Electronic supplementary material (ESM)

Risk phenotypes of diabetes and association with COVID-19 severity and death – a living systematic review and meta-analysis

Sabrina Schlesinger[1,2], Manuela Neuenschwander[1,2], Alexander Lang[1], Kalliopi Pafili[2,3], Oliver Kuss[1,2,4], Christian Herder[2,3,5], Michael Roden[2,3,5]

[1] Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany;

[2] German Center for Diabetes Research (DZD), Partner Düsseldorf, Germany;

[3] Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany;

[4] Centre for Health and Society, Faculty of Medicine, Heinrich-Heine-University, Düsseldorf, Germany;

[5] Department of Endocrinology and Diabetology, Medical Faculty and University Hospital, Heinrich-Heine University , Düsseldorf, Germany.

Correspondence:

Sabrina Schlesinger PhD, Institute for Biometrics and Epidemiology, German Diabetes Center, Auf'm Hennekamp 65, 40225 Düsseldorf, Germany. Tel. +49 211 3382231. Email: sabrina.schlesinger@ddz.de

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ESM Methods 1: Details on risk of bias assessment

Each domain was rated as low, moderate or high risk of bias, or no information. Determining the overall risk of bias of each study, we put special emphasis on the domains comprising study confounding, statistical analysis/reporting and study participation. Studies were judged as high risk of bias if one of these domains was judged as high risk of bias. Studies were judged as low risk of bias, if all domains were judged as low risk of bias, or if confounding and statistical analysis/reporting were low risk of bias, and none of the other domains were judged as high risk of bias. In other cases, studies were rated as moderate risk of bias.

ESM Table 1: Search strategy for e.g. PubMed

#1	diabetes mellitus[MeSH Terms]) OR diabetes OR diabetic*
#2	covid19 OR covid-19 OR covid OR corona OR new-corona OR novel-corona OR coronavir* OR SARS-CoV-2 OR nCoV OR 2019-nCoV
#3	Combine: #1 AND #2

ESM Table 2: Extracted data

Information of included publications	• The first author's last name • Date of publication • Study design • Geographic area • Number of participants • Number of cases
Patients' characteristics	• Age • Sex • BMI • Smoking status • Ethnicity
Diabetes-specific characteristics	• Type of diabetes • Duration of diabetes • Glycaemic control • Diabetes treatment
Metabolic parameters	• Blood pressure/ hypertension • Inflammatory biomarkers • Liver enzymes • Specific laboratory markers
Diabetes-related complications	• Macrovascular diseases (CVD: coronary heart diseases and stroke etc.) • Microvascular diseases (nephropathy, neuropathy, retinopathy)
Comorbidities	• Respiratory diseases • Cancer • Immunosuppressive conditions
Outcome	• Definition of outcome • Outcome assessment
Findings	• Crude risk estimates and 95% CIs • If available multivariable-adjusted risk estimates with 95% CIs • Confounders

ESM Table 3: Signaling questions for risk of bias assessment using QUIPS

Risk of Bias assessment using the Cochrane QUIPS tool	
Signalling question	**Authors‘ judgement**
Study participation: yes/partial yes/no/partial no/unclear	**The study sample adequately represents the population of interest**
a) Adequate participation in the study by eligible people	Patients with confirmed COVID-19 (PCR or clinically) and diagnosed diabetes mellitus according to the ADA or other internationally recognized standards. High risk of bias, if high proportion of participants without confirmed COVID diagnosis were included
b) Description of the source population or population of interest	Source population or population of interest is clearly described (e.g. region, setting e.g. hospital)
c) Description of the baseline study sample	Baseline study sample is clearly described (characteristics table)
d) Adequate description of the sampling frame and recruitment	Recruitment, selection criteria and key characteristics of the source population clearly described, e.g. low risk of bias for sampling in hospitals using medical files
e) Adequate description of the period and place of recruitment	Time period and place of recruitment are clearly described, e.g. name of hospital and date. Answer partial yes, if date is not specified, because we know the approximate time (beginning 2020).
f) Adequate description of inclusion and exclusion criteria	Inclusion and exclusion criteria are clearly described and presented. Answer unclear, if no exclusion criteria are defined
Study participation: risk of bias rating (high/low/unclear)	**High**: most items are answered with ’no’ or if signalling question a is answered with ‘no’; **Low**: all items answered with ’yes’; **Unclear**: most items are answered with ’unclear’ Note: potentially a single item may introduce a high risk of bias, depending on study specifics
Study attrition: Yes/partial yes/no/partial no/unclear	**The study data available (i.e., participants not lost to follow-up) adequately represent the study sample**
a) Adequate response rate for study participants	Response rate during follow-up sufficient. For most of the studies not applicable because patients were in hospital and followed-up for this time period.
b) Attempts to collect information on participants who dropped out described	Attempts to collect information on participants who dropped out are described (e.g. via registers). Can be ignored, if loss to follow-up is low.

c) Reasons for loss to follow-up provided	Information about the reason participants were lost to follow-up are set up (e.g. participants refused). Can be ignored, if loss to follow-up is low.
d) Adequate description of participants lost to follow-up	Key characteristics of participants lost to follow-up are described (Age, sex, comorbidities). Can be ignored, if loss to follow-up is low.
e) No important differences between participants who completed the study and those who did not	No important differences in baseline characteristics between responders and non-responders. Can be ignored, if loss to follow-up is low.
Study attrition: risk of bias rating (high/low/unclear)	**High**: most items are answered with 'no'; **Low**: all items answered with 'yes'; **Unclear**: most items are answered with 'unclear' Note: potentially a single item may introduce a high risk of bias, depending on study specifics
Prognostic factor measurements: yes/partial yes/no/partial no/unclear	**The PF is measured in a similar way for all participants**
a) Clear definition or description provided	Clear definition of the investigated phenotypes: patients' characteristics (age, sex, BMI, smoking status, ethnicity), metabolic parameters (e.g. glycaemic control, blood pressure, blood lipids, inflammatory biomarkers, liver enzymes), diabetes-related complications (macro- and microvascular diseases), comorbidities (respiratory diseases, cancer, immunosuppressive conditions)
b) Adequately valid and reliable method of measurement	Valid and reliable methods of assessment of the phenotypes listed above. The following methods were considered as reliable and valid: assessed at hospital admission/data collection from medical files, contact of the patient's general/specialist practitioners, regular pharmacist or biomedical laboratory
c) Continuous variables reported or appropriate cut points used	Appropriate cut points: BMI: ≥25 kg/m² for overweight and ≥30 kg/m² for obesity HbA1c >53 mmol/mol/ >7%
d) Same method and setting of measurement used in all study participants	Measurements of the phenotypes are the same for all study participants
e) Adequate proportion of the study sample had complete data	Number in final model with complete data

f) Appropriate methods of imputation were used for missing data	Multiple imputations is a valid method. Complete case analysis for exposure and outcome variables are required.
Prognostic factor measurements: risk of bias rating (high/low/unclear)	**High**: most items are answered with 'no'; **Low**: all items answered with 'yes'; **Unclear**: most items are answered with 'unclear' Note: potentially a single item may introduce a high risk of bias, depending on study specifics
Outcome measurement: yes/partial yes/no/partial no/unclear	**The outcome of interest is measured in a similar way for all participants**
a) Clear definition of the outcome provided	Clear definition for the outcomes: death and composite endpoint/severity of COVID-19. How was the composite endpoint/severity of COVID-19 defined? Answer yes, if outcome is defined as in-hospital mortality. Answer unclear, if outcome is defined as "all-cause mortality" or mortality/death/lethality without further specification
b) Use of adequately valid and reliable methods of outcome measurement	Valid and reliable methods of assessment of the outcomes. E. g. collection of COVID-19-related clinical data during the hospital stay
c) Use of same method and setting of outcome measurement in all study participants	Measurements of the outcomes are the same for all study participants.
Outcome measurement: risk of bias rating (high/low/unclear)	**High**: most items are answered with 'no'; **Low**: all items answered with 'yes'; **Unclear**: most items are answered with 'unclear' Note: potentially a single item may introduce a high risk of bias, depending on study specifics
Study confounding: yes/partial yes/no/partial no/unclear	**Important potential confounding factors are appropriately accounted for**
a) Measurement of all important confounders	Minimal adjusted models should include: Age, sex, BMI/overweight/obesity, at least one comorbid condition, as most important confounders
b) Provision of clear definitions of the important confounders measured	Measurements of confounders are described and defined
c) Adequately valid and reliable measurements of all important confounders	Measurements of confounding factors are valid and reliable (assessed at hospital admission, medical records, contact of the patient's general/specialist practitioners or regular pharmacist)
d) Use of the same method and setting of confounding measurement in all study participants	The method and setting of confounding measurement are the same for all participants
e) Appropriate imputation methods used for missing confounders (if applicable)	Appropriate methods of imputation for missing covariate data are applied and described.

f) Important potential confounders were accounted for the study design	Most important potential confounders are accounted for in the study design (e.g., matching for key variables, stratification). Minimal adjusted models should include: Age, sex, BMI/overweight/obesity, at least one comorbid condition, as most important confounders
g) Important confounders were accounted for in the analysis	Most important potential confounders are accounted for in the analysis (i.e., use of multivariable analysis). Minimal adjusted models should include: Age, sex, BMI/overweight/obesity, at least one comorbid condition, as most important confounders
Study confounding measurement: risk of bias rating (high/low/unclear)	**High**: most items are answered with 'no' or if signalling questions f) and g) are answered with 'no'; **Low**: all items answered with 'yes'; **Unclear**: most items are answered with 'unclear' Note: potentially a single item may introduce a high risk of bias, depending on study specifics
Statistical analysis and reporting: yes/partial yes/no/partial no/unclear	**Statistical Analysis and Reporting**
a) Sufficient presentation of data to assess the adequacy of the analytic strategy	There is sufficient presentation of data to assess the adequacy of the analysis (e.g. findings are displayed in a table or in the text). The results are expressed as risk ratios (e.g. hazard ratios, relative risks, odds ratios) with corresponding 95% confidence intervals
b) Strategy for model building is appropriate and based on conceptual framework model	The selection of the confounders are described and appropriate (e.g. selection of existing knowledge). Stepwise regression is not appropriate, with the exception that the known important confounders were selected.
c) Statistical model is adequate for the study design	Multivariable logistic regression or cox proportional hazard model or Weibull analysis are applied. Univariate methods are not appropriate.
d) No selective reporting of results	There is no selective reporting of results (e.g. findings are shown for a specific age group, time period etc.). Answer yes (no selective reporting), if data were missing in the manuscript and authors sent additional information via email, but note in the judgement that data were missing in the article and additional information was received via email.
Statistical analysis and reporting: risk of bias rating (high/low/unclear)	**High**: most items are answered with 'no'; **Low**: all items answered with 'yes'; **Unclear**: most items are answered with 'unclear' Note: potentially a single item may introduce a high risk of bias, depending on study specifics

ESM Table 4: List of excluded studies

Reasons for exclusion	**References**
Not relevant population/ not relevant comparison group, e.g. patients without diabetes and/or without COVID-19	1-52
Not relevant data	53-70
No risk estimates	71-117
Abstract/letter/editorial/comment/protocol	118-169
Review/meta-analysis	170-192
Not in English	193,194
Duplicate cohort	195,196

ESM Table 5: Characteristics of included studies									
Author, year	**Country, setting, time period**	**Study design, Follow-up**	**Sex, mean age, type of diabetes**	**Number of participants and cases**	**Outcome**	**Outcome assessment**	**Relevant exposure**	**Exposure assessment**	**Adjustment factors**
Acharya, 2020[197]	South Korea Hospitals-based Dongguk University Gyeongju Hospital or Andong Medical Center, Gyeongsangbuk-do, 18th February to 30th June 2020	Retrospective study, ND	m/w, 69.8 years, T2D	55 participants, 11 cases	Mortality	Medical records	Age, BMI, SBP, DBP, sex, smoking, alcohol intake, being resident in care facility, hypertension, CVD, cerebrovascular disease, dementia, malignancy, blood glucose, HbA1c, leukocytes, lymphocytes, AST, LDH, creatinine, anaemia (haemoglobin), albumin, CRP	Medical records	Age
Agarwal, 2020[198]	USA Hospitals-based Montefiore Medical Center, 11th March to 7th May 2020	Retrospective study, ND	m/w, 67.9 years, T1D and T2D	1279 participants, 394 cases	In-hospital death	Electronic health records	HbA1c, diabetes treatment (noninsulin, insulin, both), hypertension, CVD, CKD, COPD	Electronic health records	Age, sex, BMI, insurance, HbA1c, insulin treatment, non-insulin treatment, hypertension, COPD, CVD, CKD
Bello-Chavolla, 2020[199]	Mexico National register data Mexican epidemiologic surveillance database, up to May 18th 2020	Retrospective study, 30 days	m/w, 57.2 years, ND	9460 participants, 2062 cases	Death	Open source dataset of the General Directorate of Epidemiology of the Mexican Ministry of Health	Smoking, COPD, asthma, CVD,CKD, hypertension, sex, age, obesity	Open source dataset of the General Directorate of Epidemiology of the Mexican Ministry of Health	Smoking, immunosuppression, COPD, asthma, CVD,CKD, hypertension, sex, age, obesity
Cariou, 2020[200]	France Hospitals-based	Prospective study, 7 days	m/w, 69.8 years, T1D and T2D	1317 participants,	MV and/or death, death	Medical files	Age, sex, type of diabetes, ethnicity, BMI, diabetes duration, HbA1c, hypertension,	Medical files, if needed, general or specialist practitioner,	Univariate and different multivariate models available e.g. age, sex, hypertension, microvascular

	All French hospitals, 10th March to 10th April 2020 CORONADO study			382 MV and/or deaths 140 deaths			dyslipidaemia, smoking, microvascular complications, severe diabetic retinopathy, diabetic kidney disease, history of diabetic foot ulcer, macrovascular complications, ischaemic heart disease, cerebrovascular disease, peripheral artery disease, heart failure, NAFLD or liver cirrhosis, active cancer, COPD, treated OSA, end stage renal failure, metformin, sulfonylurea/ glinides, DPP-4 inhibitors, GLP1-RA, insulin, loop diuretics, thiazide diuretics, potassium-sparing diuretics, MRA, β-blocker, ACE inhibitors, ARBs, ARBs and/or ACE inhibitors, statins, admission plasma glucose, plasma creatinine, eGFR, ALT, AST, GGT, haemoglobin, white cell count, lymphocyte count, platelet count, d-dimers, CRP, LDH, CPK, fibrinogen	regular pharmacist or biomedical laboratory	diseases, macrovascular disease, heart failure, cancer, treated OSA, β-blocker, metformin, insulin, loop diuretics, ARBs and/or ACE inhibitors and/or MRAs
Chen, 2020[201]	China Hospitals-based Central Hospital of Wuhan,	Retrospective study, ND	m/w, 66.0 years, ND	136 participants, 26 in-hospital death,	In-hospital death, poor prognosis	Electronic medical records, CT, evaluation by experienced clinicians	Age, sex, hypertension, CVD, CKD, nervous system disease, white blood cells, neutrophils, lymphocytes, albumin, ALT, AST, LDH, urea,	Electronic medical records	Analyses for sex, hypertension, CVD, CKD, nervous system disease, white blood cells, neutrophils, lymphocytes, ALT, AST, LDH, urea,

	1st January to 17th March 2020			93 poor prognosis defined as progression to severe or critical illness, and in-hospital death			creatinine, creatine kinase, blood glucose at admission, CRP, d-dimer, metformin, insulin, α-glucosidase inhibitors, secretagogues, DPP4 inhibitor		creatine kinase and d-dimer unadjusted Analyses for age, albumin, creatinine, glucose, CRP, metformin, insulin, α-glucosidase inhibitors, secretagogues and DPP4 inhibitors adjusted for age, albumin, creatinine, glucose, CRP, and usage of a specific medication (yes/no)
Chung, 2020[202]	Korea Hospitals-based Yeungnam University Medical Center in Daegu, time period not specified	Retrospective study, 28 days	m/w, 66.3 years, ND	29 participants, 13 severe and critical outcome, 8 acute cardiac injuries, 5 acute kidney injuries	Severe and critical outcome, acute cardiac injury, acute kidney injury	Electronic medical records	Age, HbA1c, serum glucose, metformin, RAS inhibitors	Electronic medical records	Age, sex, smoking, HbA1c, serum glucose levels
Crouse, 2020[203]	USA Hospitals-based University of Alabama at Birmingham Hospital, 25th February to 22nd June 2020	Retrospective study, ND	m/w, ND, T1D and T2D	239 participants, 45 deaths	Death	Electronic medical records	Age, ethnicity, sex, obesity, hypertension, diabetes type, insulin, metformin	Electronic medical records	Age, sex, hypertension, BMI, metformin, insulin, ethnicity (mutual adjustment for the covariates)
Dalan, 2020[204]	Singapore Hospitals-based National Centre of Infectious diseases, up to 15th April 2020	Retrospective study, ND	m/w, ND, T2D	76 participants, na	Supple-mentary oxygen, ICU admis-sion, MV	Medical records	DPP4 inhibitors, SGLT2 inhibitors, sulfonylureas	Medical records	Age, sex, BMI, statin, ethnicity, HbA1c, antihypertensive medication, diabetes medication, SBP, DBP

de Abajo, 2020[205]	Spain Hospitals-based Seven hospitals in Madrid, 1st March to 24th March 2020	Case-population study, ND	m/w, 69.1 years (for the entire population, na for participants with diabetes), ND	1440 participants, 182 hospital admissions	Admission to hospital	Electronic primary health-care records	RAAS inhibitors	Hospital medical records	Age, sex, hypertension, COPD, asthma, dyslipidaemia, cerebrovascular disease, cancer, ischaemic heart disease, heart failure, atrial fibrillation, thromboembolic disease, chronic renal failure
Li, 2020[206]	China Hospitals-based Wuhan Union hospital of Tongji Medical College and Jinyintan Hospital, 31st December 2019 to 5th April 2020	Retrospective study, ND	m/w, 65.0 years, T1D and T2D	132 participants, 15 in-hospital deaths, 31 in-hospital complications	In-hospital death, in-hospital complications	Electronic medical records	Age, sex, diabetes duration, comorbidities, hypertension, CVD, malignancy, cerebrovascular disease, chronic pulmonary disease, CKD, chronic liver disease, white blood cells, lymphocytes, platelet count, haemoglobin, d-dimer, prothrombin time, activated partial thromboplastin time, fibrinogen, glucose, albumin, ALT, AST, serum creatinine, total bilirubin, creatine kinase, LDH, myoglobin, high-sensitivity troponin I, serum ferritin, interleukin-6, procalcitonin, total CT score of the pulmonary involvement	Electronic medical records	Analyses for d-dimer and glucose and in-hospital death, as well as glucose and in-hospital complications adjusted for age, hypertension, total CT score of the pulmonary involvement, lymphocyte count, fasting plasma glucose, d-dimer, ALT, LDH creatinine, CRP Other analyses unadjusted

Liu, 202[207]0	China Hospitals-based Guanggu branch of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 3rd to 26th February 2020	Retrospective study, ND	m/w, 66.0 years, ND	64 participants, 12 MV and/or deaths	MV and/or death	Electronic medical records	HbA1c, in-hospital blood glucose, lymphocytes, CRP, prothrombin time, metformin, insulin, α-glucosidase inhibitors, ARBs/ACE inhibitors, calcium channel blockers, statins	Electronic medical records	Plasma glucose at admission
Luo, 2020[208]	China Hospitals-based Tongji Hospital of Wuhan, 27th January to 24th March 2020	Retrospective study, ND	m/w, 64.3 year, ND	283 participants, 25 in-hospital deaths	In-hospital death	Electronic medical records	Metformin, statins	Electronic medical records	Na
Merzon, 2020[209]	Israel Health insurance data Leumit Health Services, 1st February to 30th April 2020	Retrospective study, ND	m/w, 61.8 years, ND	183 participants, 46 hospitalizations	Hospitalization	LHS electronic medical records	HbA1c, age, sex, SES, smoking, depression/anxiety, schizophrenia, dementia, hypertension, ischaemic heart disease, cerebrovascular accident, congestive heart failure, chronic lung disease, obesity	LHS electronic medical records	Age, sex, SES, depression/anxiety, schizophrenia, dementia, hypertension, ischaemic heart disease, cerebrovascular accident, congestive heart failure, chronic lung disease, obesity
Rastad, 2020[210]	Iran Hospitals-based Hospitalized inpatients in Alborz province,	Retrospective study, ND	m/w, 54.8 years (for the entire population, ND for participants with	267 participants, ND	In-hospital death	Electronic medical records	Age, sex, comorbidities, white blood cells, lymphocytes, neutrophils, AST, ALT, albumin, creatinine, LDH, CRP, erythrocyte	Electronic medical records	Age, sex, laboratory tests

	20th February to 25th March 2020		diabetes), ND				sedimentation rate, haemoglobin		
Rhee, 2020[211]	Korea Health insurance data Korean population, up to 17th May 2020	Retrospective study, ND	m/w, 61.8 years, ND	832 participants, 34 Intensive care or deaths	Intensive care or death	HIRA database	DPP-4 inhibitor, RAS blockade, RAS blockade and DPP-4 inhibitor	HIRA database	Age, sex, hypertension, dyslipidemia, CVD, cerebrovascular disease, CKD, asthma, COPD, cancer, metformin, sulfonylurea, meglitinide, TZD, DPP-4 inhibitor, SGLT2 inhibitor, AGI, insulin, ACEi, ARB, beta blocker, diuretics, CCB, statin, fibrate
Seiglie, 2020[212]	USA Hospitals-based Massachusetts General Hospital, 11th March to 30th April 2020	Prospective study, 14 days	m/w, 66.7 years, ND	168 participants, 75 ICU admissions, 66 MV, 28 deaths	ICU admission, MV, death	Manual chart review	HbA1c, BMI, age, sex, race/ethnicity	Manual chart review and Enterprise Data Warehouse (EDW)	Age, sex, ethnicity, coronary artery disease or myocardial infarction, chronic heart failure, hypertension, COPD/asthma, cancer, liver disease, renal disease
Shah, 2020[213]	USA Hospitals-based Three Phoebe Putney hospitals, 2nd March to 22nd May 2020	Retrospective study, ND	m/w, 60.1 years (for the entire population, na for participants with diabetes), ND	228 participants, ND	In-hospital death, new dialysis requirement, MV, ICU care, composite endpoint	Electronic medical records	ACE-inhibitor/AT1 blocker	Electronic medical records	Age, BMI, sex, hypertension, coronary artery disease, congestive heart failure, COPD, asthma, CKD, cancer, immunosuppression, chronic liver disease, drug abuse, alcohol abuse, smoking, ESRD on dialysis and presentation severity

Shang, 2020[214]	China Hospitals-based Wuhan No.7 Hospital, 25th December 2019 to 20th March 2020	Retrospective study, ND	m/w, 59.0 years (for the entire population, na for participants with diabetes), ND	84 participants, 17 deaths	Death	Electronic medical records	Insulin	Electronic medical records	Unadjusted
Shi, 2020[215]	China Hospitals-based Renmin Hospital of Wuhan University and Zhongnan Hospital of Wuhan University, 1st January to 8th March 2020	Retrospective study, ND	m/w, 64.0 years, ND	153 participants, 31 in-hospital deaths	In-hospital death	Electronic medical records	Age, sex, hypertension, CVD, COPD, blood glucose, white blood cells, neutrophils, lymphocytes, platelet count, CRP, prothrombin time, creatinine, eGFR, total cholesterol, triglyceride, PaO_2, SpO_2, glucose at admission, lactate, procalcitonin, $CD3^+$ cell count, $CD4^+$ cell count, $CD8^+$ cell count, $CD19^+$ cell count, $CD16^+56^+$ cell count	Electronic medical records	Mutual adjustment for covariates in the analyses for age, sex, hypertension, CVD and COPD Other analyses unadjusted
Solerte, 2020[216]	Italy Hospitals-based Seven academic medical centers in Northern Italy, 1st March to 30th April 2020	Retrospective case-control study, 30 days	m/w, 69.0 years, T2D	338 participants 94 in-hospital deaths, 40 intensive cares, 23 MVs	In-hospital death, Intensive care, MV	Electronic medical records	Sitagliptin, sex, age, cancer, CVD, CKD, antiviral agents, hydroxychloroquine	Electronic medical records	Age, sex, cancer, CVD, CKD, sitagliptin, hydroxychloroquine, antiviral agents
Xu, 2020[217]	China Hospitals-based Renmin Hospital of Wuhan University, 30th January to April 26th 2020	Case series study, ND	m/w, 66.0 years, T2D	114 participants, 27 deaths	Death	Electronic medical records	Glucocorticoid treatment, fasting blood glucose	Electronic medical records	Age, sex, cerebral diseases cardiovascular diseases, chronic renal diseases, digestive diseases pulmonary diseases, NEWS2

Zhu, 2020[218]	China Hospitals-based 19 hospitals in Hubei Province, 30th December 2019 to 20th March 2020	Retrospective study, 28 days	m/w, 62.7 years, T2D	810 participants, 61 deaths, 133 acute respiratory distress,	Death, acute respiratory distress	Electronic medical records	Blood glucose control	Electronic medical records	Age, sex, hospital sites, indicators of the severity of COVID-19, hypertension, CHD, cerebrovascular diseases, chronic liver diseases, and chronic renal diseases

ND: no data

ACE: angiotensin converting enzyme, ALT: alanine aminotransferase, ARB: angiotensin II receptor blocker, AST: aspartate aminotransferase, AT1: angiotensin II receptor type 1, BMI: body mass index, CCB: calcium channel blocker, CHD: coronary heart disease, CKD: chronic kidney disease, COPD: chronic obstructive pulmonary disease, CORONADO: Coronavirus SARS-CoV-2 and Diabetes Outcomes, CPK: creatine phosphokinase, CRP: C-reactive protein, CT: computed tomography, CVD: cardiovascular disease, DBP: diastolic blood pressure, DPP-4: dipeptidyl peptidase 4, eGFR: estimated glomerular filtration rate, ESDR: end-stage renal disease GGT: γ-glutamyl transferase, GLP-1 RA: glucagon-like peptide 1-receptor agonist, HIRA: Health Insurance Review & Assessment Service ICU: intensive care unit, LDH: lactate dehydrogenase, LHS: Leumit Health Services, MRA: mineralocorticoid-receptor antagonist, MV: mechanical ventilation, NAFLD: non-alcoholic fatty liver disease, NEWS2: National Early Warning Score 2, OSA: obstructive sleep apnoea, PCR: polymerase chain reaction,RAAS: renin-angiotensin-aldosterone system, RAS: renin-angiotensin system, SBP: systolic blood pressure, SES: socioeconomic status, SGLT-2: sodium-glucose co-transporter-2, T1D: type 1 diabetes, T2D: type 2 diabetes, TZD: thiazolidinediones.

ESM Table 6: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Male sex								
10	observational studies	not serious	not serious	not serious	not serious	none	**RR 1.28** (1.02 to 1.61)	⊕⊕⊕⊕ HIGH
Age >65 years								
6	observational studies	serious [a]	serious [b]	not serious	not serious	strong association	**RR 3.49** (1.82 to 6.69)	⊕⊕⊕◯ MODERATE
Age per 5 years								
5	observational studies	very serious [a]	not serious [c]	not serious	not serious	dose response gradient	**RR 1.43** (1.12 to 1.83)	⊕⊕⊕◯ MODERATE
Overweight								
2	observational studies	very serious [d]	not serious	not serious	serious [e]	none	**RR 0.72** (0.45 to 1.16)	⊕◯◯◯ VERY LOW
Obesity								
4	observational studies	serious [a]	not serious	not serious	very serious [f]	none	**RR 1.06** (0.76 to 1.49)	⊕◯◯◯ VERY LOW
Smoking (smoker vs not smoker)								
3	observational studies	not serious	not serious	not serious	serious [e]	none	**RR 0.91** (0.79 to 1.06)	⊕⊕⊕◯ MODERATE
Type 2 vs type 1 diabetes								
2	observational studies	extremely serious [g]	not serious	not serious	very serious [f]	none	**RR 1.65** (0.64 to 4.26)	⊕◯◯◯ VERY LOW

ESM Table 6: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Diabetes duration, per 5 years								
2	observational studies	extremely serious [g]	not serious	not serious	not serious	none	**RR 1.06** (0.94 to 1.20)	⊕◯◯◯ VERY LOW
HbA1c, 53-75 vs <53 mmol/mol (7-9 vs <7%)								
2	observational studies	very serious [d]	not serious	not serious	very serious [f]	none	**RR 1.08** (0.57 to 2.06)	⊕◯◯◯ VERY LOW
HbA1c, >75 vs <53 mmol/mol (>9 vs <7%)								
2	observational studies	very serious [d]	serious [h]	not serious	very serious [f]	none	**RR 0.95** (0.50 to 1.79)	⊕◯◯◯ VERY LOW
HbA1c per 20 mmol/mol increase								
4	observational studies	not serious	serious	not serious	serious [e]	none	**RR 1.04** (0.80 to 1.35)	⊕⊕◯◯ LOW
Blood glucose at admission 6-11 mmol/l compared to <6 mmol/l								
2	observational studies	very serious [d]	not serious	not serious	very serious [f]	strong association dose response gradient	**RR 2.76** (0.56 to 13.51)	⊕⊕◯◯ LOW
Blood glucose at admission >11 mmol/l compared to <6 mmol/l								
2	observational studies	very serious [d]	not serious	not serious	very serious [i]	very strong association dose response gradient	**RR 8.60** (2.25 to 32.83)	⊕⊕⊕◯ MODERATE
Blood glucose at admission, per 1 mmol/l								
2	observational studies	extremely serious [g]	not serious	not serious	not serious	dose response gradient	**RR 1.10** (1.05 to 1.16)	⊕⊕◯◯ LOW

ESM Table 6: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Poorly controlled								
1	observational studies	not serious	na	not serious	very serious [i]	very strong association	**RR 7.69** (2.32 to 25.52)	⊕⊕⊕◯ MODERATE
Use of insulin								
5	observational studies	not serious	not serious	not serious	not serious	none	**RR 1.75** (1.01 to 3.03)	⊕⊕⊕⊕ HIGH
Use of metformin								
4	observational studies	serious [a]	not serious	not serious	not serious	none	**RR 0.50** (0.28 to 0.90)	⊕⊕⊕◯ MODERATE
Use of DPP-4 inhibitors								
2	observational studies	extremely serious [g]	serious	not serious	very serious [f]	none	**RR 0.90** (0.59 to 1.36)	⊕◯◯◯ VERY LOW
Use of sulfonylurea/glinide								
2	observational studies	extremely serious [g]	serious [j]	not serious	serious [e]	none	**RR 0.73** (0.49 to 1.09)	⊕◯◯◯ VERY LOW
Hypertension								
8	observational studies	not serious	serious	not serious	very serious [f]	none	**RR 1.09** (0.77 to 1.53)	⊕◯◯◯ VERY LOW
Total CVD								
8	observational studies	not serious	serious	not serious	not serious	none	**RR 1.56** (1.09 to 2.24)	⊕⊕⊕◯ MODERATE

ESM Table 6: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Cerebrovascular disease								
2	observational studies	extremely serious [g]	not serious	not serious	not serious	strong association	**RR 2.11** (1.36 to 3.26)	⊕⊕◯◯ LOW
CKD								
6	observational studies	serious [a]	not serious	not serious	not serious	none	**RR 1.93** (1.28 to 2.90)	⊕⊕⊕◯ MODERATE
COPD								
5	observational studies	not serious	not serious	not serious	not serious	none	**RR 1.40** (1.21 to 1.62)	⊕⊕⊕⊕ HIGH
Cancer								
3	observational studies	not serious	not serious	not serious	serious [e]	none	**RR 1.54** (0.94 to 2.51)	⊕⊕⊕◯ MODERATE
Any comorbidity								
2	observational studies	extremely serious [g]	not serious	not serious	very serious [f]	none	**RR 0.94** (0.45 to 1.98)	⊕◯◯◯ VERY LOW
Use of renin inhibitors								
2	observational studies	not serious	not serious	not serious	very serious [f]	none	**RR 1.04** (0.64 to 1.68)	⊕⊕◯◯ LOW
Use of statins								
2	observational studies	extremely serious [g]	not serious	not serious	very serious [f]	none	**RR 1.38** (0.71 to 2.66)	⊕◯◯◯ VERY LOW

ESM Table 6: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
CRP, per 10 mg/l								
3	observational studies	very serious [d]	not serious	not serious	serious [e]	none	**RR 1.18** (0.98 to 1.42)	⊕◯◯◯ VERY LOW
ALT, per 5 unit/l								
2	observational studies	extremely serious [g]	not serious	not serious	serious [e]	none	**RR 1.08** (0.93 to 1.25)	⊕◯◯◯ VERY LOW
AST, per 5 unit/l								
2	observational studies	extremely serious [g]	not serious	not serious	very serious [f]	none	**RR 1.50** (0.73 to 3.08)	⊕◯◯◯ VERY LOW
Creatinine, per 10 µmol/l								
3	observational studies	very serious [d]	not serious	not serious	serious [e]	none	**RR 1.09** (0.97 to 1.22)	⊕◯◯◯ VERY LOW
White blood cell count, per 1x10^9/l								
3	observational studies	extremely serious [g]	not serious	not serious	not serious	dose response gradient	**RR 1.33** (1.12 to 1.57)	⊕◯◯◯ VERY LOW
Lymphocyte count, per 1x10^9/l								
4	observational studies	very serious [d]	serious [k]	not serious	serious [i]	strong association dose response gradient	**RR 0.28** (0.09 to 0.87)	⊕⊕◯◯ LOW
Neutrophils, per 1x10^9/l								
3	observational studies	extremely serious [g]	not serious	not serious	not serious	dose response gradient	**RR 1.24** (1.17 to 1.32)	⊕⊕◯◯ LOW

ESM Table 6: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Lactatdehydrogenase, per 10 unit/l								
2	observational studies	extremely serious [g]	not serious	not serious	serious [e]	none	**RR 1.10** (0.90 to 1.34)	⨁◯◯◯ VERY LOW
Albumin, per 5 g/l								
2	observational studies	extremely serious [g]	serious [l]	not serious	very serious [f]	none	**RR 0.27** (0.04 to 1.83)	⨁◯◯◯ VERY LOW

CI: Confidence interval; RR: Risk ratio

a. High proportion (>25-50%) of evidence from studies with high risk of bias
b. RR ranged from 0.87 to 17.42 and some 95% CIs did not overlap
c. One study with large effect included, but it has a small weight
d. Very high proportion (>50-90%) of evidence from studies with high risk of bias
e. 95% CI includes the null value and includes important benefit OR harm
f. 95% CI includes the null value and includes important benefit AND harm
g. Extreme high proportion (>90-100%) of evidence from studies with high risk of bias
h. RRs ranged from beneficial to harmful associations and minimal overlap of 95% CIs
i. 95% CI excludes the null value, but is very wide and includes implausibly high benefit or harm
j. RR ranged from 1.03 to 8.68 and minimal overlap of 95% CIs
k. RR ranged from 0.01 to 0.81 and minimal overlap of 95% CIs
l. RR ranged from 0.64 to 0.94, no overlap of 95% CIs

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Male sex								
11	observational studies	not serious	not serious	not serious	not serious	none	**RR 1.36** (1.13 to 1.64)	⊕⊕⊕⊕ HIGH
Age >65 years								
6	observational studies	serious [a]	serious [b]	not serious	not serious	none	**RR 1.67** (1.00 to 2.76)	⊕⊕◯◯ LOW
Age per 5 years								
7	observational studies	very serious [c]	not serious	not serious	not serious	dose response gradient	**RR 1.25** (1.11 to 1.40)	⊕⊕⊕◯ MODERATE
Overweight								
2	observational studies	serious [a]	not serious	not serious	serious [d]	none	**RR 1.34** (0.96 to 1.87)	⊕⊕◯◯ LOW
Obesity								
5	observational studies	serious [a]	not serious	not serious	serious [d]	none	**RR 1.31** (0.94 to 1.84)	⊕⊕◯◯ LOW
Smoking (smoker vs not smoker)								
4	observational studies	serious [a]	not serious	not serious	very serious [e]	none	**RR 1.31** (0.78 to 2.19)	⊕◯◯◯ VERY LOW

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Diabetes duration, per 5 years								
2	observational studies	extremely serious [f]	not serious	not serious	not serious	none	**RR 1.00** (0.93 to 1.08)	⊕◯◯◯ VERY LOW
HbA1c, 53-75 vs <53 mmol/mol (7-9 vs <7%)								
3	observational studies	very serious [c]	serious [b]	not serious	very serious [e]	none	**RR 1.33** (0.66 to 2.67)	⊕◯◯◯ VERY LOW
HbA1c, >75 vs <53 mmol/mol (>9 vs <7%)								
3	observational studies	very serious [c]	serious [b]	not serious	very serious [e]	none	**RR 1.40** (0.59 to 3.31)	⊕◯◯◯ VERY LOW
HbA1c, per 20 mmol/mol increase								
5	observational studies	serious [a]	serious [b]	not serious	very serious [e]	none	**RR 0.96** (0.61 to 1.52)	⊕◯◯◯ VERY LOW
Blood glucose at admission 6-11 mmol/l compared to <6 mmol/l								
2	observational studies	very serious [c]	not serious	not serious	very serious [e]	dose response gradient	**RR 1.69** (0.53 to 5.45)	⊕◯◯◯ VERY LOW
Blood glucose at admission >11 mmol/l compared to <6 mmol/l								
2	observational studies	very serious [c]	not serious	not serious	serious [g]	strong association dose response gradient	**RR 3.94** (1.58 to 9.87)	⊕⊕⊕◯ MODERATE

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Blood glucose at admission, per 1 mmol/l								
3	observational studies	extremely serious [f]	not serious	not serious	not serious	dose response gradient	**RR 1.10** (1.04 to 1.16)	⊕⊕◯◯ LOW
Poorly controlled								
1	observational studies	not serious	na	not serious	not serious	strong association	**RR 2.44** (1.50 to 3.96)	⊕⊕⊕◯ MODERATE
Use of insulin								
6	observational studies	very serious [c]	not serious	not serious	serious [d]	none	**RR 1.75** (0.98 to 3.12)	⊕◯◯◯ VERY LOW
Use of metformin								
6	observational studies	very serious [c]	serious [b]	not serious	very serious [e]	none	**RR 0.61** (0.29 to 1.27)	⊕◯◯◯ VERY LOW
Use of DPP-4 inhibitors								
4	observational studies	very serious [c]	not serious	not serious	very serious [e]	none	**RR 0.97** (0.50 to 1.87)	⊕◯◯◯ VERY LOW
Use of sulfonylurea/glinide								
3	observational studies	serious [a]	not serious	not serious	very serious [e]	none	**RR 1.74** (0.71 to 4.25)	⊕◯◯◯ VERY LOW

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Use of alpha-glucosidase inhibitors								
2	observational studies	extremely serious [f]	not serious	not serious	very serious [e]	strong association	**RR 0.43** (0.09 to 2.09)	⊕◯◯◯ VERY LOW
Hypertension								
9	observational studies	serious [a]	serious [b]	not serious	serious [d]	none	**RR 1.16** (0.94 to 1.44)	⊕◯◯◯ VERY LOW
Total CVD								
8	observational studies	serious [a]	not serious	not serious	serious [d]	none	**RR 1.28** (1.00 to 1.65)	⊕⊕◯◯ LOW
Cerebrovascular disease								
4	observational studies	extremely serious [f]	not serious	not serious	very serious [e]	none	**RR 0.97** (0.68 to 1.37)	⊕◯◯◯ VERY LOW
Ischaemic heart disease								
2	observational studies	very serious [c]	not serious	not serious	very serious [e]	none	**RR 0.83** (0.39 to 1.77)	⊕◯◯◯ VERY LOW
Heart failure								
2	observational studies	not serious	serious [h]	not serious	very serious [e]	strong association	**RR 2.01** (0.43 to 9.36)	⊕⊕◯◯ LOW

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
CKD								
6	observational studies	serious [a]	not serious	not serious	serious [d]	none	**RR 1.44** (0.96 to 2.15)	⊕⊕◯◯ LOW
COPD								
6	observational studies	not serious	not serious	not serious	not serious	none	**RR 1.36** (1.11 to 1.66)	⊕⊕⊕⊕ HIGH
Liver disease								
2	observational studies	extremely serious [f]	not serious	not serious	serious [d]	none	**RR 1.21** (0.80 to 1.83)	⊕◯◯◯ VERY LOW
Cancer								
4	observational studies	very serious [c]	not serious	not serious	serious [d]	none	**RR 1.17** (0.86 to 1.59)	⊕◯◯◯ VERY LOW
Dementia								
2	observational studies	very serious [c]	not serious	not serious	very serious [e]	strong association	**RR 0.41** (0.09 to 1.76)	⊕◯◯◯ VERY LOW
Use of renin inhibitors								
6	observational studies	not serious	not serious	not serious	serious [d]	none	**RR 0.75** (0.50 to 1.14)	⊕⊕⊕◯ MODERATE

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Use of statins								
3	observational studies	extremely serious [f]	serious [i]	not serious	very serious [e]	none	**RR 1.01** (0.31 to 3.30)	⊕◯◯◯ VERY LOW
CRP, per 10 mg/l								
4	observational studies	very serious [c]	not serious	not serious	serious [d]	none	**RR 1.25** (0.96 to 1.63)	⊕◯◯◯ VERY LOW
ALT, per 5 unit/L								
2	observational studies	extremely serious [f]	not serious	not serious	serious [d]	none	**RR 1.06** (0.92 to 1.22)	⊕◯◯◯ VERY LOW
AST, per 5 unit/l								
2	observational studies	extremely serious [f]	not serious	not serious	very serious [e]	none	**RR 1.50** (0.73 to 3.08)	⊕◯◯◯ VERY LOW
Creatinine, per 10 µmol/l								
3	observational studies	very serious [c]	not serious	not serious	not serious	dose response gradient	**RR 1.14** (1.05 to 1.23)	⊕⊕⊕◯ MODERATE
White blood cell count, per 1x10^9/l								
3	observational studies	extremely serious [f]	not serious	not serious	not serious	dose response gradient	**RR 1.21** (1.04 to 1.40)	⊕⊕◯◯ LOW

ESM Table 7: Certainty of evidence for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

Certainty assessment							Relative risk (95% CI)	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Lymphocyte count, per 1x10^9/l								
4	observational studies	very serious [c]	not serious	not serious	serious [g]	strong association dose response gradient	**RR 0.33** (0.14 to 0.79)	⊕⊕⊕◯ MODERATE
Neutrophils, per 1x10^9/l								
3	observational studies	extremely serious [f]	not serious	not serious	not serious	dose response gradient	**RR 1.22** (1.16 to 1.28)	⊕⊕◯◯ LOW
Lactatdehydrogenase, per 10 unit/l								
2	observational studies	extremely serious [f]	not serious	not serious	serious [d]	none	**RR 1.10** (0.90 to 1.34)	⊕◯◯◯ VERY LOW
Albumin								
2	observational studies	extremely serious [f]	not serious	not serious	very serious [e]	strong association	**RR 0.26** (0.05 to 1.40)	⊕◯◯◯ VERY LOW

CI: Confidence interval; RR: Risk ratio

a. High proportion (>25-50%) of evidence from studies with high risk of bias
b. RRs ranged from beneficial to harmful associations and minimal overlap of 95% CIs
c. Very high proportion (>50-90%) of evidence from studies with high risk of bias
d. 95% CI includes the null value and includes important benefit OR harm
e. 95% CI includes the null value and includes important benefit AND harm
f. Extreme high proportion (>90-100%) of evidence from studies with high risk of bias
g. 95% CI excludes the null value, but is very wide and includes implausibly high benefit or harm
h. RR range from 1.08 to 5.41, minimal overlap of 95% CIs
i. RR range from 0.10 to 2.98, minimal overlap of 95% CIs

ESM Table 8: Comparison of the 95% CIs derived by the DerSimonian-Laird method versus the Hartung-Knapp-Sidik-Jonkman method for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 death

	Summary RR	95% CIs from the DerSimonian-Laird method		95% CIs from the Hartung-Knapp-Sidik-Jonkman method	
General risk factors					
Sex (n=10)	1.28	1.02	1.61	0.96	1.71
Age >65y (n=6)	3.49	1.82	6.69	1.49	8.20
Age per 5 y (n=5)	1.43	1.12	1.83	0.66	3.05
Overweight (n=2)	0.72	0.45	1.16	0.03	15.85
Obesity (n=4)	1.06	0.76	1.49	0.57	2.00
Smoking (n=3)	0.91	0.79	1.06	0.66	1.26
Diabetes-specific risk factors					
Type 2 vs type 1 (n=2)	1.65	0.64	4.26	0.004	774.57
Diabetes duration (n=2)	1.06	0.94	1.20	0.47	2.29
HbA1c, 53-75 vs <75 mmol/mol (n=2)	1.08	0.57	2.06	0.02	71.07
HbA1c, >75 vs <53 mmol/mol (n=2)	0.95	0.50	1.79	0.02	57.45
HbA1c, per 20 mmol/mol (n=4)	1.04	0.80	1.35	0.66	1.63
Glucose >6 mmol/l (n=2)	2.76	0.56	13.51	0.0001	82,518.97
Glucose >11 mmol/l (n=2)	8.60	2.25	32.83	0.002	50,734.76
Glucose per 1 mmol/l (n=2)	1.10	1.05	1.16	0.79	1.55
poorly controlled (n=1)	7.69	2.32	25.52	2.32	25.52
Metformin use (n=4)	0.50	0.28	0.90	0.20	1.30
DDP-4 use (n=2)	0.90	0.59	1.36	0.06	13.27
Sulfonylurea/glinides use (n=2)	0.73	0.49	1.09	0.06	9.38
Insulin use (n=5)	1.75	1.01	3.03	0.73	4.18
Comorbidities and complications					
Hypertension (n=8)	1.09	0.77	1.53	0.71	1.67
CVD (n=8)	1.56	1.09	2.24	0.99	2.44
Cerebrovascular disease (n=2)	2.11	1.36	3.26	0.13	35.69
CKD (n=6)	1.93	1.28	2.90	1.04	3.58
COPD (n=5)	1.40	1.21	1.62	1.14	1.72
Cancer (n=3)	1.54	0.94	2.51	0.53	4.51
Any comorbidities (n=2)	0.94	0.45	1.98	0.01	118.89
Other medication use					
RAAS (n=2)	1.04	0.64	1.68	0.05	24.11
Statins (n=2)	1.38	0.71	2.66	0.02	97.71
Laboratory parameters on admission					
Albumin, per 1 g/l (n=2)	0.78	0.53	1.13	0.07	8.91
CRP, per 1 mg/l (n=3)	1.02	1.00	1.04	0.97	1.07
Creatinine, per 1 µmol/l (n=3)	1.01	1.00	1.02	0.98	1.04
AST, per 1 unit/l (n=2)	1.08	0.94	1.25	0.43	2.76
ALT, per 1 unit/l (n=2)	1.02	0.99	1.05	0.84	1.23
LDH, per 1 unit/l (n=2)	1.01	0.99	1.03	0.89	1.15
White blood cell count, per $1x10^9$ (n=3)	1.33	1.12	1.57	0.91	1.93
Neutrophils, per $1x10^9$ (n=3)	1.24	1.17	1.32	1.08	1.44
Lymphocyte count, per $1x10^9$ (n=4)	0.28	0.09	0.87	0.02	5.00

Grey highlighted rows present associations that exclude the null value when applying the DerSimonian-Laird method, but include the null value when calculating the 95% CI using the Hartung-Knapp-Sidik-Jonkman method.

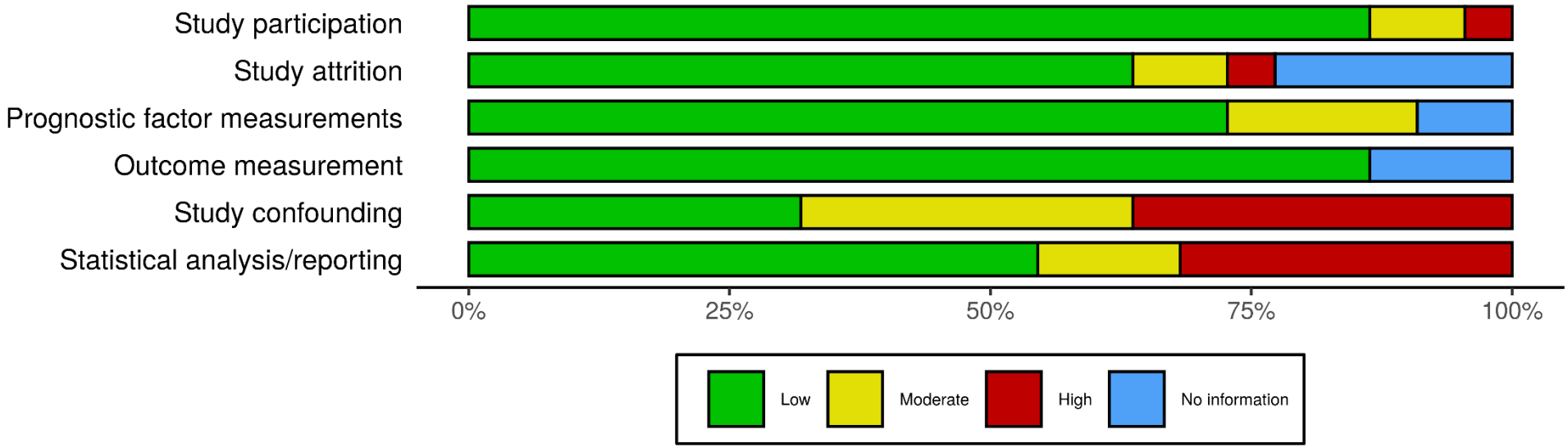
ESM Table 9: Comparison of the 95% CIs derived by the DerSimonian-Laird method versus the Hartung-Knapp-Sidik-Jonkman method for associations between phenotypes of patients with diabetes and SARS-CoV-2 regarding COVID-19 severity

	Summary RR	95% CIs from the DerSimonian-Laird method		95% CIs from the Hartung-Knapp-Sidik-Jonkman method	
General risk factors					
Sex (n=11)	1.36	1.13	1.64	1.09	1.71
Age >65y (n=6)	1.67	1.00	2.76	0.69	4.02
Age per 5 y (n=7)	1.25	1.11	1.40	1.05	1.47
Overweight (n=2)	1.34	0.96	1.87	0.15	11.83
Obesity (n=5)	1.31	0.94	1.84	0.82	2.12
Smoking (n=4)	1.31	0.78	2.19	0.56	3.03
Diabetes-specific risk factors					
Diabetes duration per 5y (n=2)	1.00	0.93	1.08	0.62	2.39
HbA1c, 53-75 vs <75 mmol/mol (n=3)	1.33	0.66	2.67	0.29	6.14
HbA1c, >75 vs <53 mmol/mol (n=3)	1.40	0.59	3.31	0.21	9.25
HbA1c per 20 mmol/mol (n=5)	0.96	0.61	1.52	0.42	2.14
Glucose >6 mmol/l (n=2)	1.69	0.53	5.45	0.001	3,325.62
Glucose >11 mmol/l (n=2)	3.94	1.58	9.87	0.01	1509.01
Glucose per 1 mmol/l (n=3)	1.10	1.04	1.16	0.98	1.23
Poorly controlled (n=1)	2.44	1.50	3.96	1.50	3.96
Metformin use (n=6)	0.61	0.29	1.27	0.21	1.72
DDP-4 use (n=4)	0.97	0.50	1.87	0.30	3.12
Sulfonylurea/glinides use (n=3)	1.74	0.71	4.25	0.20	14.79
Alpha-glucosidase inhibitors use (n=2)	0.43	0.09	2.09	0.00002	12,089.17
Insulin use (n=6)	1.75	0.98	3.12	0.78	3.91
Comorbidities and complications					
Hypertension (n=9)	1.16	0.94	1.44	0.89	1.53
CVD (n=8)	1.28	1.00	1.65	0.91	1.81
Cerebrovascular disease (n=4)	0.97	0.68	1.37	0.55	1.70
Ischaemic heart disease (n=2)	0.83	0.39	1.77	0.01	113.68
Heart failure (n=2)	2.01	0.43	9.36	0.0001	42,830.87
Liver disease (n=2)	1.21	0.80	1.83	0.08	17.45
CKD (n=6)	1.44	0.96	2.15	0.79	2.60
COPD (n=6)	1.36	1.11	1.66	1.04	1.78
Cancer (n=4)	1.17	0.86	1.59	0.71	1.92
Dementia (n=2)	0.41	0.09	1.76	0.0003	5,527.15
Other medication use					
RAAS (n=6)	0.75	0.50	1.14	0.44	1.30
Statins (n=3)	1.01	0.31	3.30	0.04	24.56
Laboratory parameters on admission					
Albumin, per 1 g/l (n=2)	0.76	0.54	1.08	0.08	7.15
CRP, per 1 mg/l (n=4)	1.02	1.00	1.05	0.96	1.09
Creatinine, per 1µmol/L (n=3)	1.01	1.01	1.02	0.99	1.03
AST, per 1 unit/l (n=2)	1.08	0.94	1.25	0.43	2.76
ALT, per 1 unit/l (n=2)	1.01	0.98	1.04	0.84	1.22
LDH, per 1 unit/l (n=2)	1.01	0.99	1.03	0.89	1.15
White blood cell count, per $1x10^9$/l (n=3)	1.21	1.04	1.40	0.79	1.84
Neutrophils, per $1x10^9$ (n=3)	1.22	1.16	1.28	1.10	1.35
Lymphocyte count, per $1x10^9$ (n=4)	0.33	0.14	0.79	0.07	1.52

Grey highlighted rows present associations that exclude the null value when applying the DerSimonian-Laird method, but include the null value when calculating the 95% CI using the Hartung-Knapp-Sidik-Jonkman method.

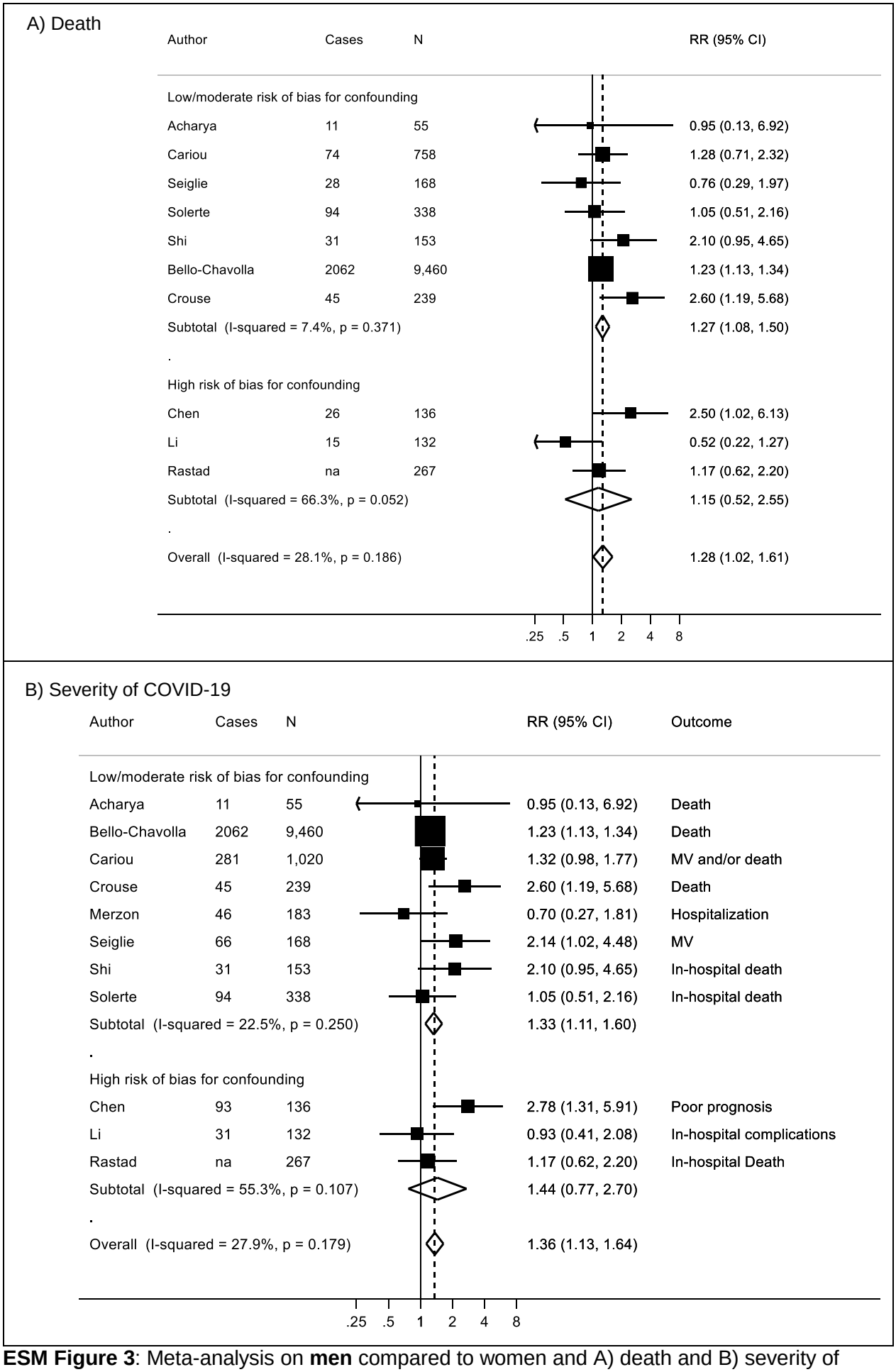
ESM Figure 1: Risk of bias of each study for each domain and overall

Risk of bias was visualized by using the robvis visualization tool.[219]

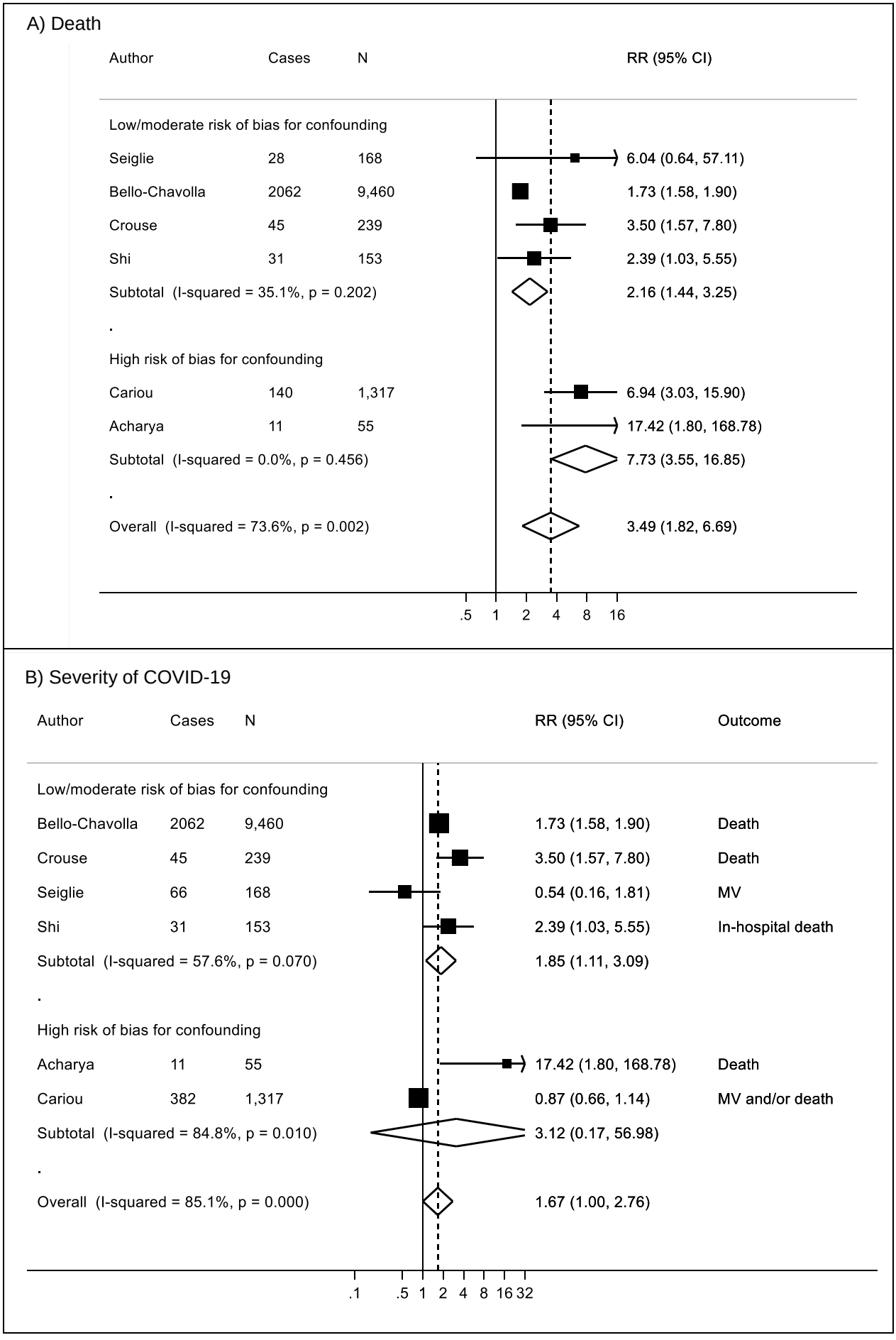


ESM Figure 2: Risk of bias of judgements within each bias domain

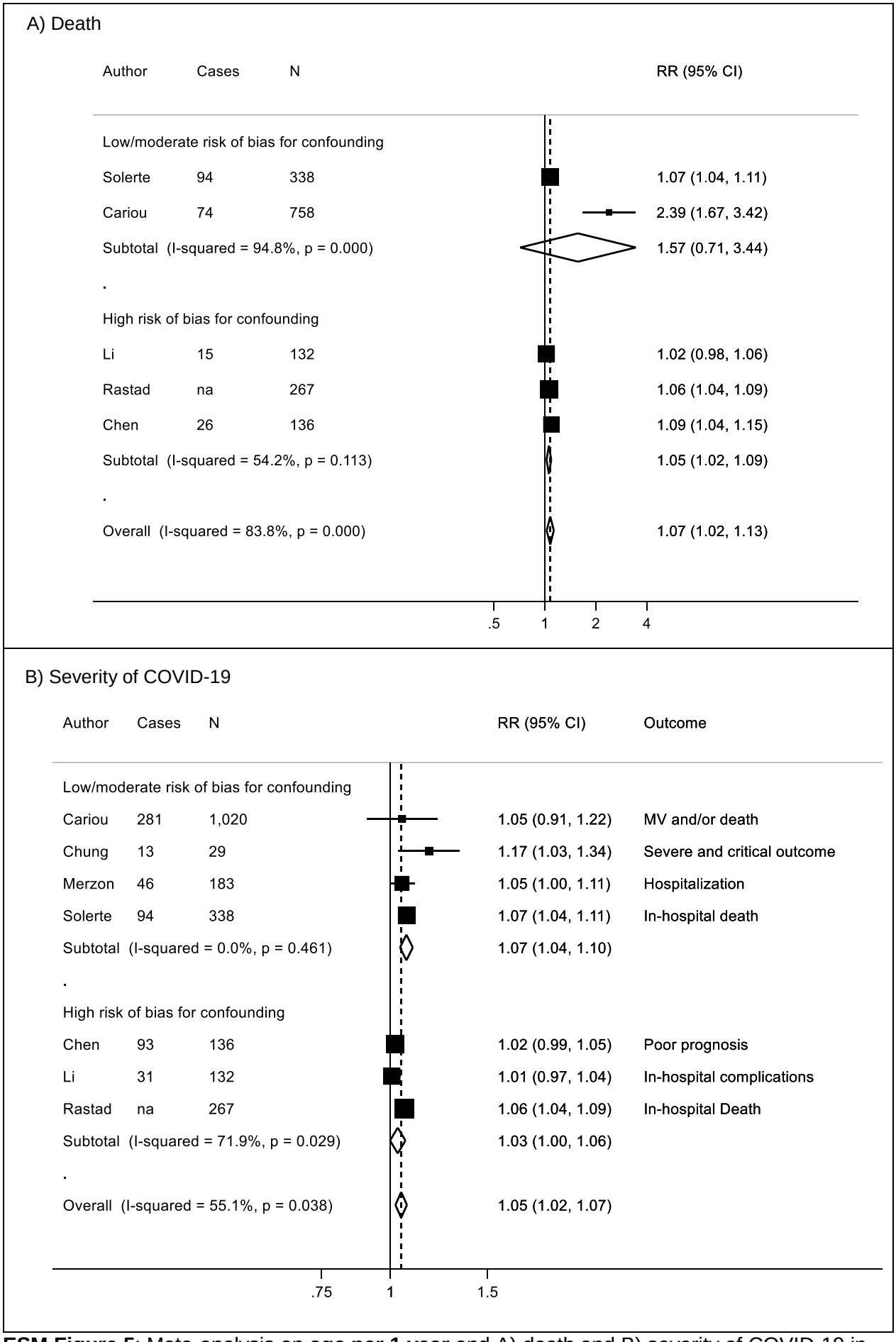
Risk of bias was visualized by using the robvis visualization tool.[219]



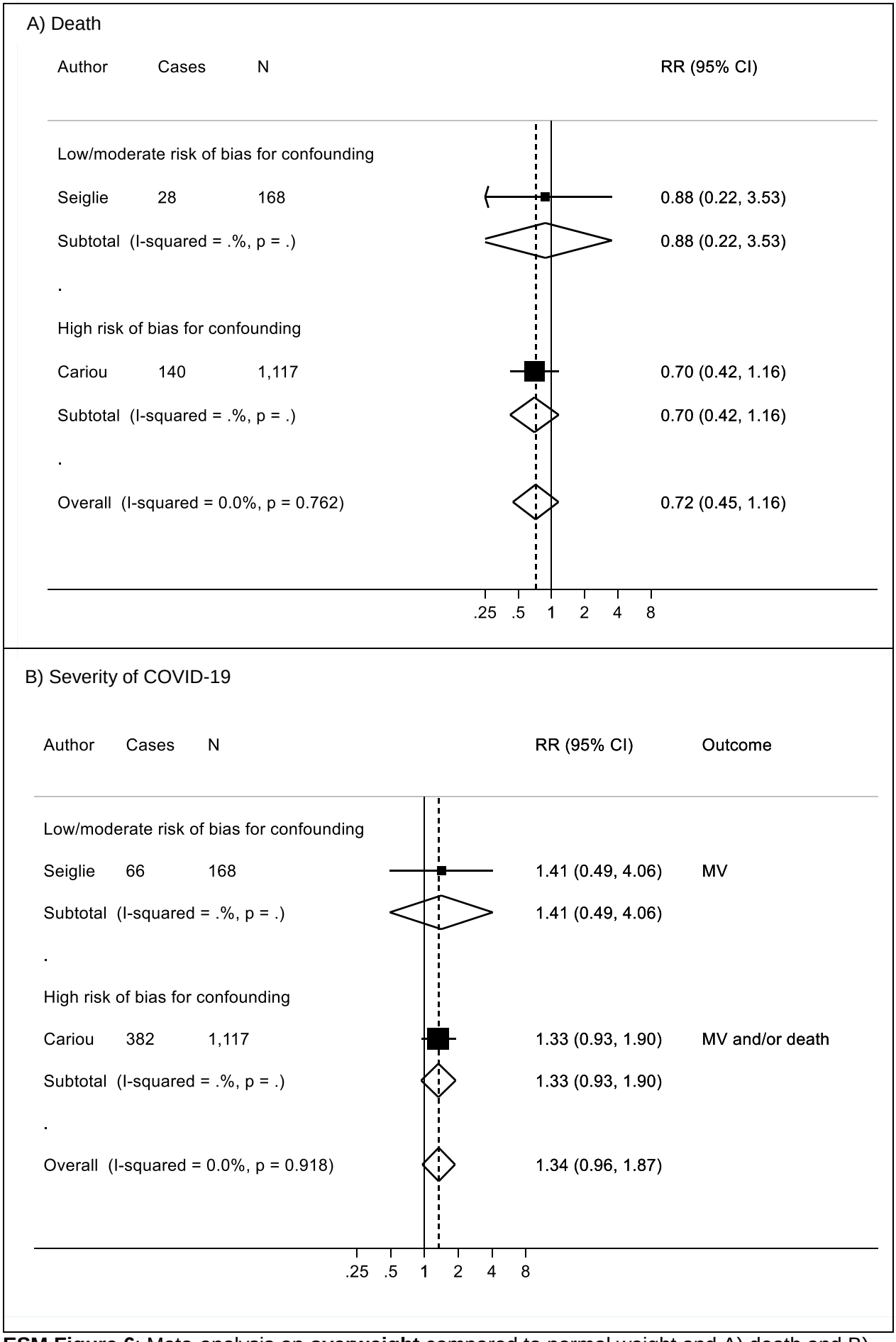
ESM Figure 3: Meta-analysis on **men** compared to women and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



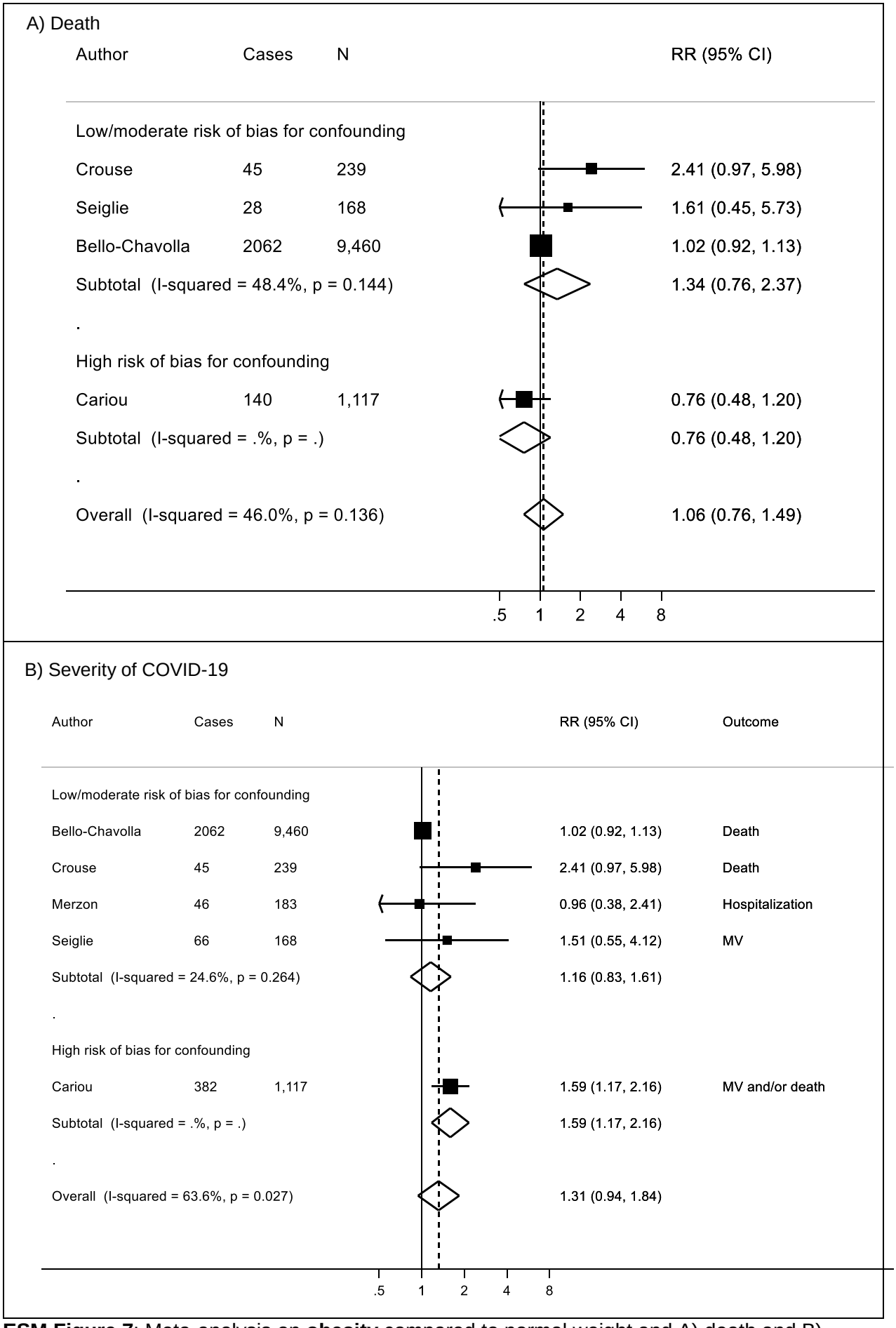
ESM Figure 4: Meta-analysis on **age >65** years and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



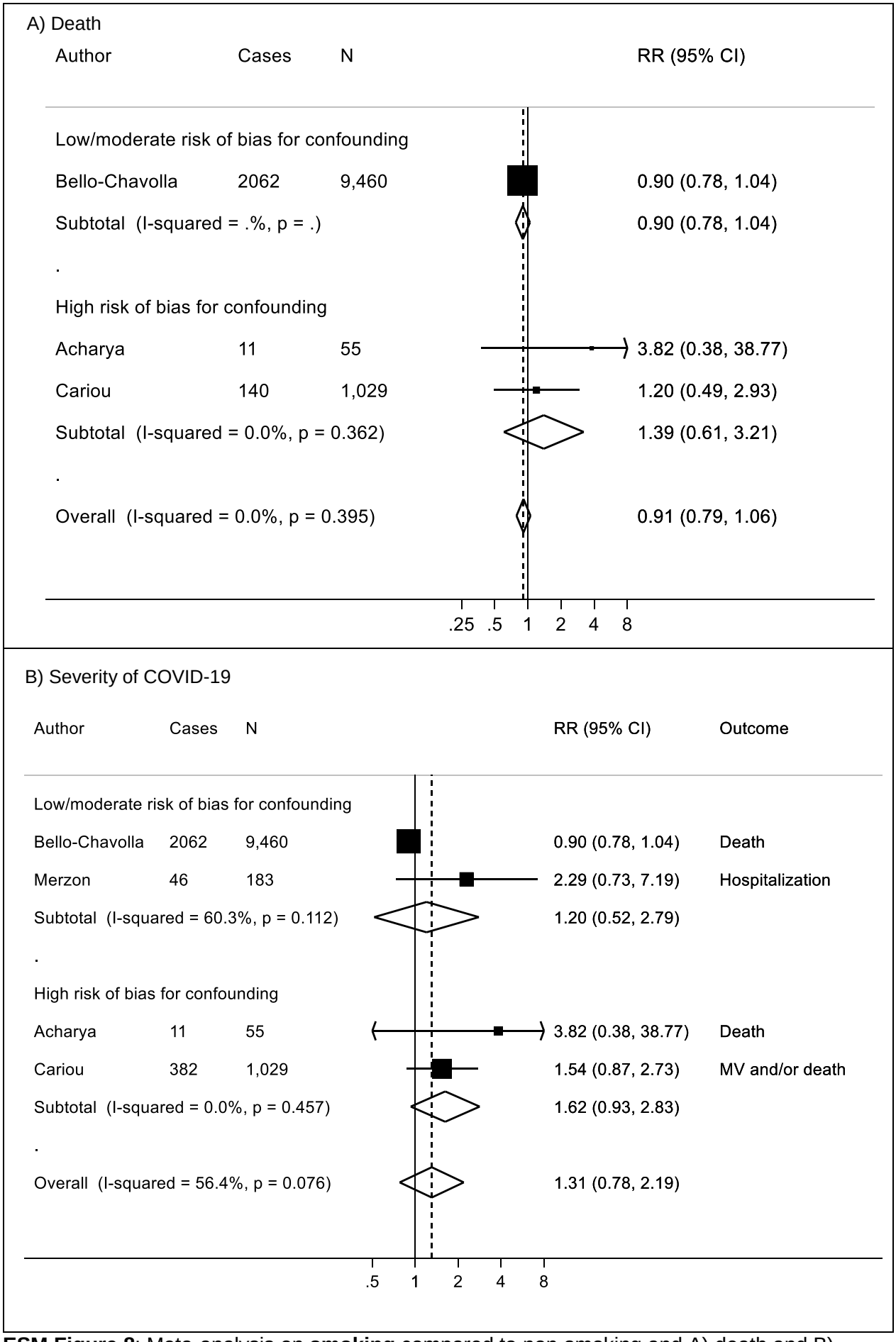
ESM Figure 5: Meta-analysis on **age per 1 year** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



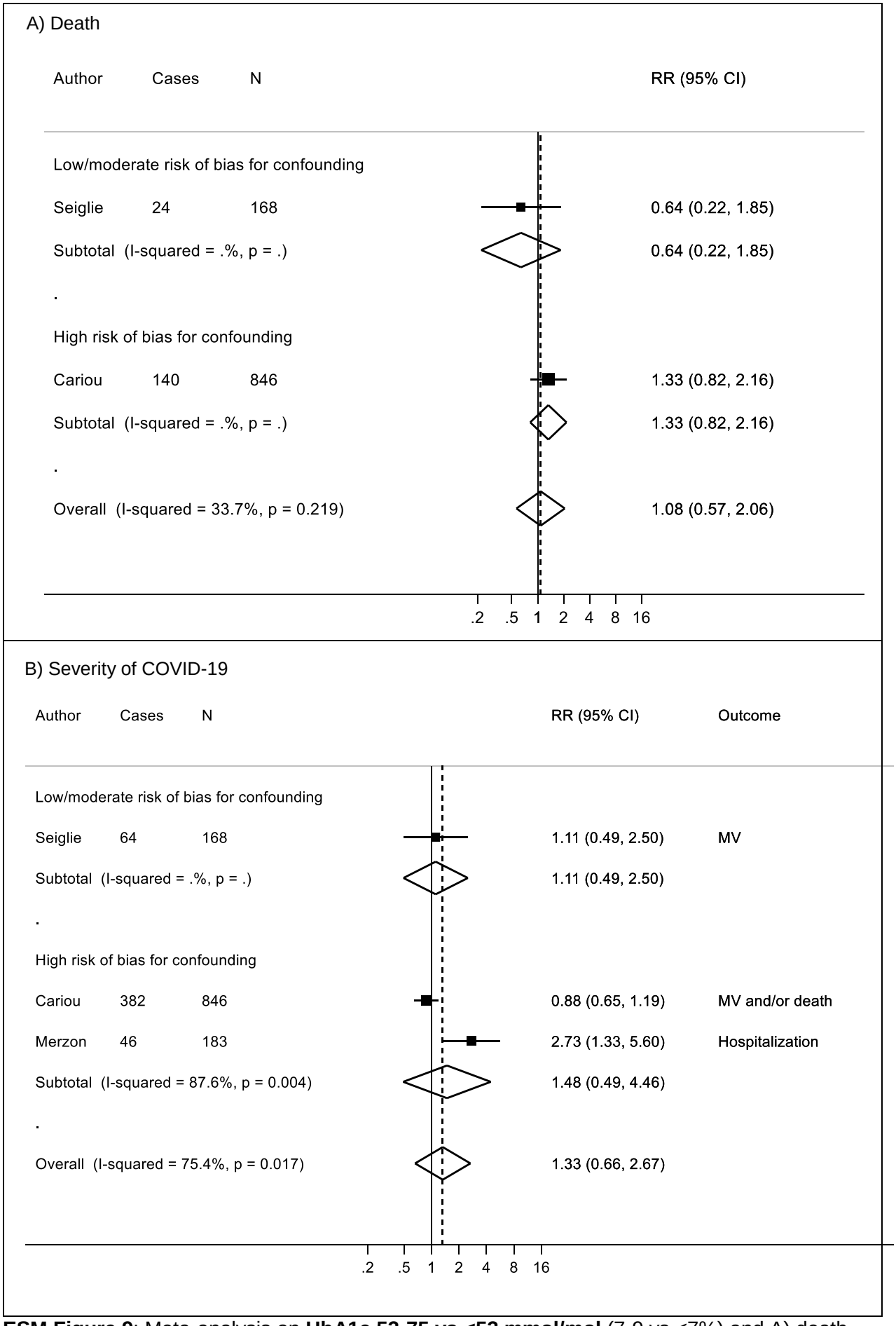
ESM Figure 6: Meta-analysis on **overweight** compared to normal weight and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



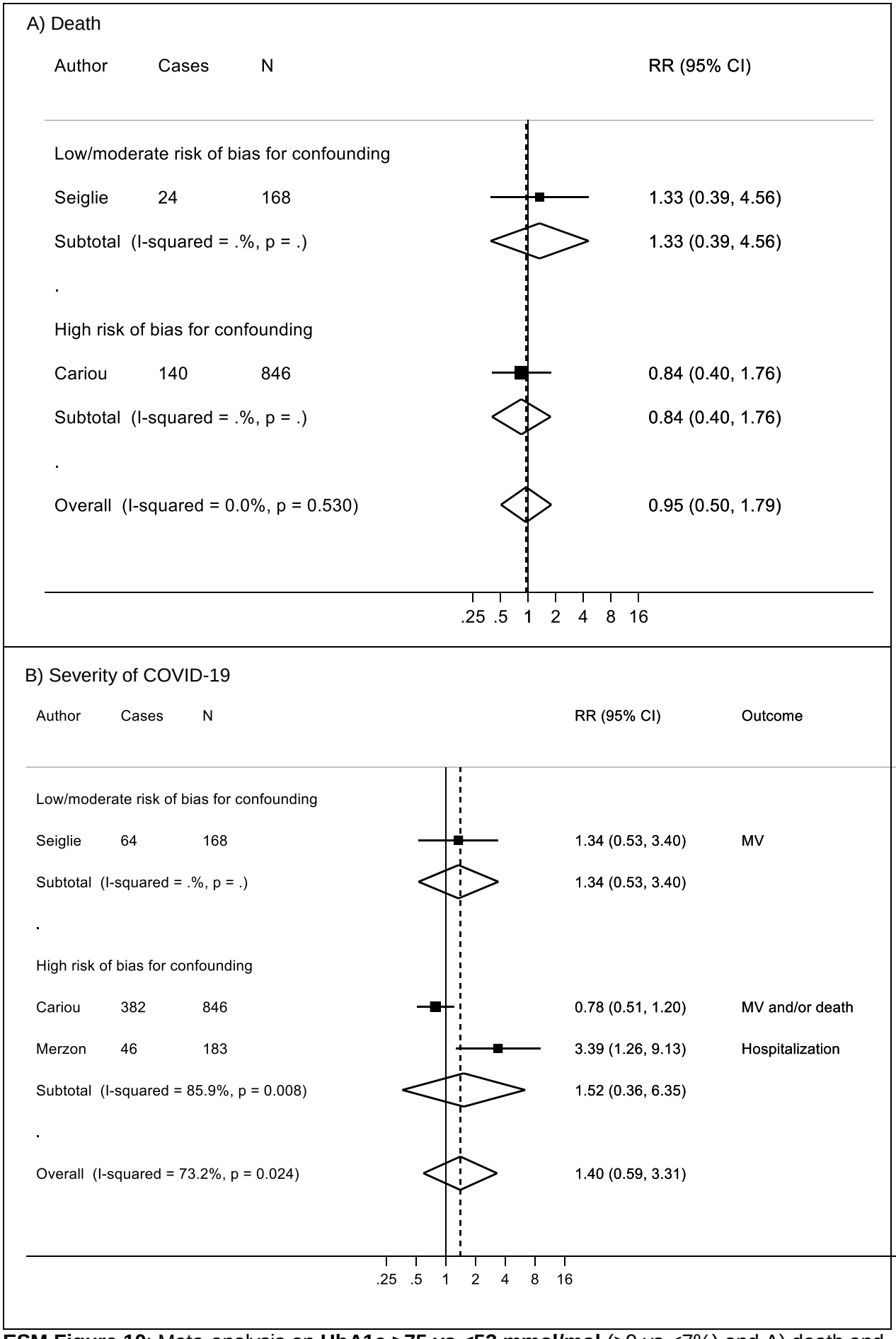
ESM Figure 7: Meta-analysis on **obesity** compared to normal weight and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



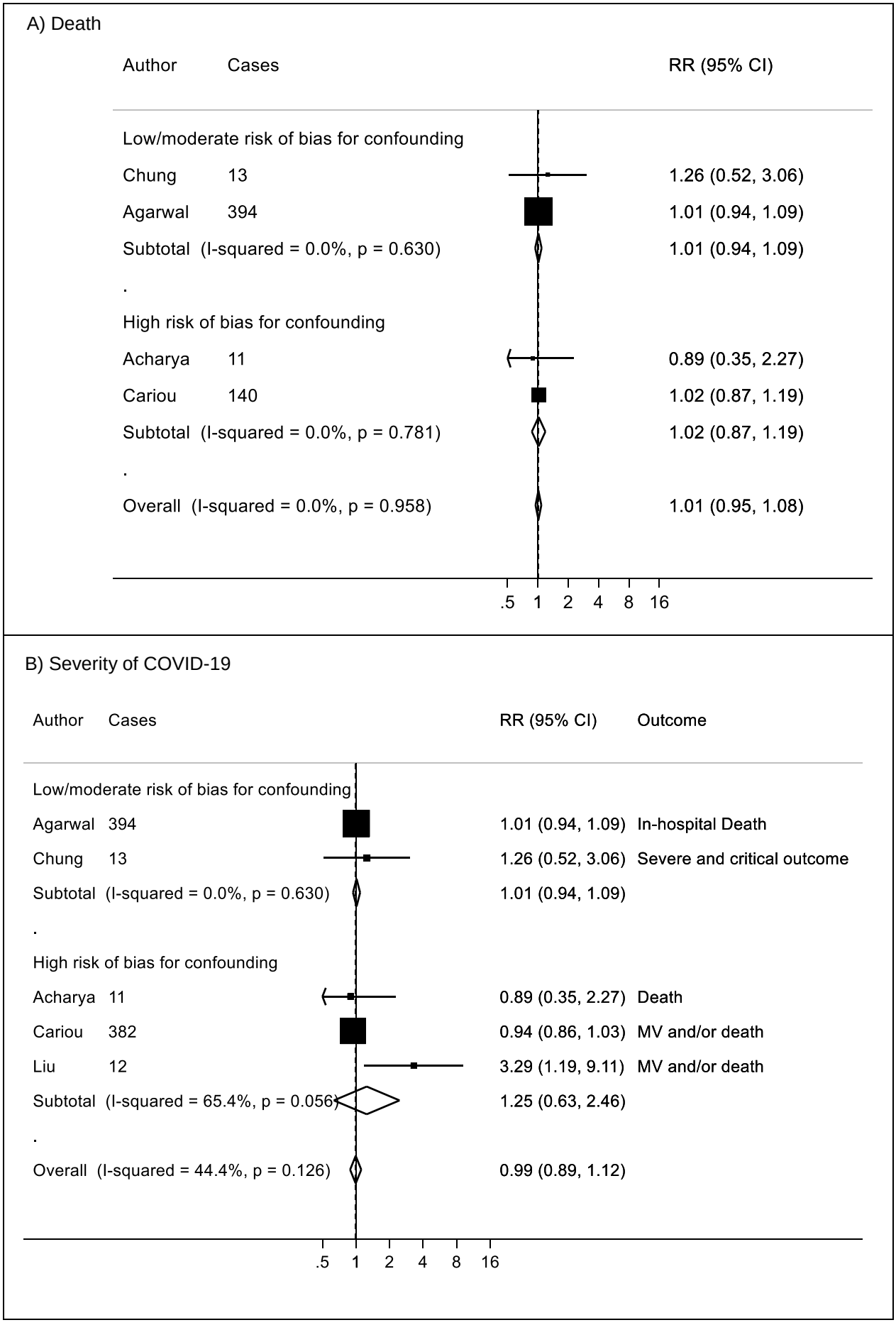
ESM Figure 8: Meta-analysis on **smoking** compared to non-smoking and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



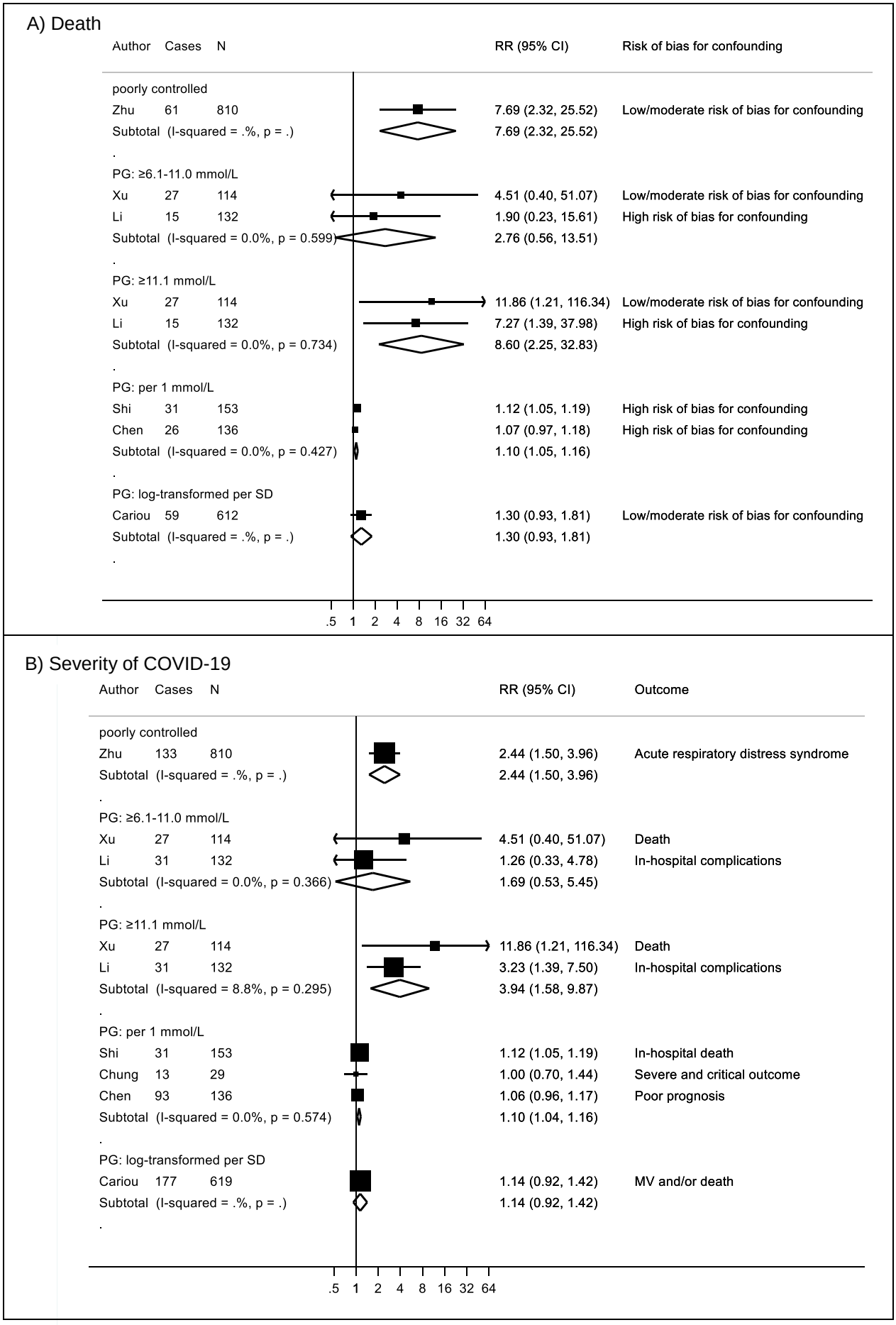
ESM Figure 9: Meta-analysis on **HbA1c 53-75 vs <53 mmol/mol** (7-9 vs <7%) and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



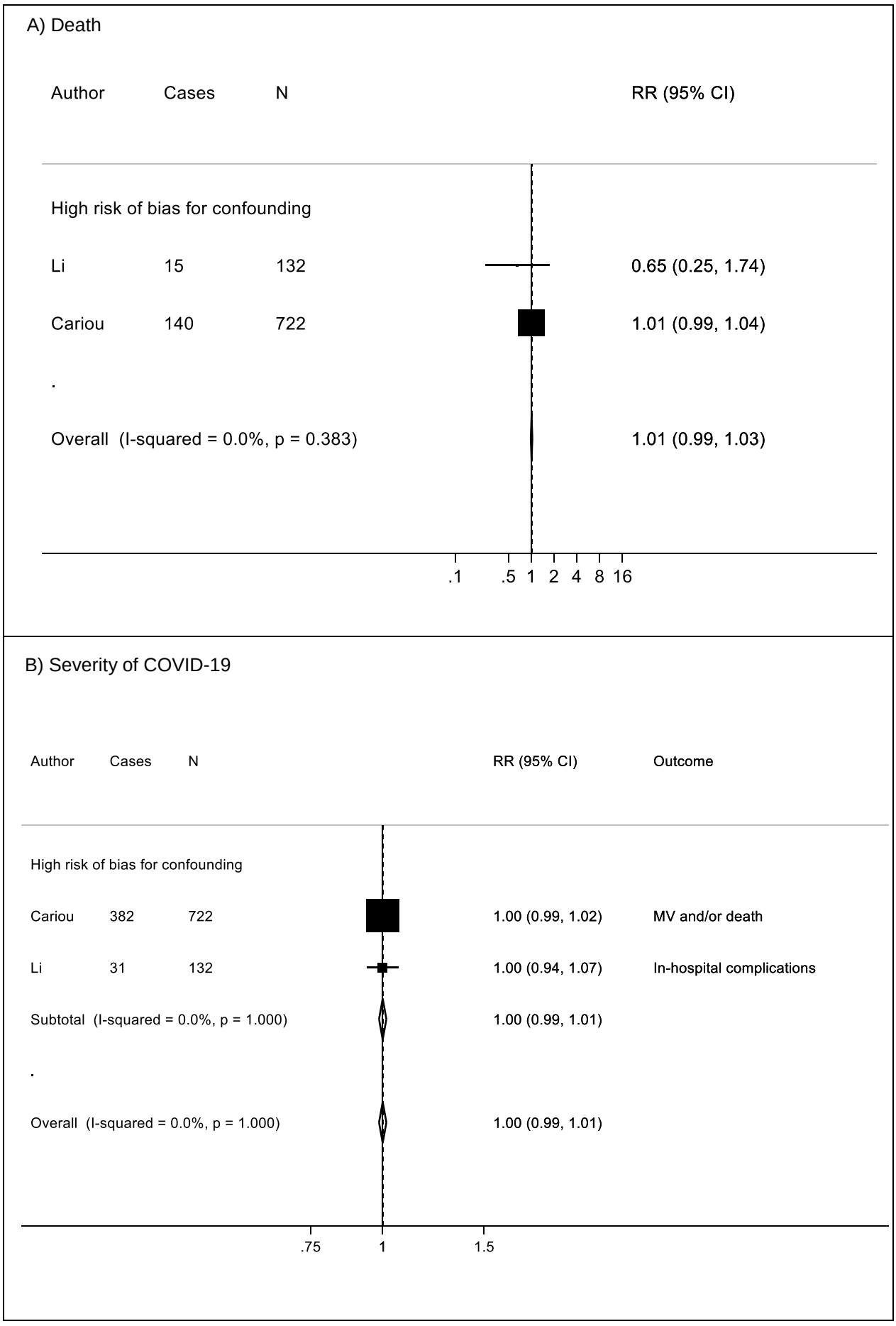
ESM Figure 10: Meta-analysis on **HbA1c >75 vs <53 mmol/mol** (>9 vs <7%) and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 11: Meta-analysis on **HbA1C per 1%** increase and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19

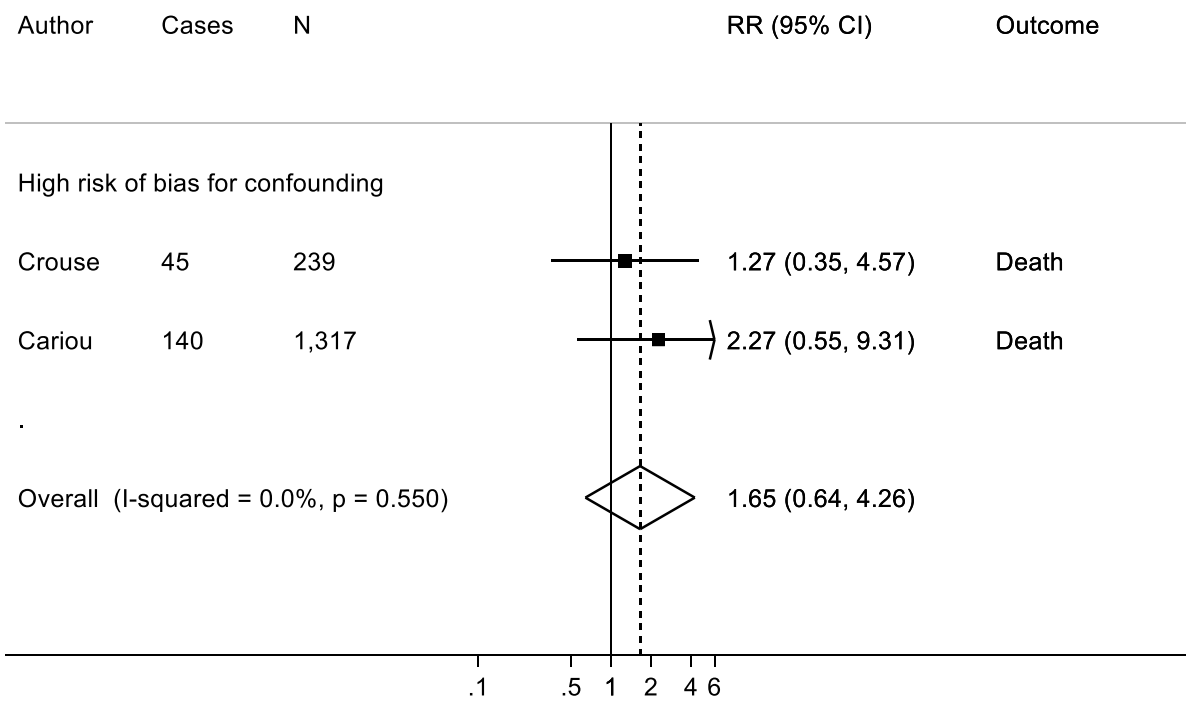


ESM Figure 12: Meta-analysis on **blood glucose** at admission and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 13: Meta-analysis on **diabetes duration** per 1 year and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19

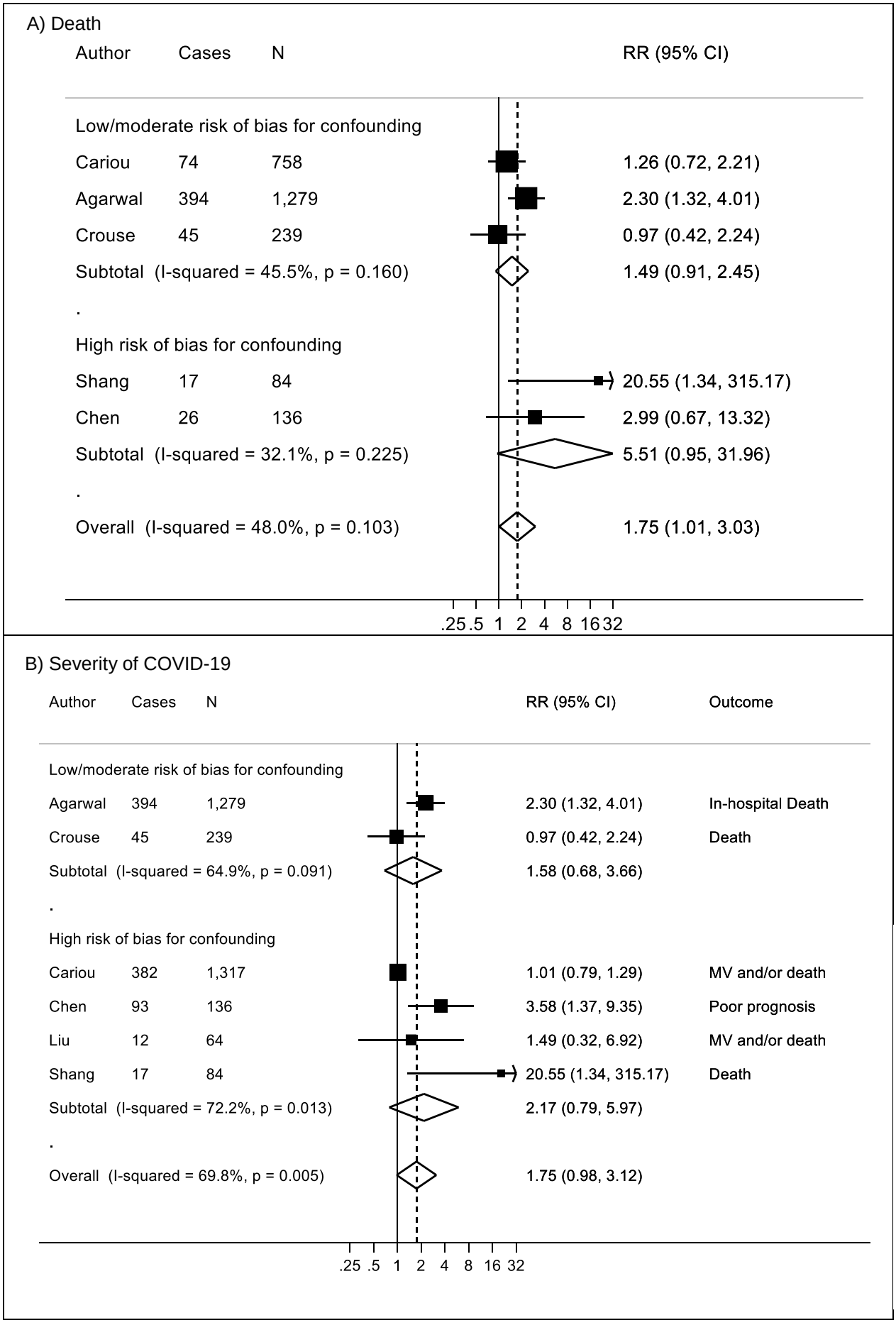
A) Death



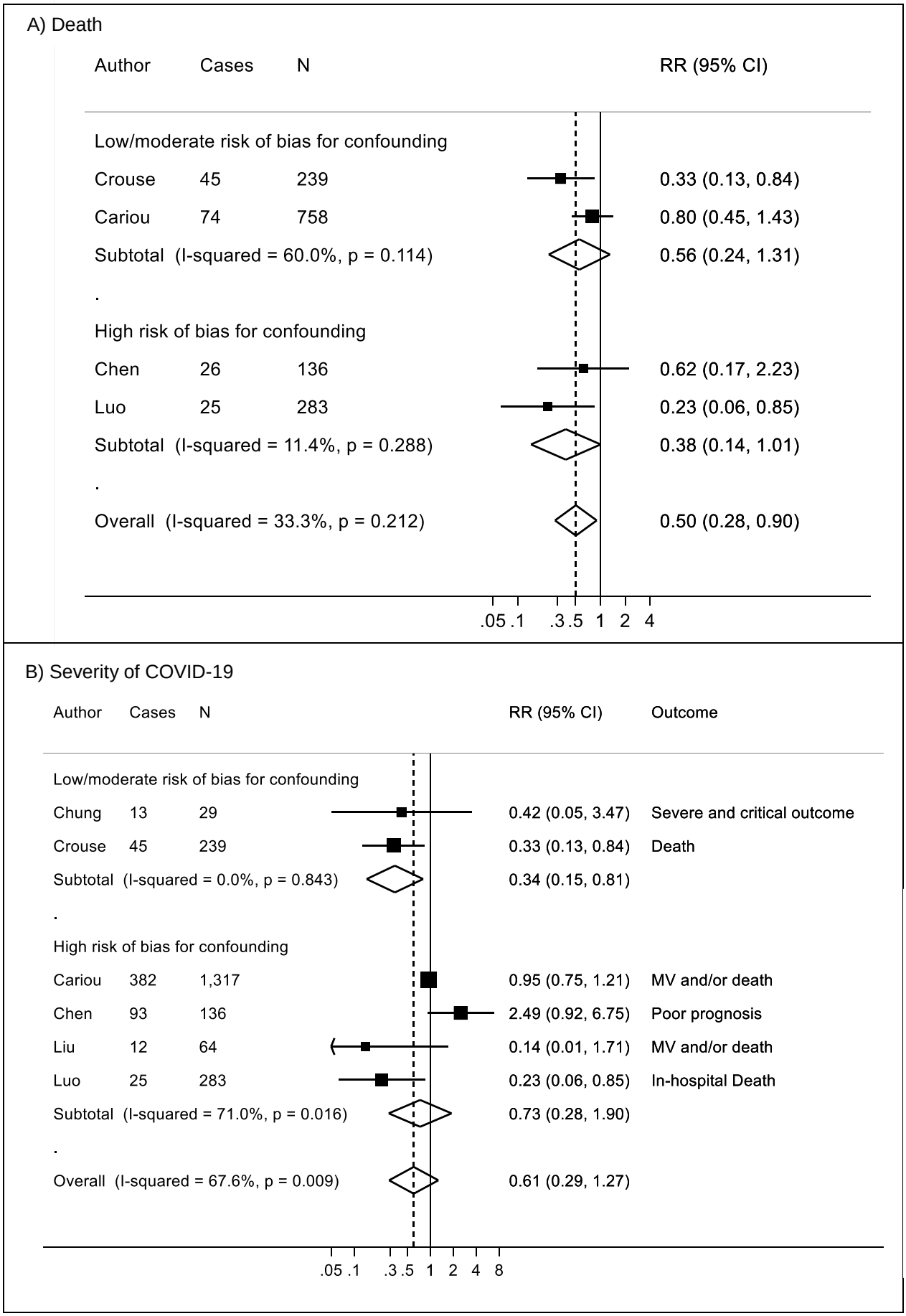
B) Severity of COVID-19

No data available

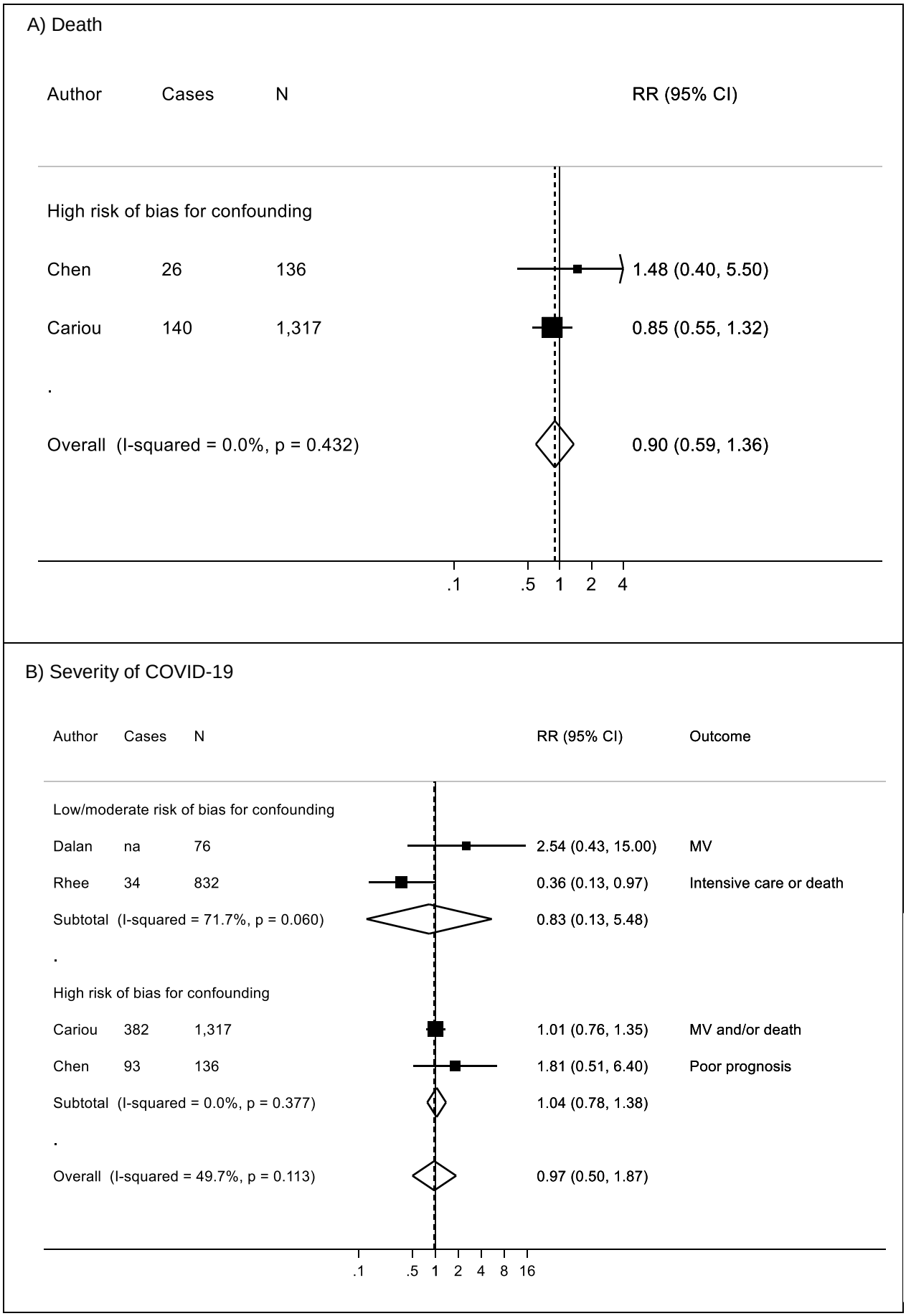
ESM Figure 14: Meta-analysis on **type 2 vs type 1** diabetes and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



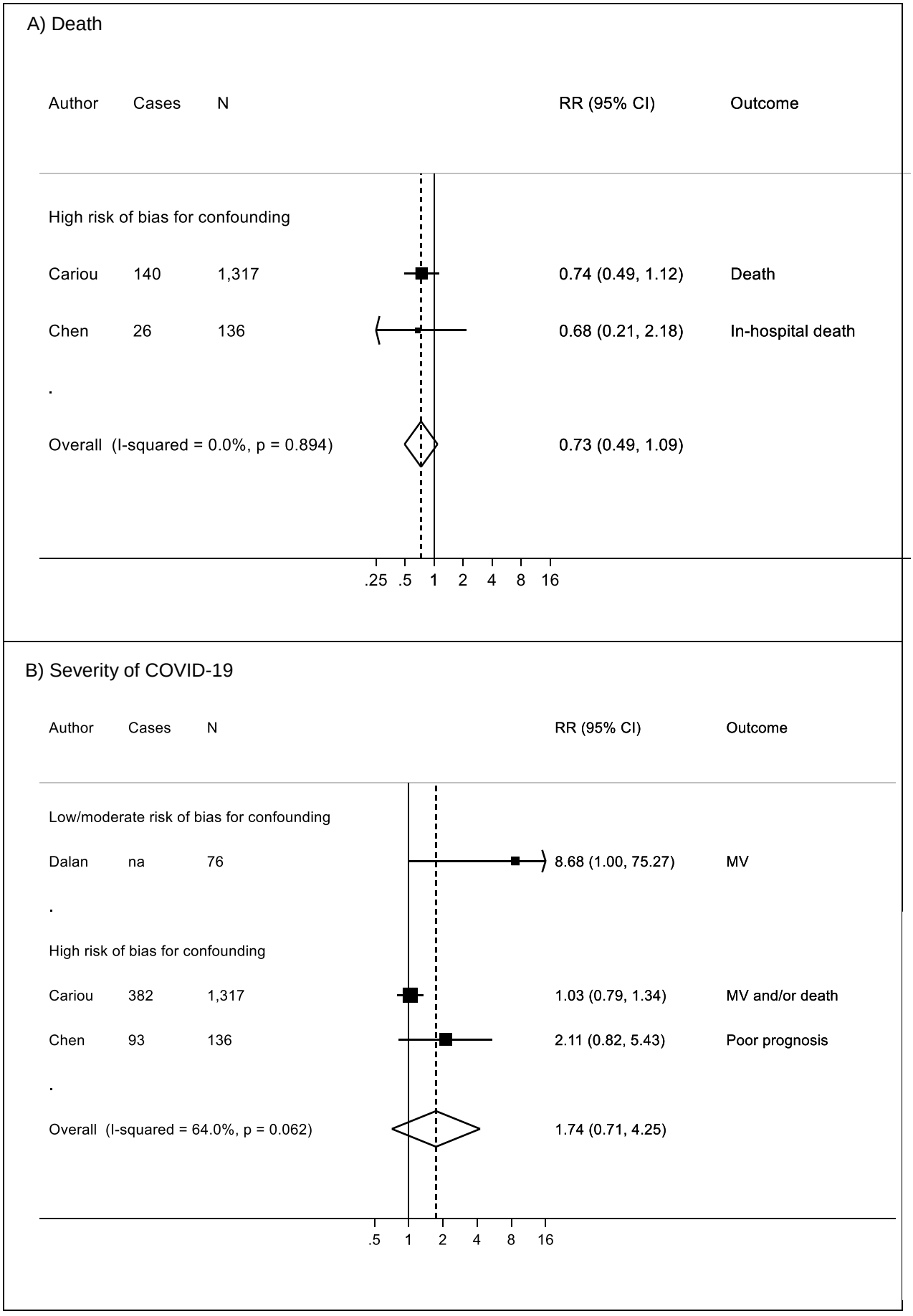
ESM Figure 15: Meta-analysis on **insulin use** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 16: Meta-analysis on **metformin use** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 17: Meta-analysis on **DPP-4-inhibitors use** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19

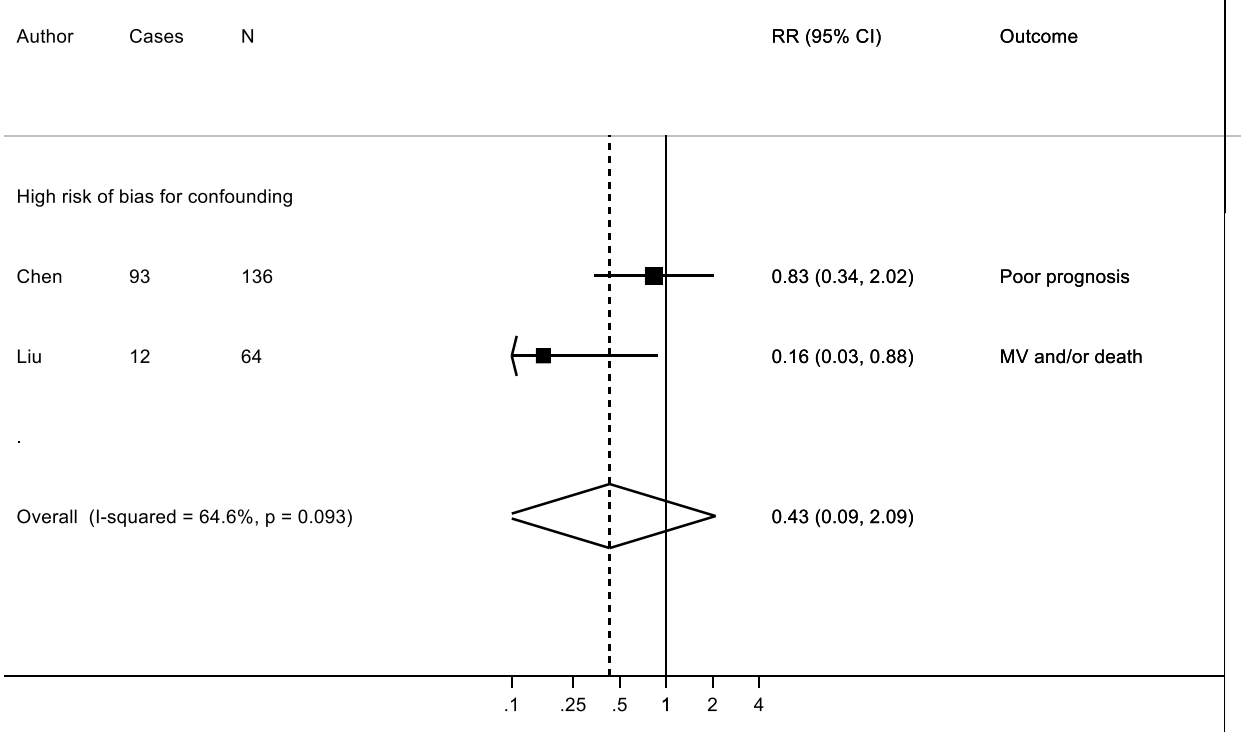


ESM Figure 18: Meta-analysis on use of **sulfonylurea/glinide** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19

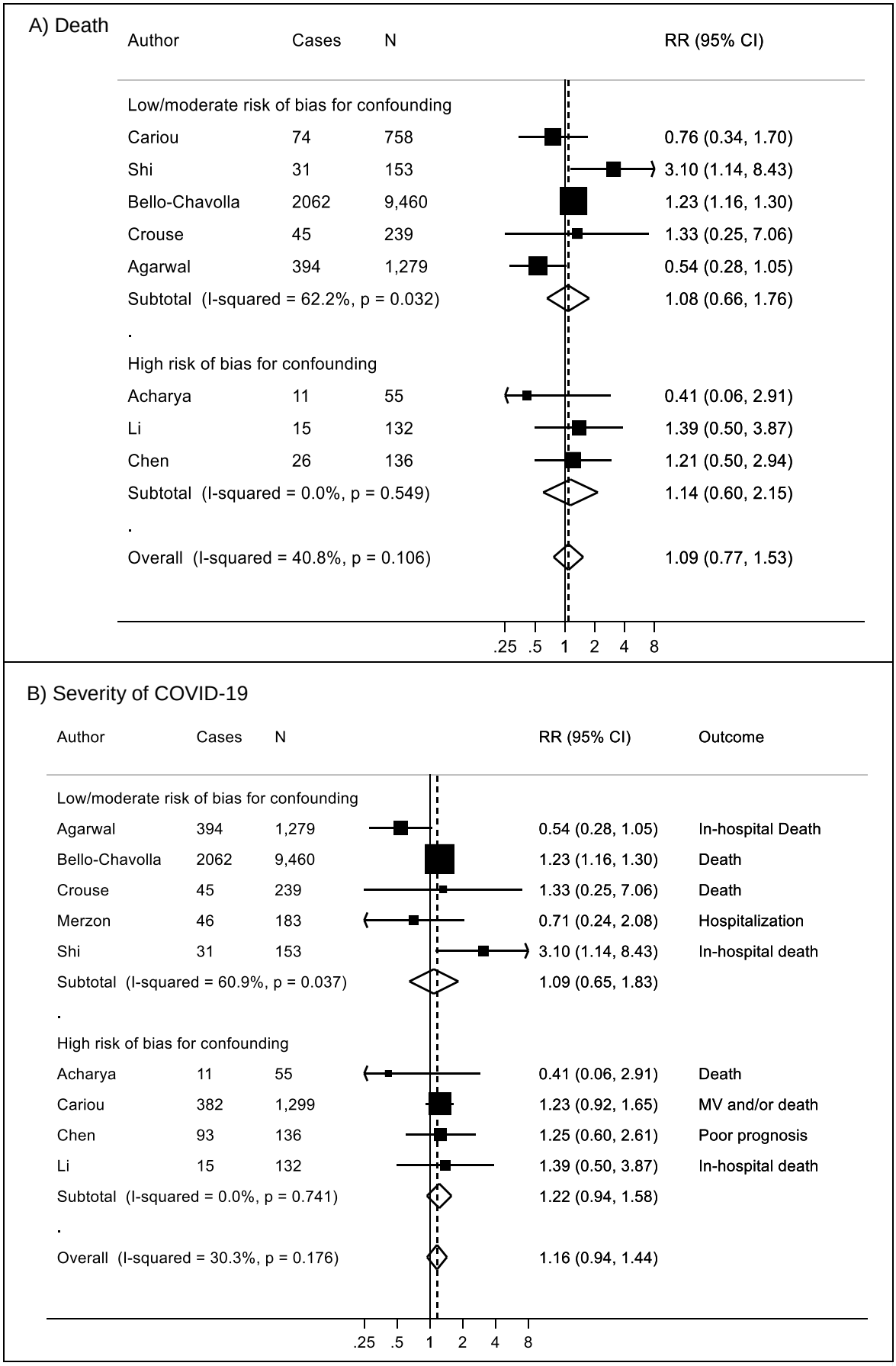
A) Death

No data available

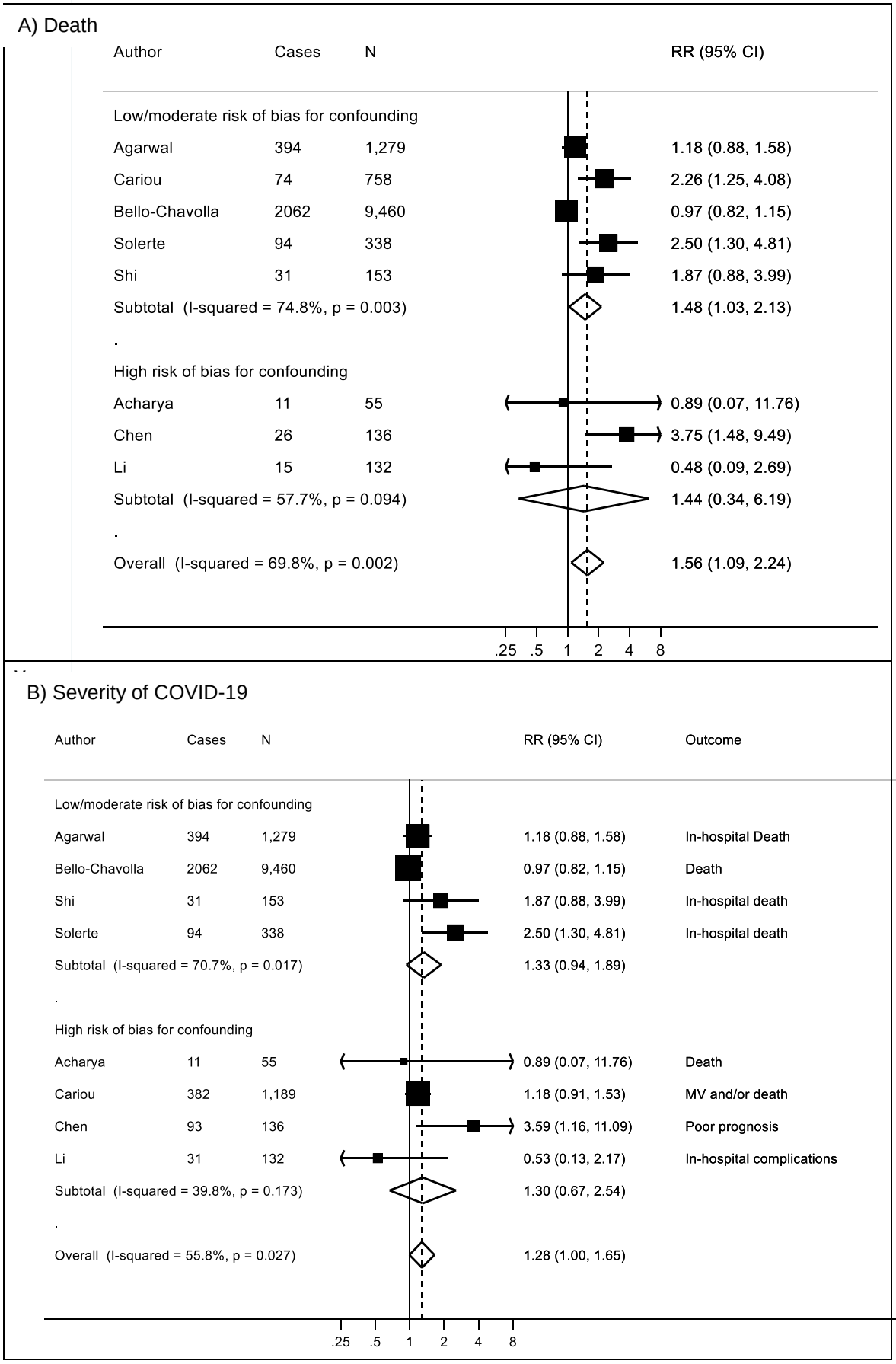
B) Severity of COVID-19



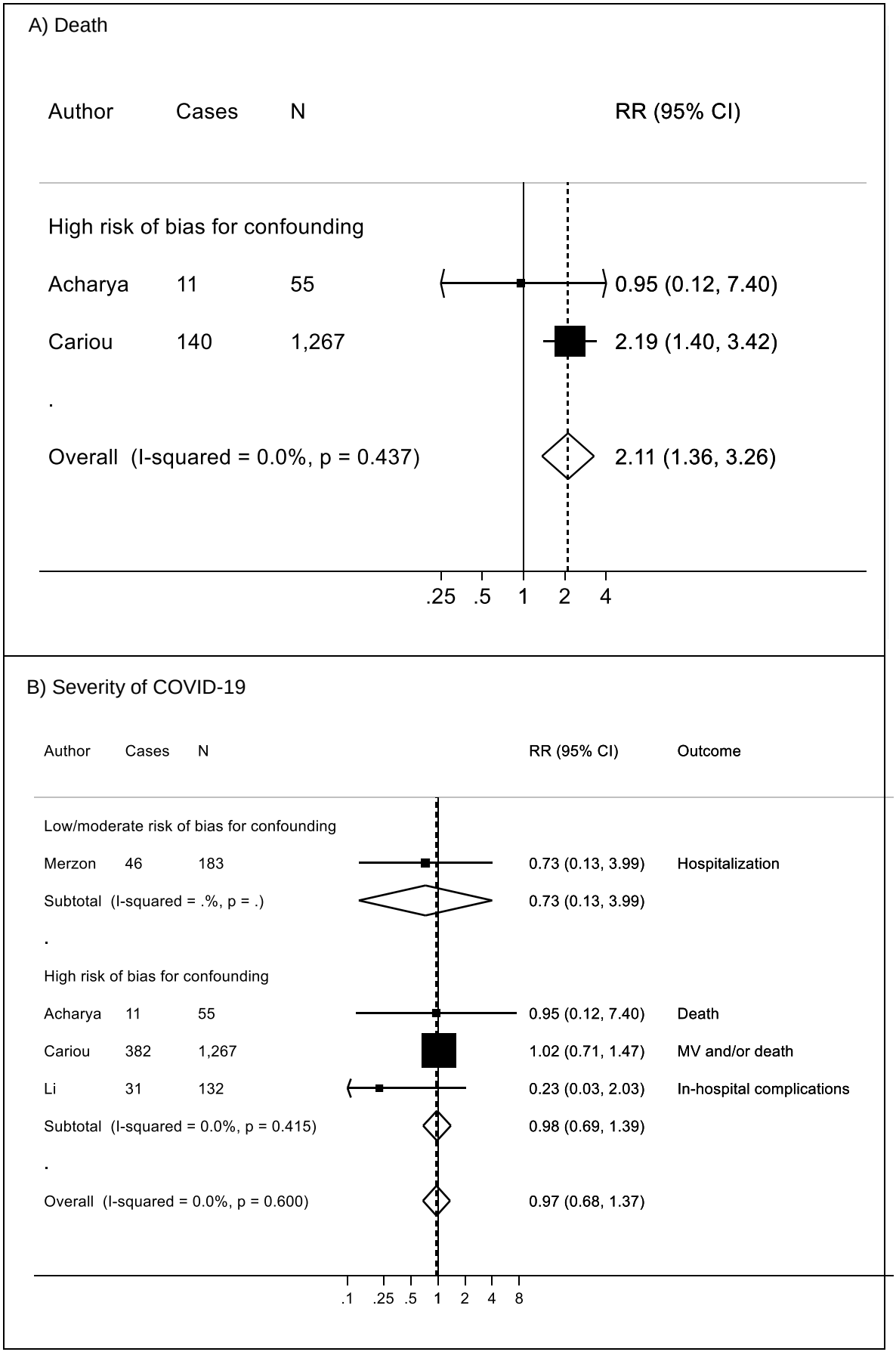
ESM Figure 19: Meta-analysis on use of **alpha-glucosidase inhibitors** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



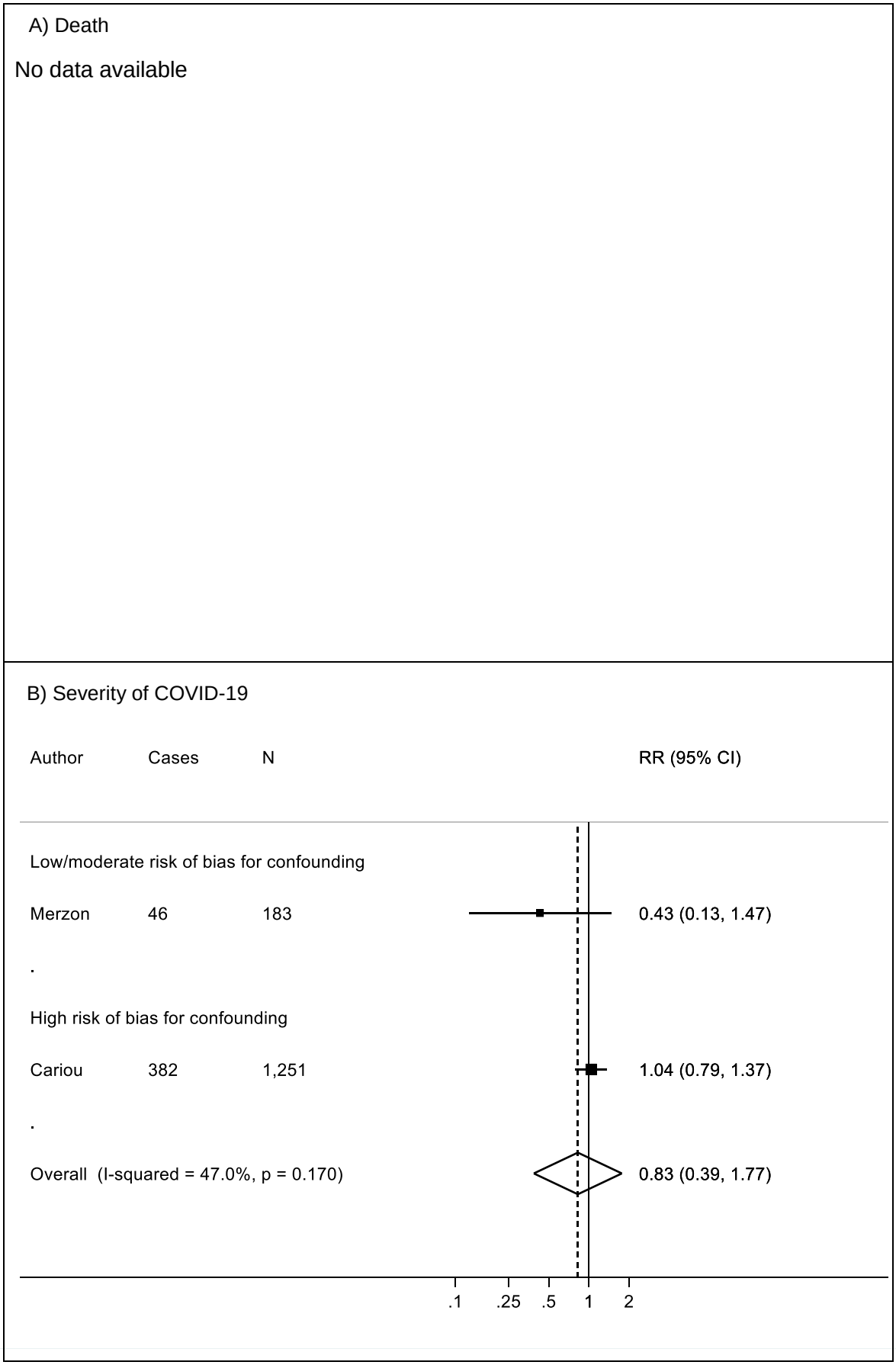
ESM Figure 20: Meta-analysis on **hypertension** compared to no hypertension and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



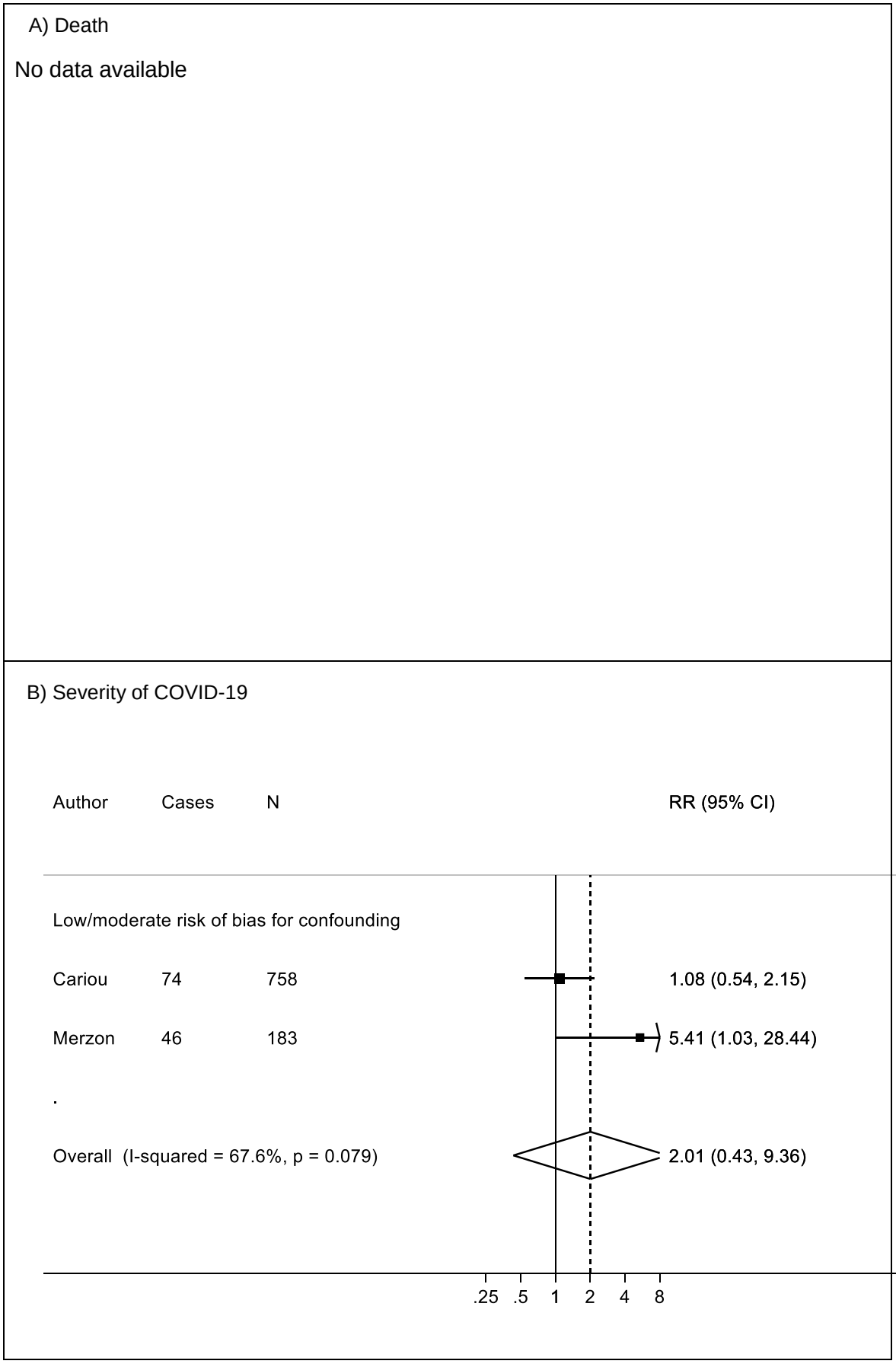
ESM Figure 21: Meta-analysis on pre-existing **cardiovascular disease** (CVD) compared to no CVD and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



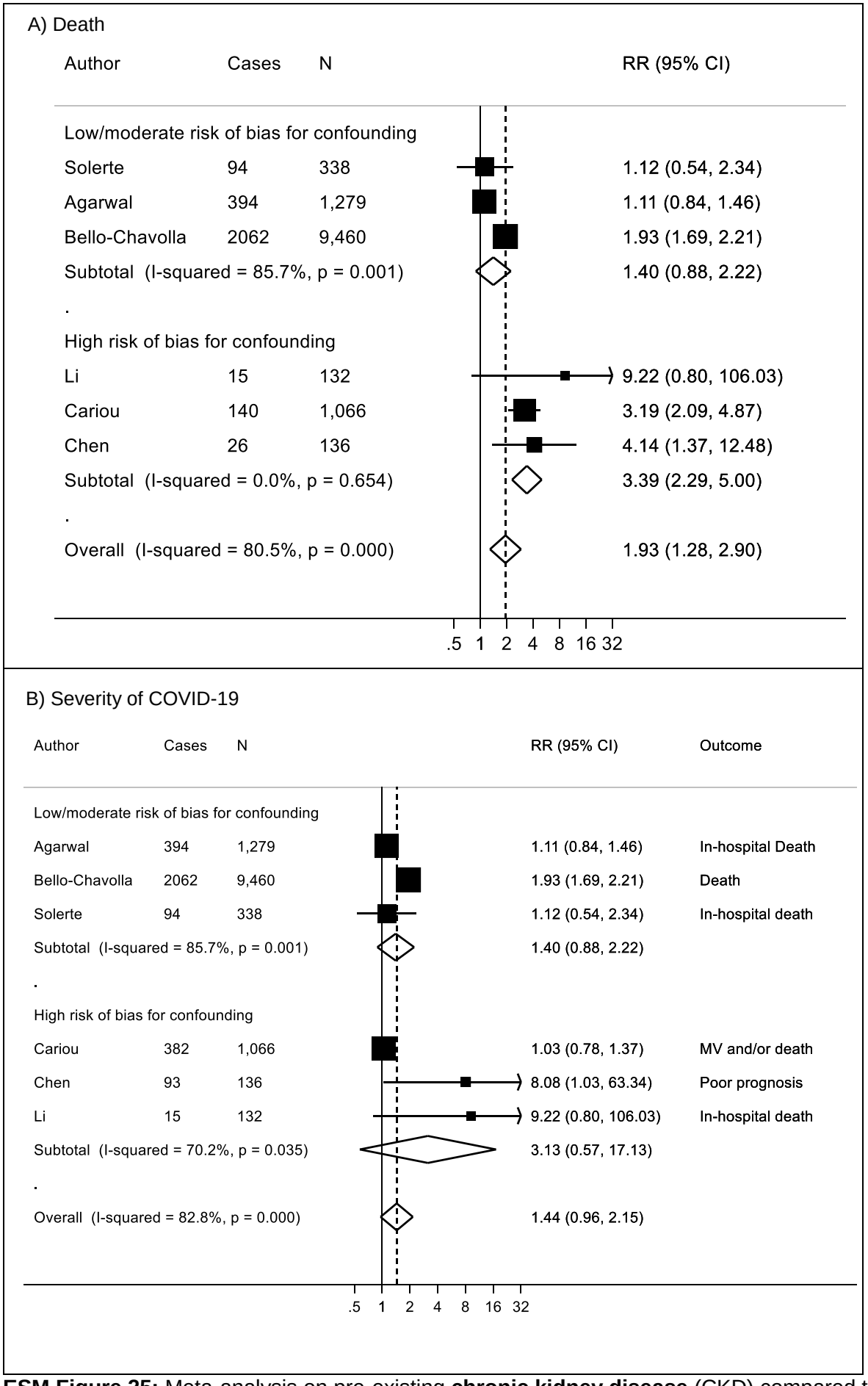
ESM Figure 22: Meta-analysis on pre-existing **cerebrovascular disease** compared to no cerebrovascular disease and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



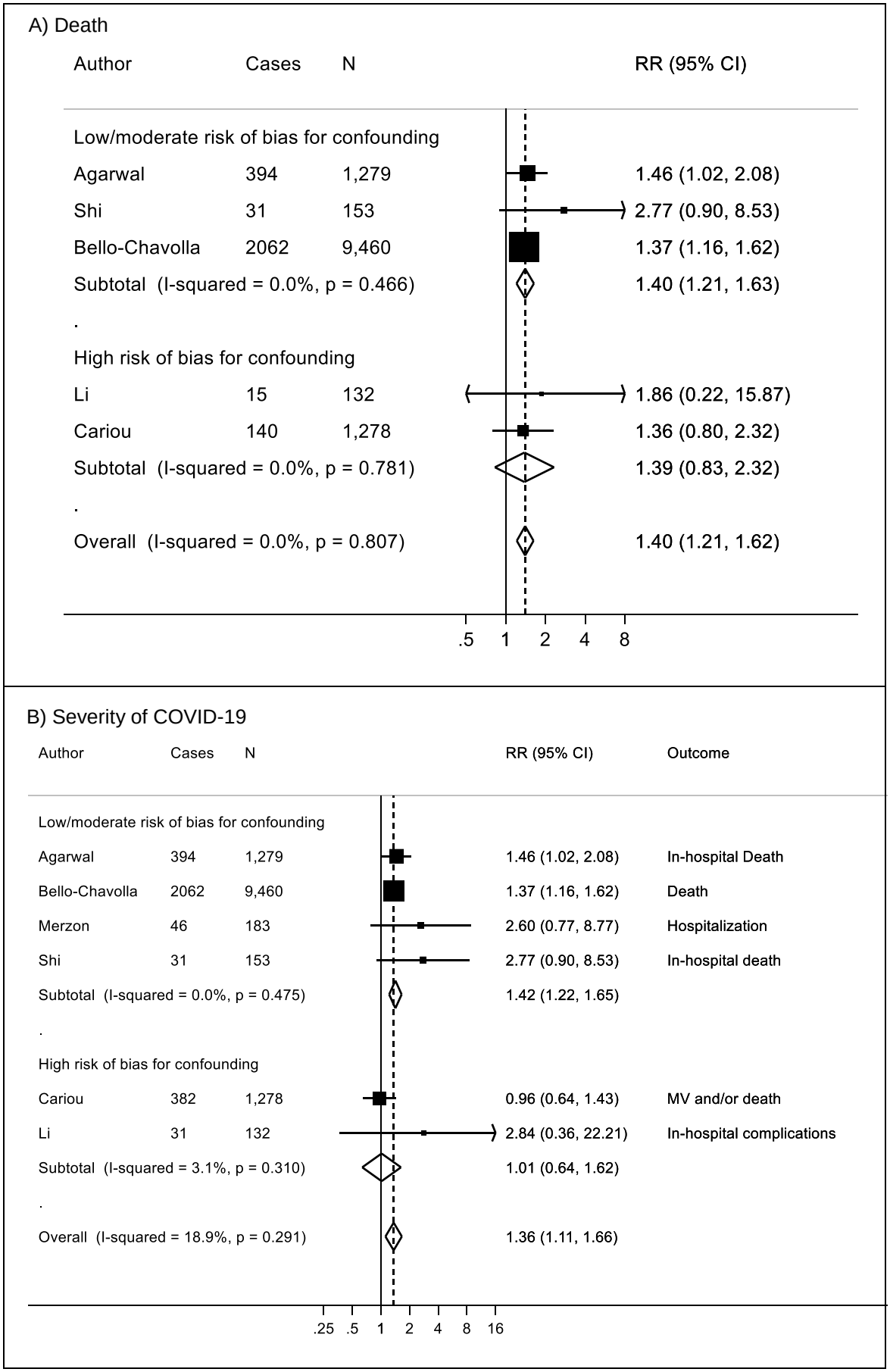
ESM Figure 23: Meta-analysis on pre-existing **ischaemic heart disease** (IHD) compared to no IHD disease and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



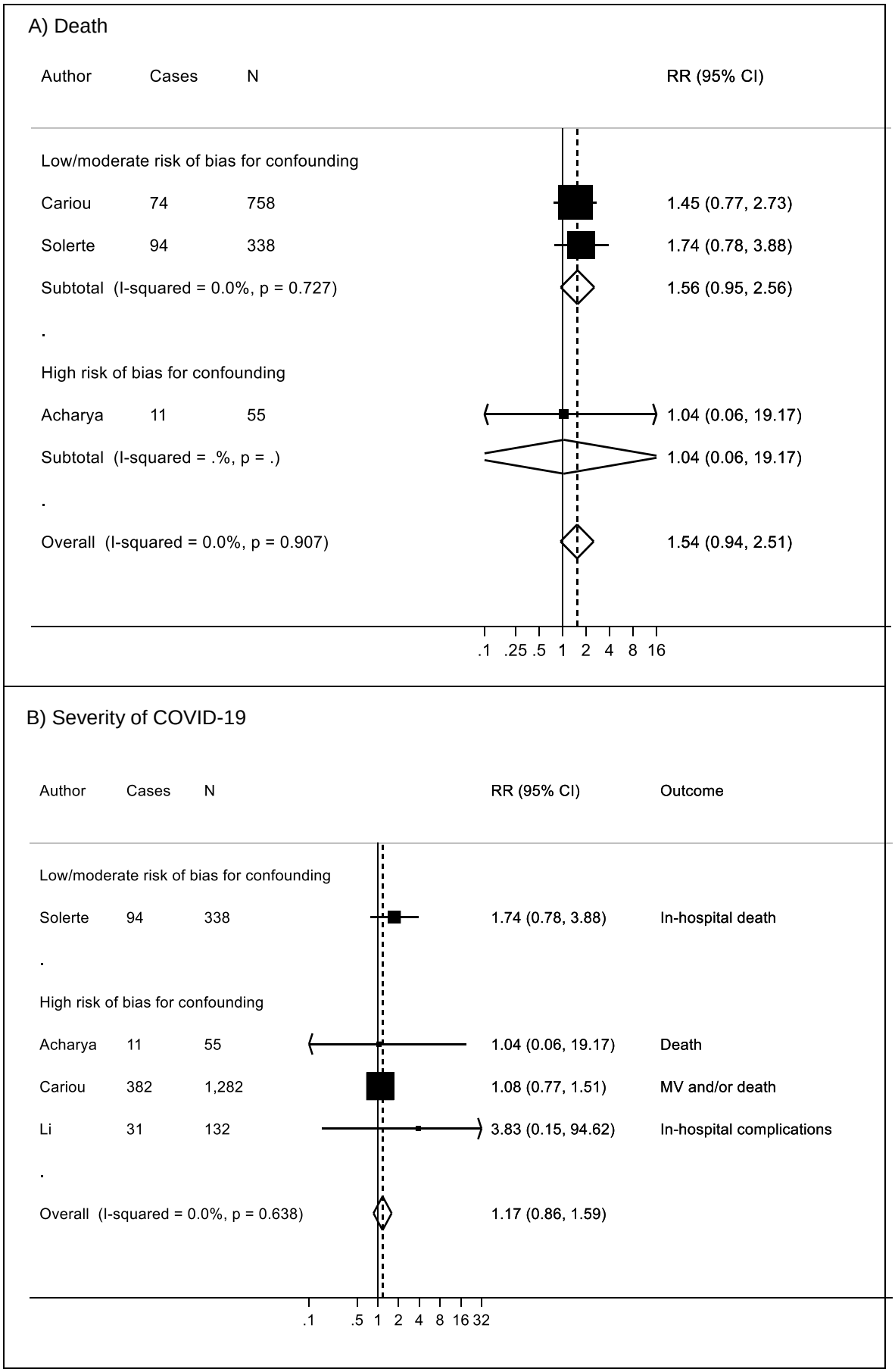
ESM Figure 24: Meta-analysis on pre-existing **heart failure** (HF) compared to no HF disease and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



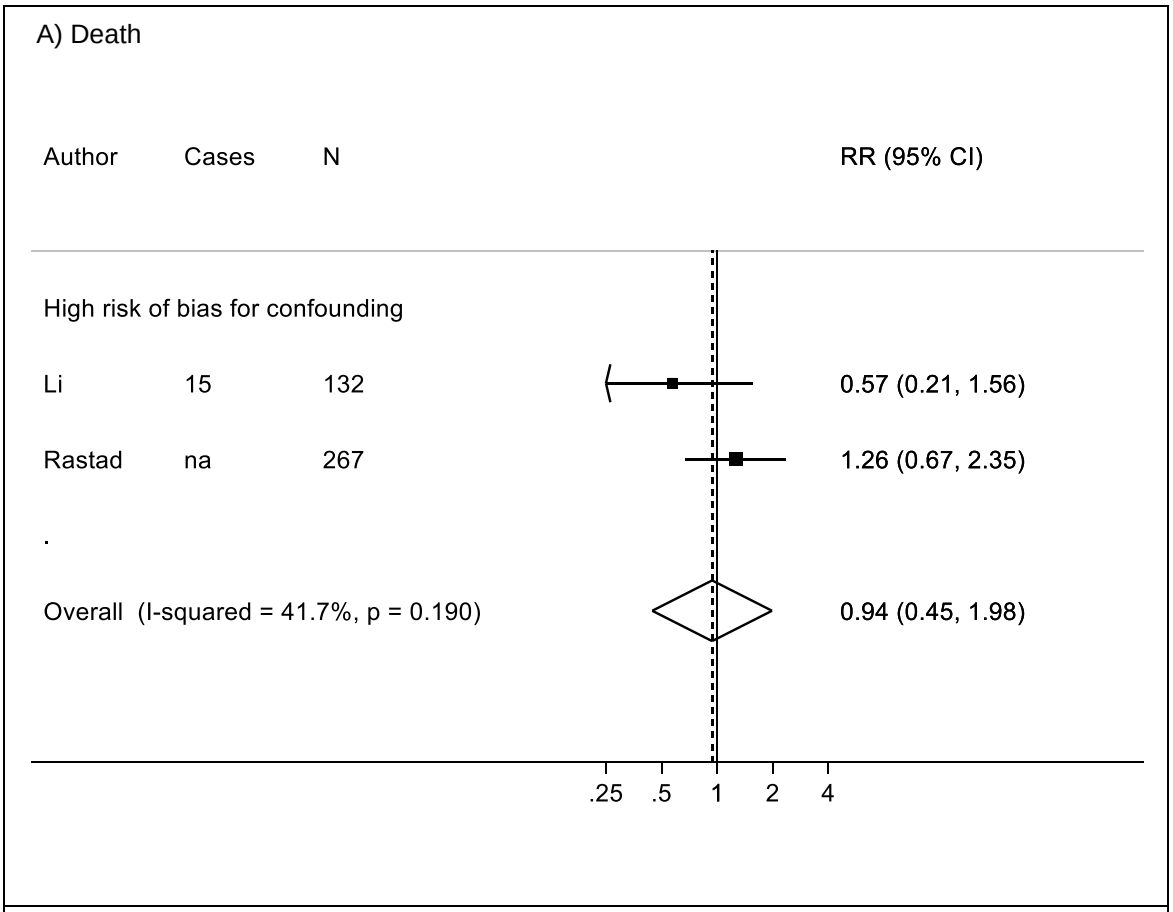
ESM Figure 25: Meta-analysis on pre-existing **chronic kidney disease** (CKD) compared to no CKD and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 26: Meta-analysis on pre-existing **chronic obstructive pulmonary disease** (COPD) compared to no COPD and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



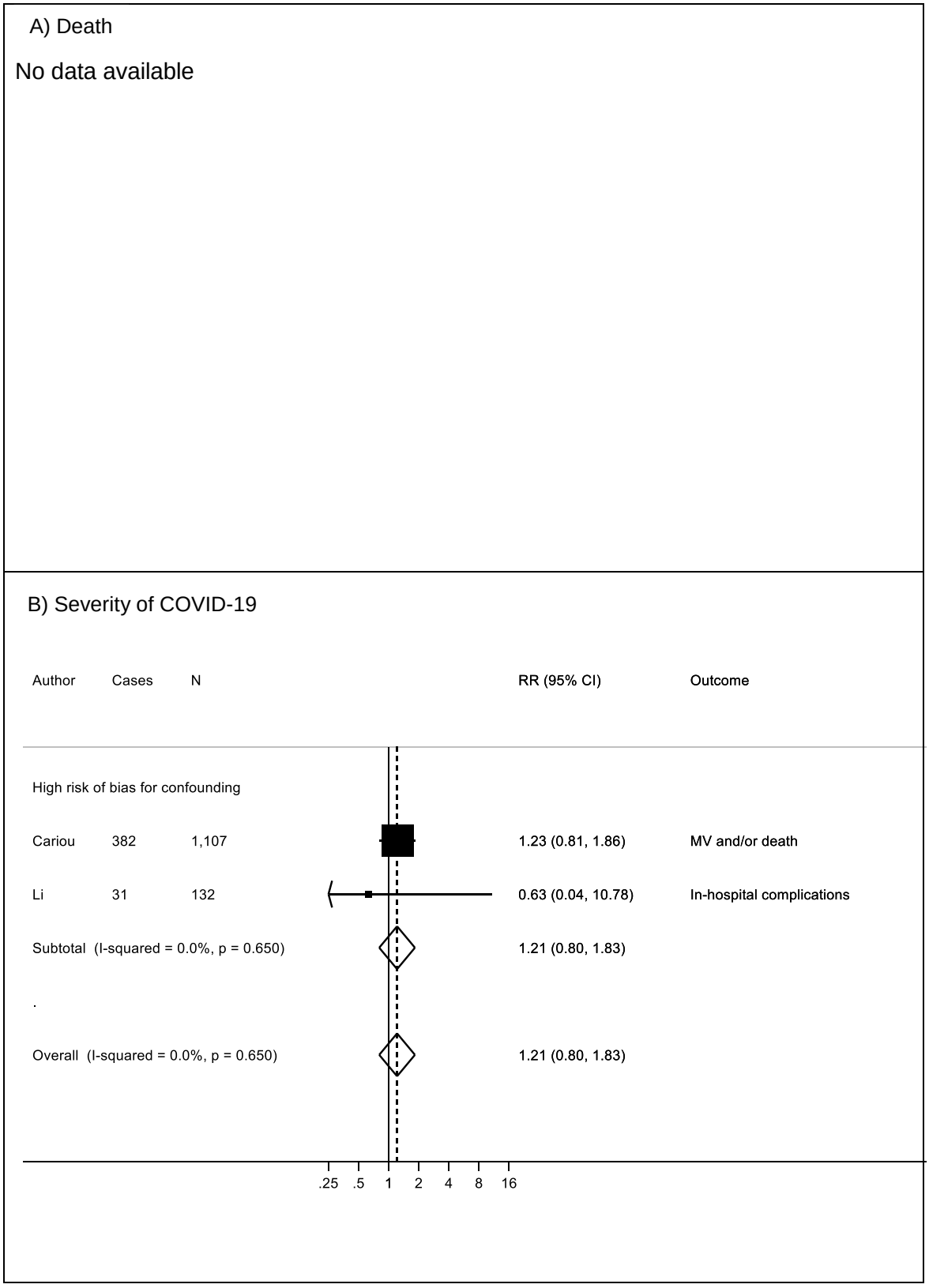
ESM Figure 27: Meta-analysis on pre-existing **cancer** compared to no cancer and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



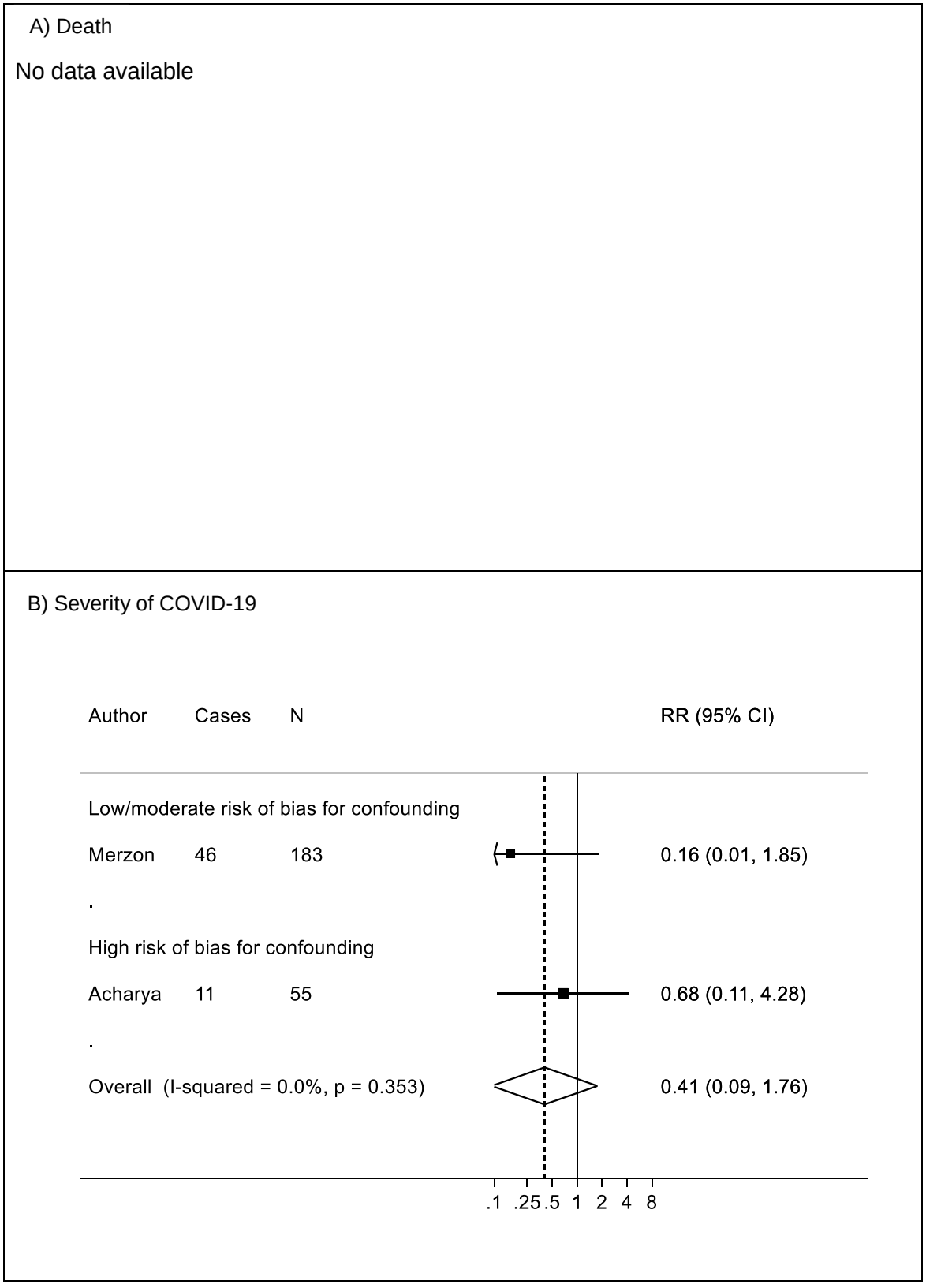
B) Severity of COVID-19

No data available

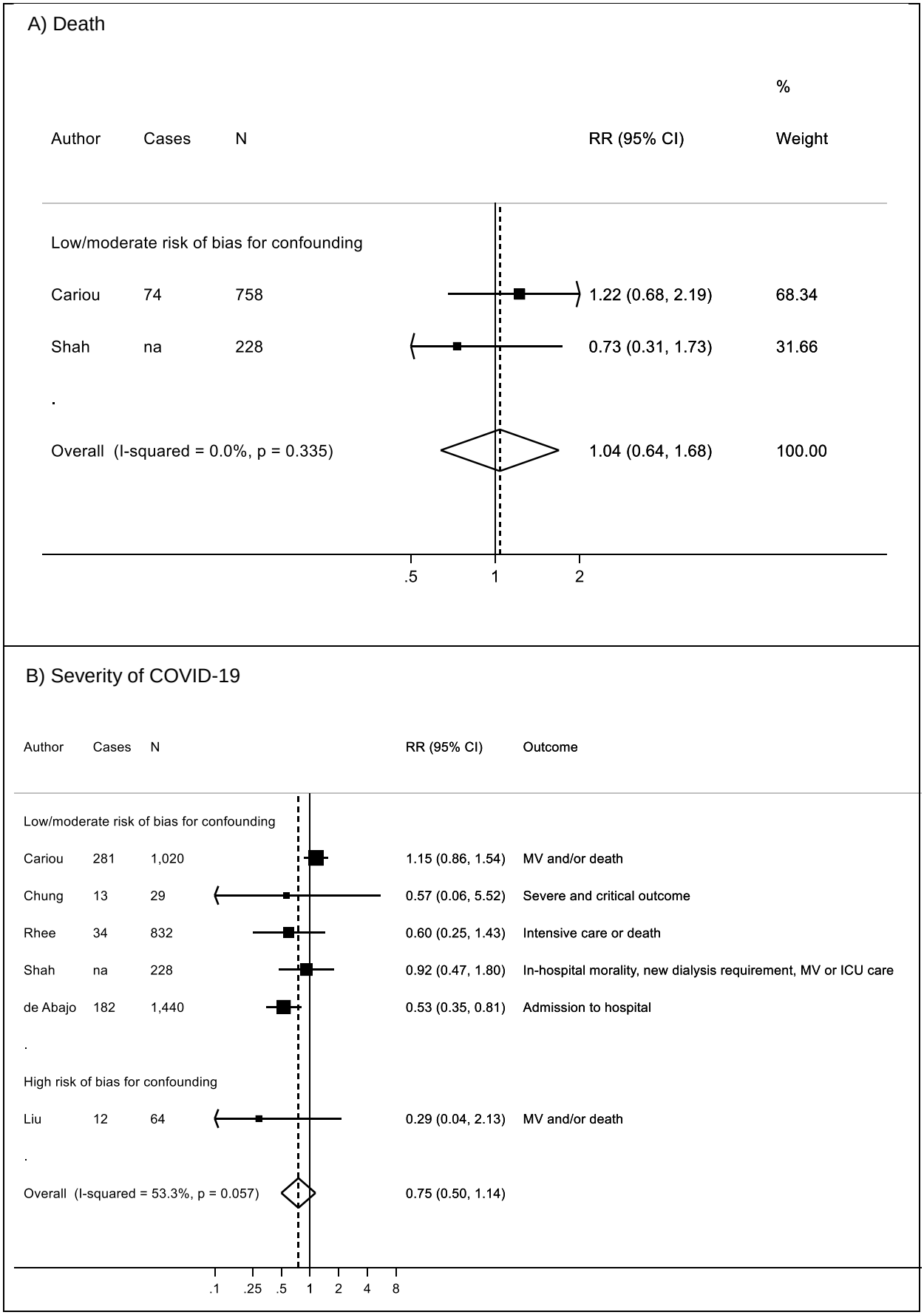
ESM Figure 28: Meta-analysis on **any comorbidities** compared to no comorbidities and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



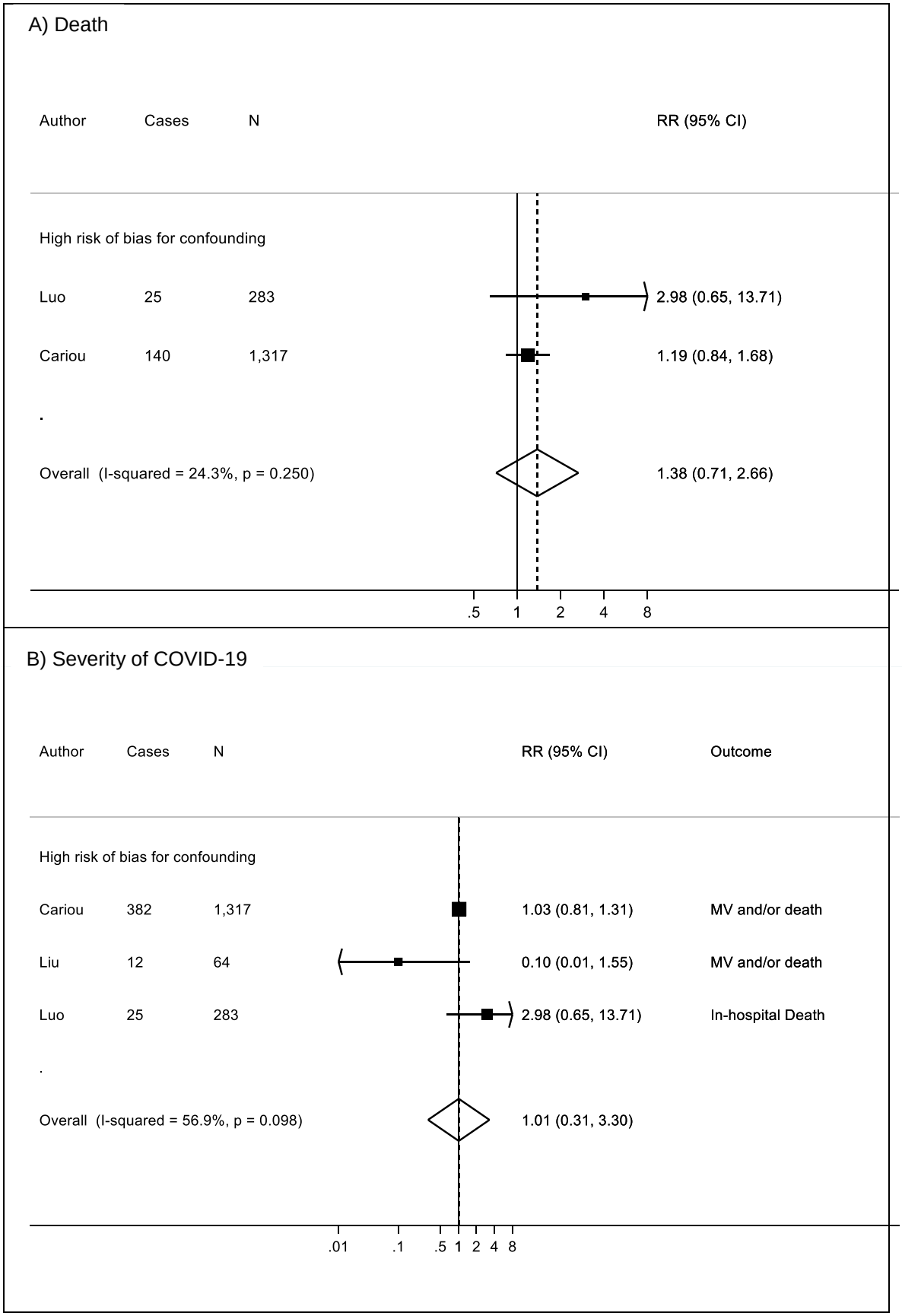
ESM Figure 29: Meta-analysis on pre-existing **liver disease** compared to no liver disease and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



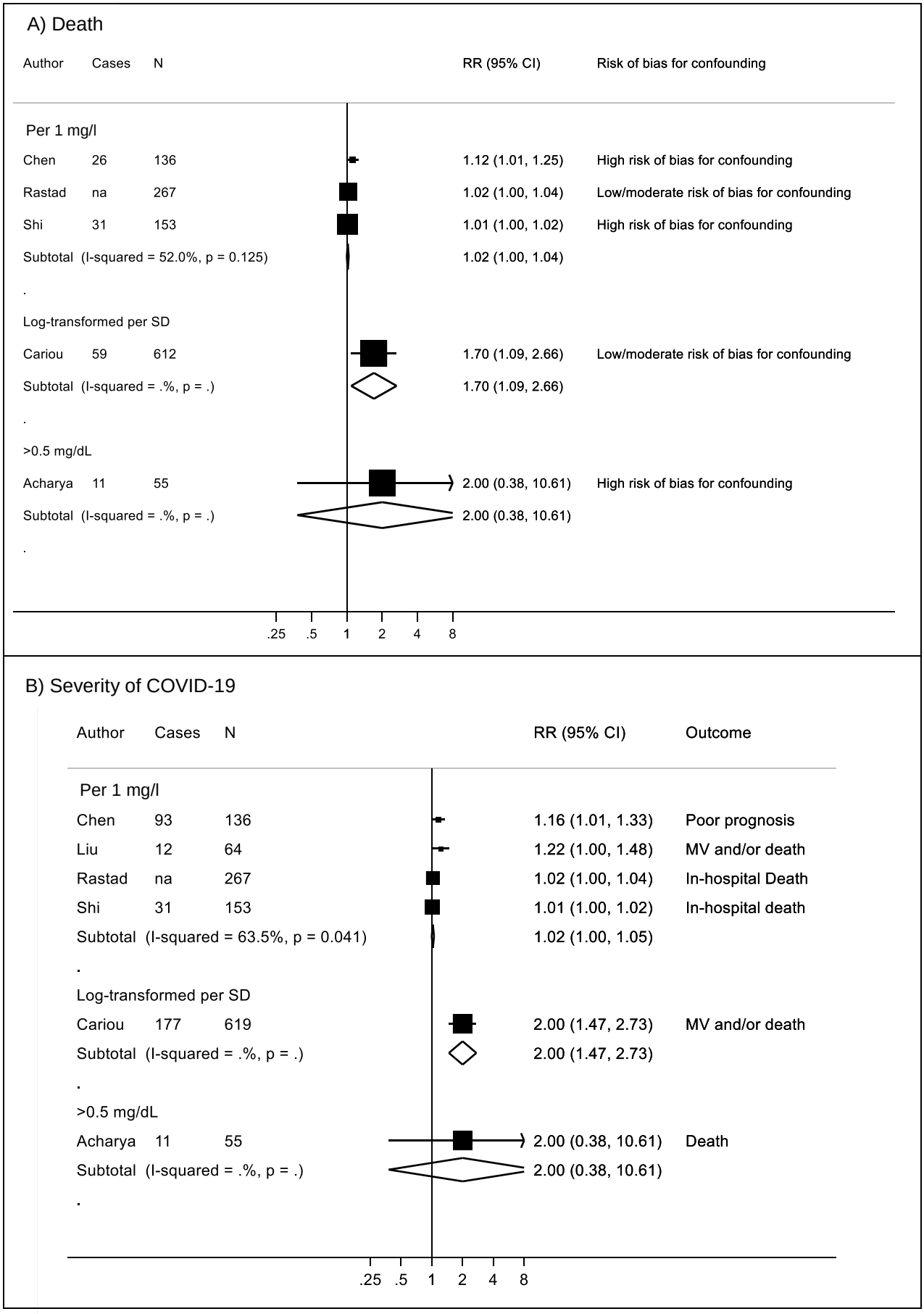
ESM Figure 30: Meta-analysis on pre-existing **dementia** compared to no dementia and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



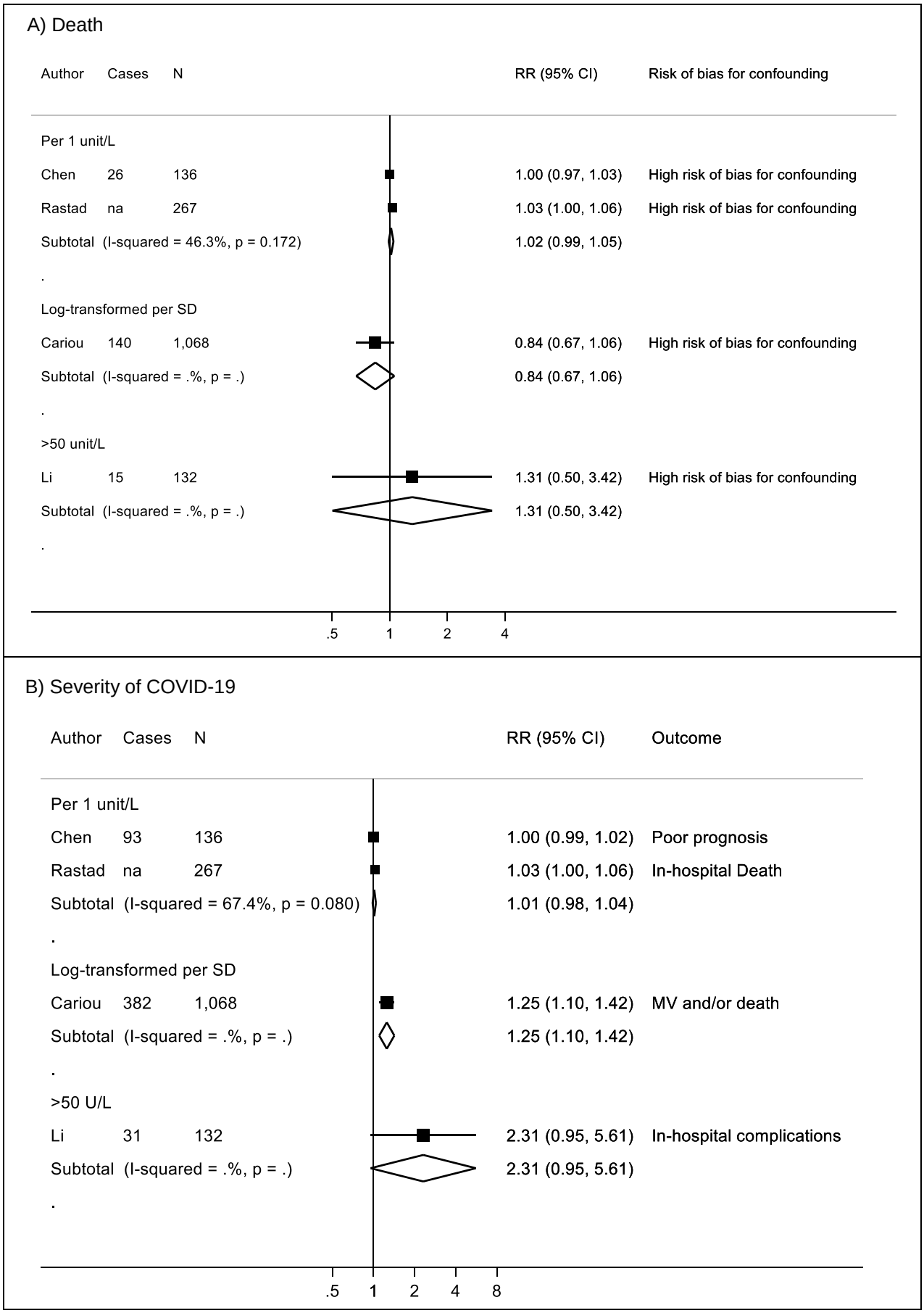
ESM Figure 31: Meta-analysis on **use of renin inhibitor** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



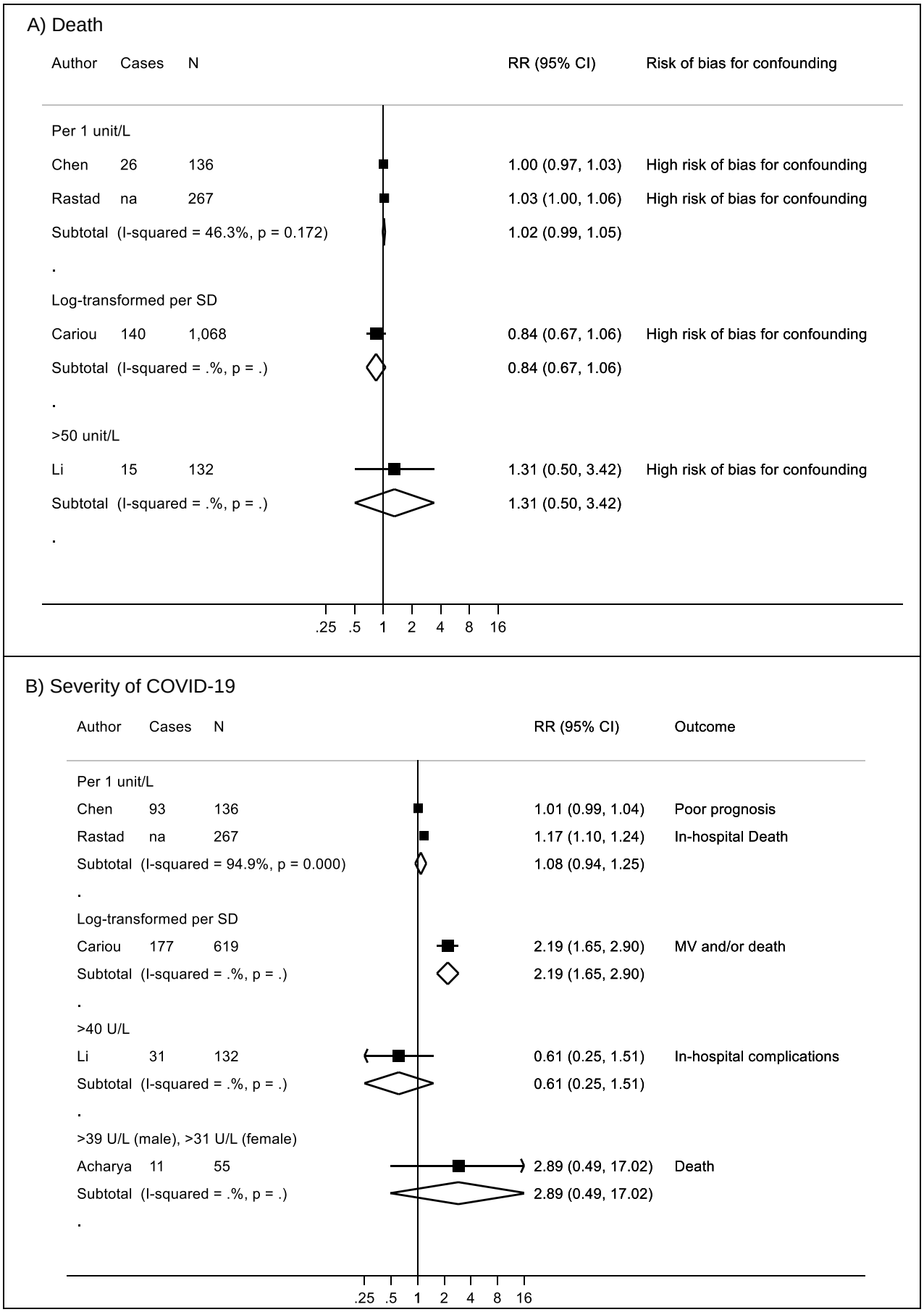
ESM Figure 32: Meta-analysis on **use of statins** compared to non-use and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



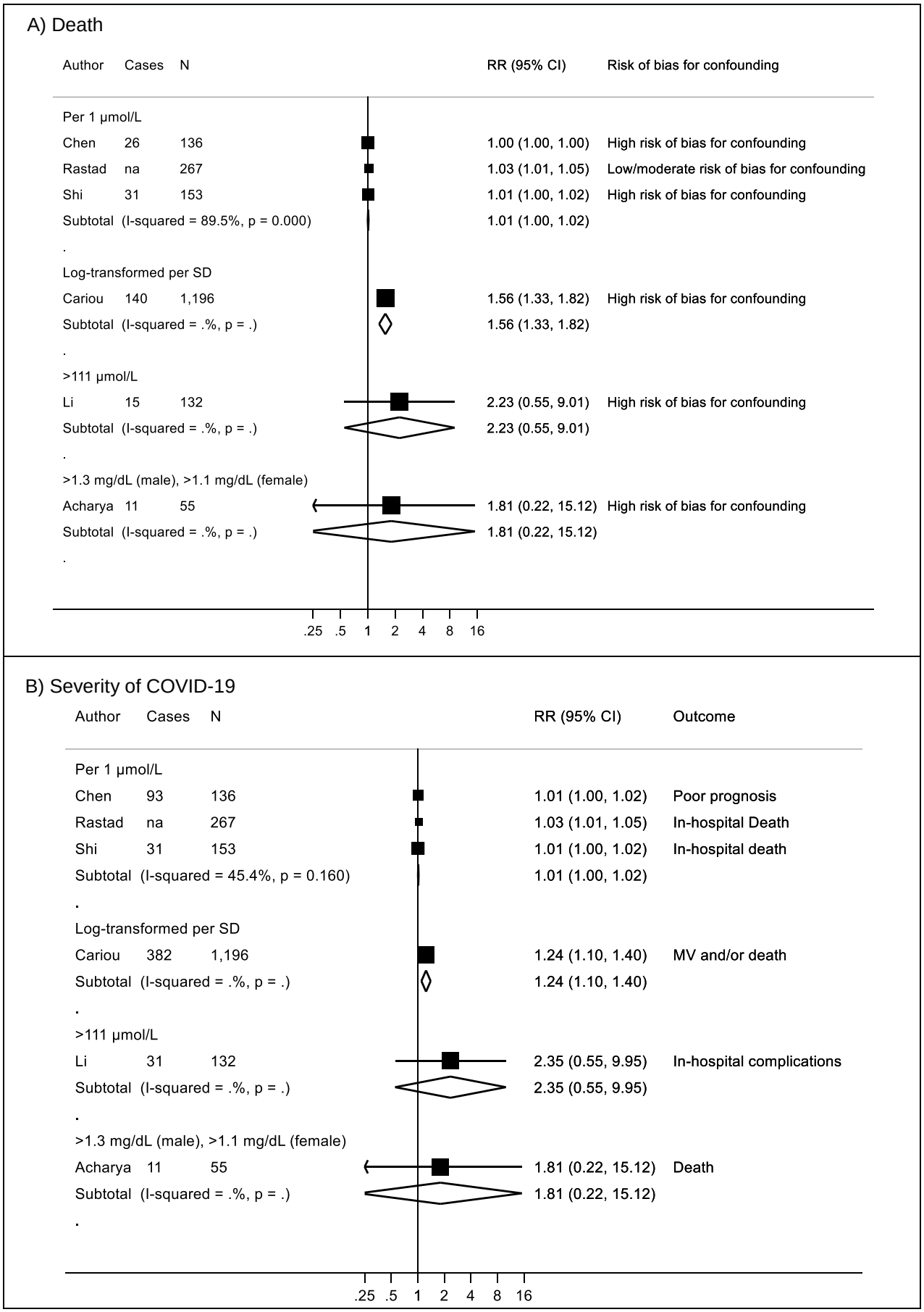
ESM Figure 33: Meta-analysis on **C-reactive protein (CRP)** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



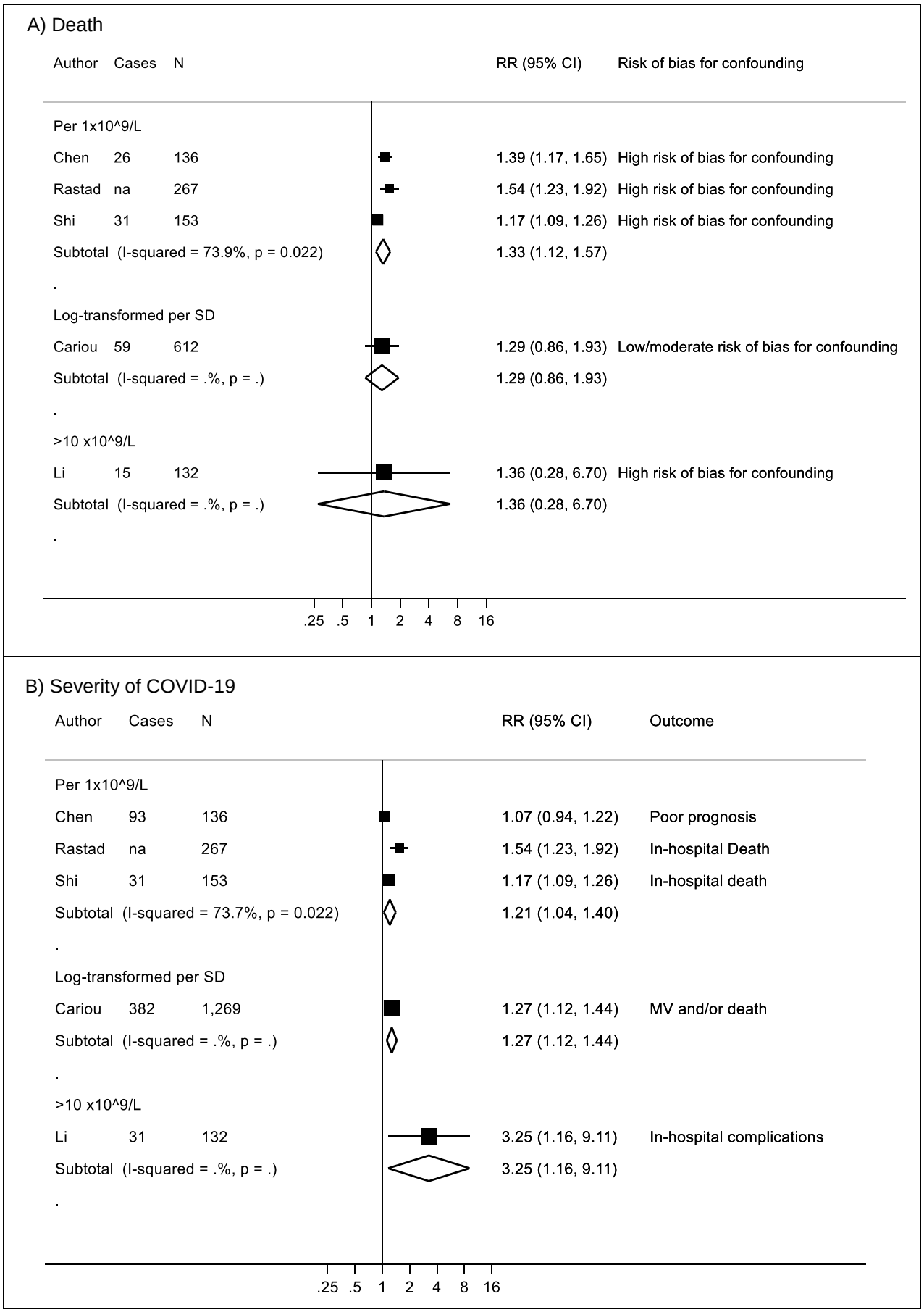
ESM Figure 34: Meta-analysis on **ALT** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



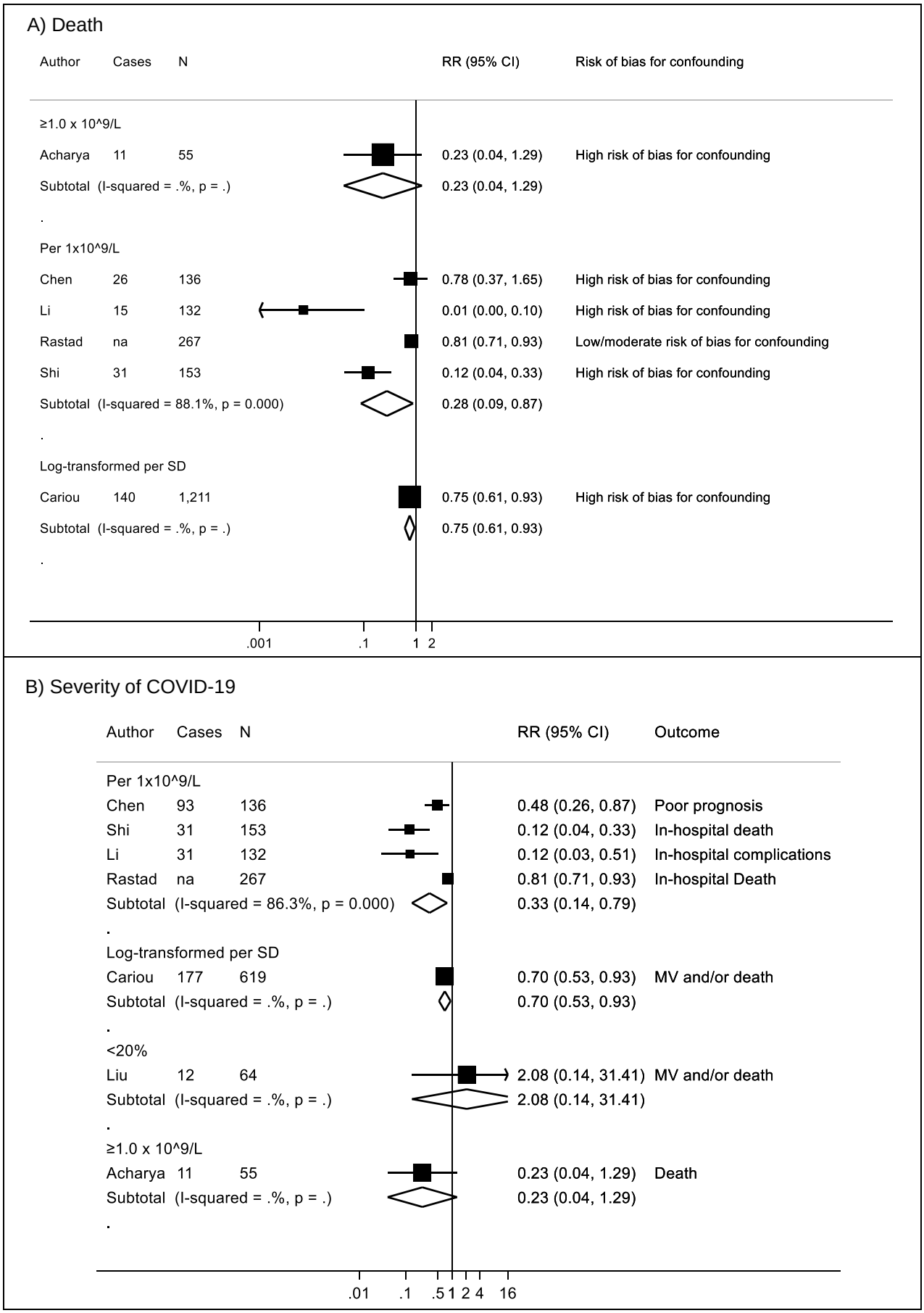
ESM Figure 35: Meta-analysis on **AST** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



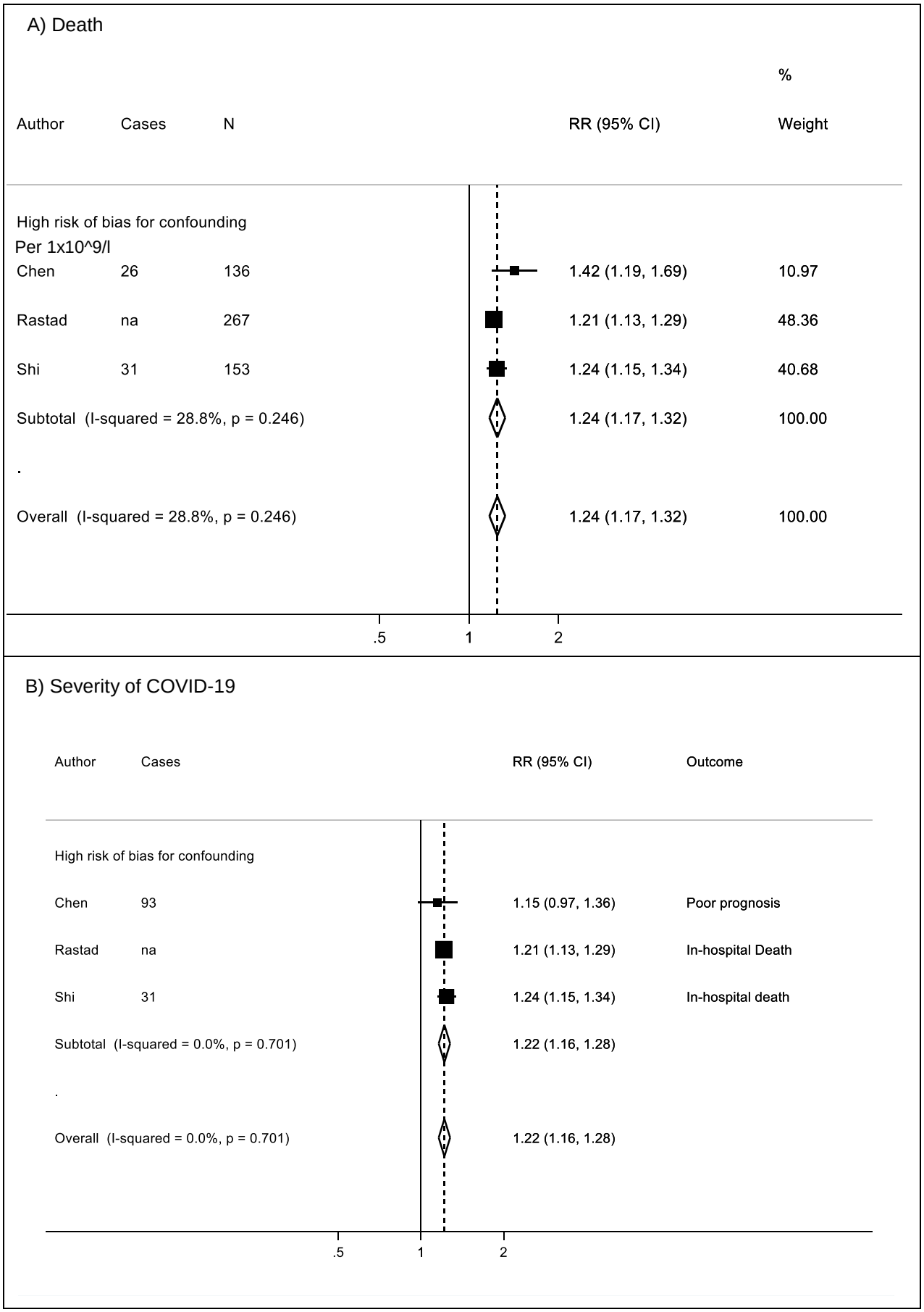
ESM Figure 36: Meta-analysis on **creatinine** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



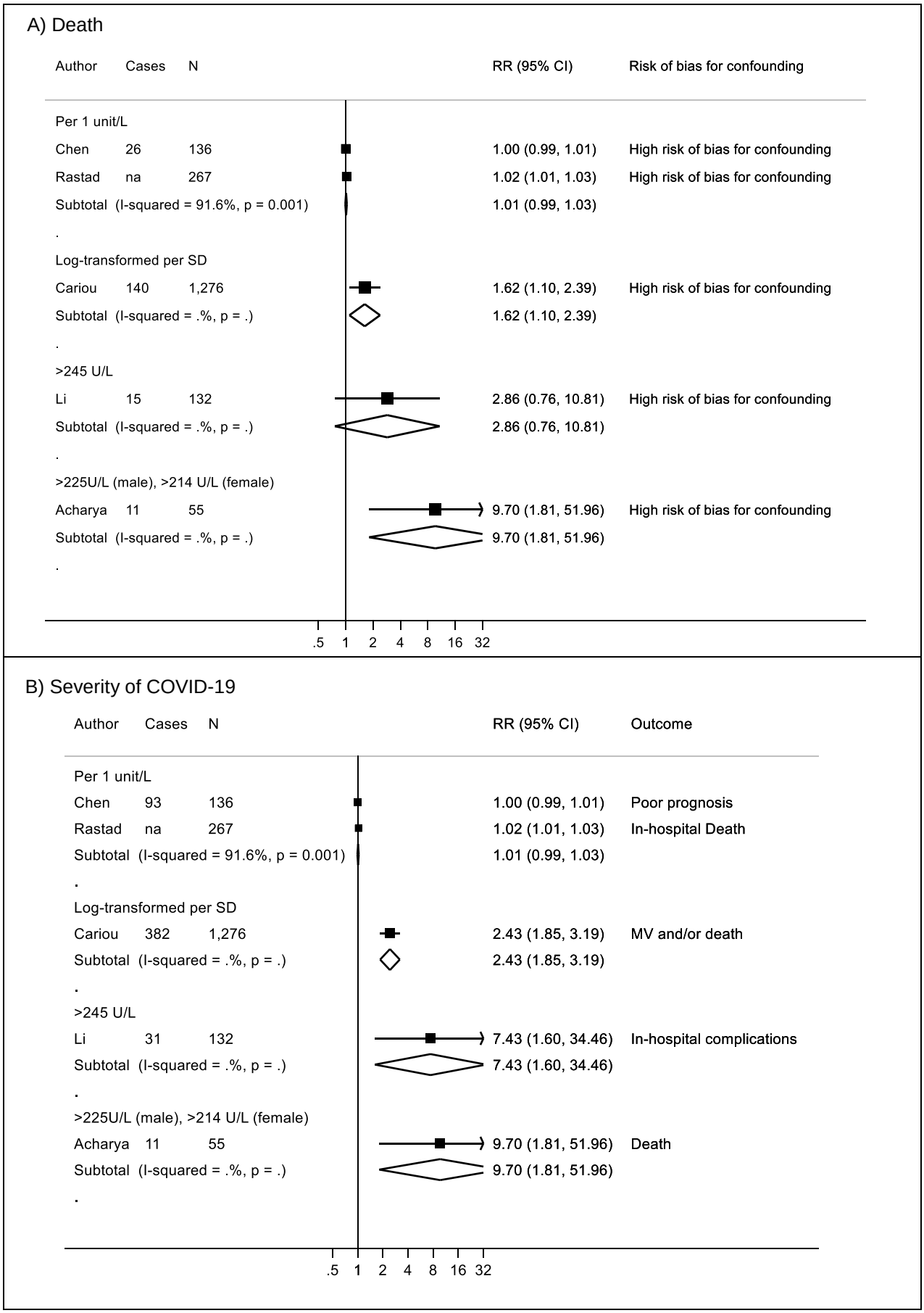
ESM Figure 37: Meta-analysis on **white blood cell count** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



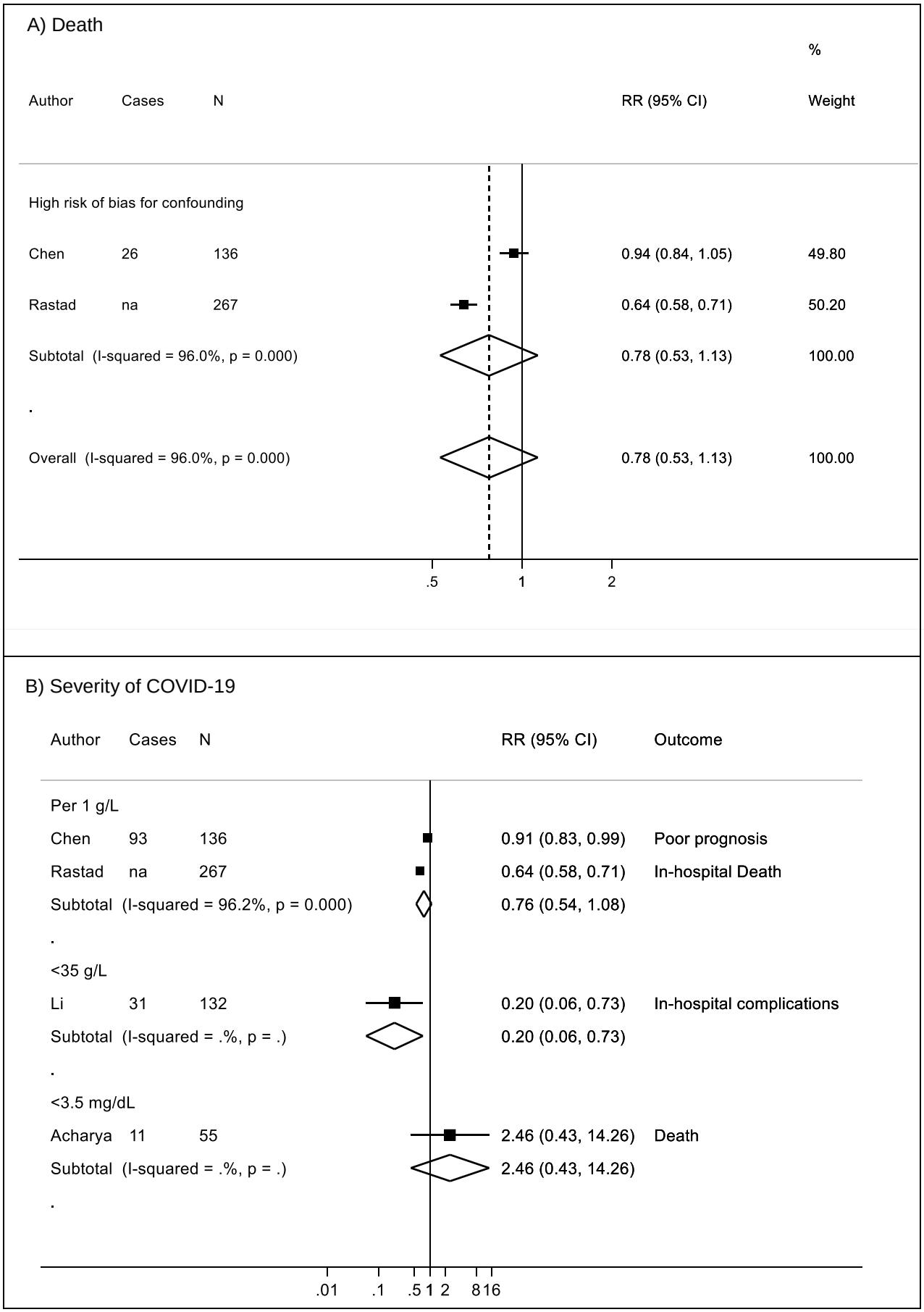
ESM Figure 38: Meta-analysis on **lymphocyte** count and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



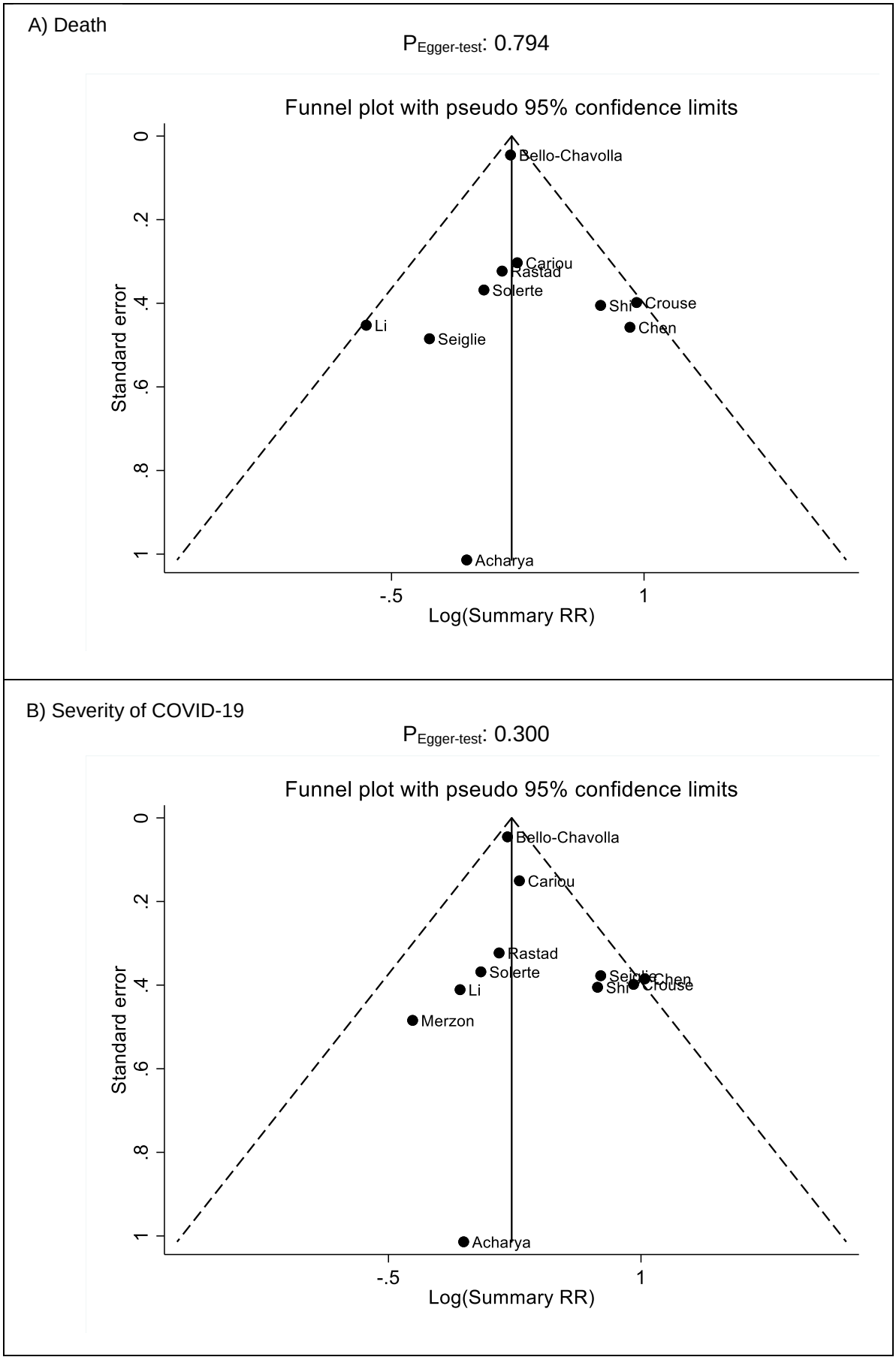
ESM Figure 39: Meta-analysis on **neutrophils** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 40: Meta-analysis on **lactate dehydrogenase** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 41: Meta-analysis on **albumin** and A) death and B) severity of COVID-19 in patients with diabetes and COVID-19



ESM Figure 42: Funnel plot for association between men versus women and A) death and B) severity of COVID-19 in patients with diabetes and COVID -19

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