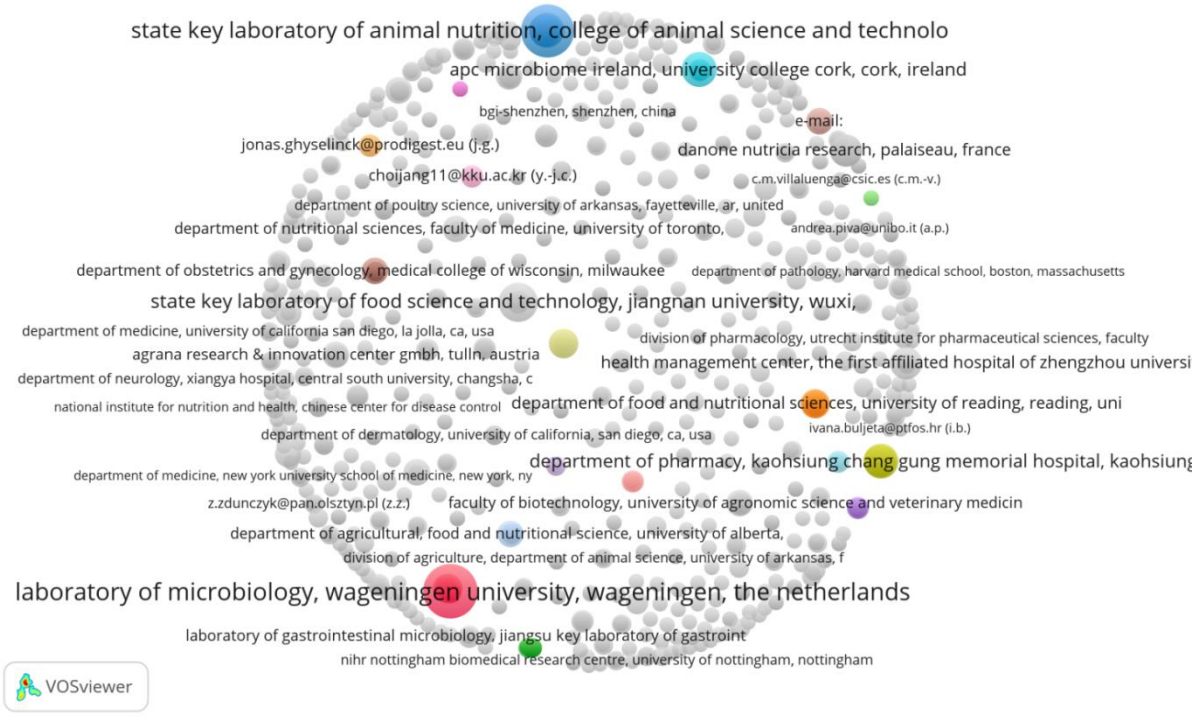


B

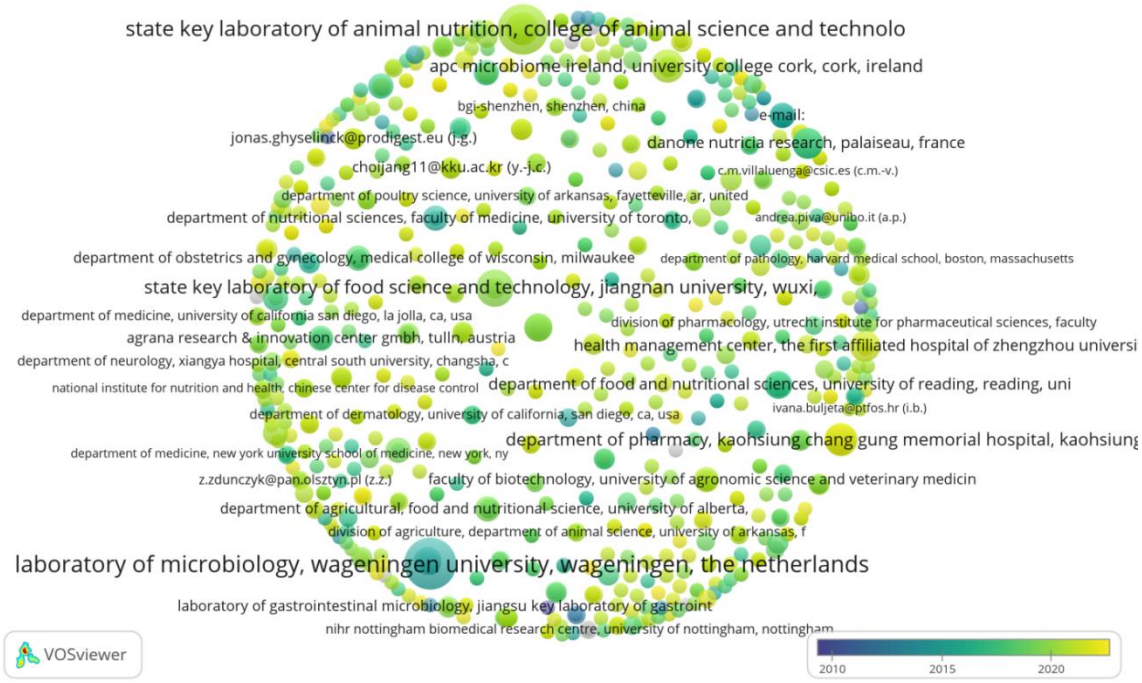


S Figure 15: Institutional collaborations for anthocyanin, gut microbiota and SCFA research (A) Network visualization (B) Overlay visualization (year wise)

A



B



S Figure 16: Independent institutional collaborations for anthocyanin, gut microbiota and SCFA research (A) Network visualization **(B)** Overlay visualization (year wise)