SUPPLEMENTARY MATERIAL

Efficacy of Probiotics Supplementation On Chronic Kidney Disease: a Systematic Review and Meta-Analysis

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Supplementary Table S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	p.1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p.2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	p.4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p.5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	p.5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	p.6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p.5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file 2

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p.6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p.7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	p.6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p.7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	p.8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^{2)}$ for each meta-analysis.	p.8

Supplementary Methods Section. Searching strategies of Pubmed, EMBASE and Cochrane Library.

For Pubmed

1# ((((((((((((((((("Renal Insufficiency, Chronic"[Mesh]) OR Chronic Renal Insufficiencies) OR Renal Insufficiencies, Chronic) OR Chronic Renal Insufficiency) OR Kidney Insufficiency, Chronic) OR Chronic Kidney Insufficiency) OR Chronic Kidney Insufficiencies) OR Kidney Insufficiencies, Chronic) OR Chronic Kidney Diseases) OR Chronic Kidney Disease) OR Disease, Chronic Kidney) OR Diseases, Chronic Kidney) OR Kidney Disease, Chronic) OR Kidney Diseases, Chronic) OR Chronic Renal Diseases) OR Chronic Renal Disease) OR Disease, Chronic Renal) OR Diseases, Chronic Renal) OR Renal Disease, Chronic) OR Renal Diseases, Chronic

2# ((((((((((((((End-Stage Kidney Disease) OR Disease, End-Stage Kidney) OR End Stage Kidney Disease) OR Kidney Disease, End-Stage) OR Chronic Kidney Failure) OR End-Stage Renal Disease) OR Disease, End-Stage Renal) OR End Stage Renal Disease) OR Renal Disease, End-Stage) OR Renal Disease, End Stage) OR Renal Failure, End-Stage) OR End-Stage Renal Failure) OR Renal Failure, End Stage) OR Renal Failure, Chronic) OR Chronic Renal Failure) OR ESRD) OR "Kidney Failure, Chronic"[Mesh]

#3 #1 OR #2

#4 ("Probiotics"[Mesh]) OR probiotic

#5 #3 AND #4

For EMBASE

#1 'chronic kidney failure'/exp OR 'chronic kidney failure'

#2 'renal insufficiency, chronic'/exp OR 'renal insufficiency, chronic' OR 'chronic renal insufficiencies' OR 'renal insufficiencies, chronic' OR 'chronic renal insufficiency'/exp OR 'chronic renal insufficiency' OR 'kidney insufficiency, chronic' OR 'chronic kidney insufficiency'/exp OR 'chronic kidney insufficiency' OR 'chronic kidney insufficiencies' OR 'kidney insufficiencies, chronic' OR 'chronic kidney diseases' OR 'chronic kidney disease'/exp OR 'chronic kidney disease' OR 'disease, chronic kidney' OR 'diseases,

chronic kidney' OR 'kidney disease, chronic'/exp OR 'kidney disease, chronic' OR 'kidney diseases, chronic' OR 'chronic renal diseases' OR 'chronic renal disease'/exp OR 'chronic renal disease' OR 'disease, chronic renal' OR 'diseases, chronic renal' OR 'renal disease, chronic' OR 'renal diseases, chronic'

#3 #1 OR #2

#4 'end stage renal disease'/exp

#5 'kidney failure, chronic'/exp OR 'kidney failure, chronic' OR 'end-stage kidney disease'/exp OR 'end-stage kidney disease' OR 'disease, end-stage kidney' OR 'end stage kidney disease'/exp OR 'end stage kidney disease' OR 'kidney disease, end-stage' OR 'chronic kidney failure'/exp OR 'chronic kidney failure' OR 'end-stage renal disease'/exp OR 'end-stage renal disease' OR 'disease, end-stage renal' OR 'end stage renal disease'/exp OR 'end stage renal disease' OR 'renal disease, end-stage' OR 'renal disease, end stage' OR 'renal failure, end-stage' OR 'end-stage renal failure'/exp OR 'end-stage renal failure' OR 'renal failure, end stage' OR 'renal failure, chronic' OR 'chronic renal failure'/exp OR 'chronic renal failure' OR 'esrd'/exp OR 'esrd'

#6 #4 OR #5

#7 #3 OR #6

#8 'probiotic agent'/exp

#9 'probiotics'/exp OR probiotics

#10 'probiotic'/exp OR probiotic

#11 #8 OR #9 OR #10

#12 #7 AND #11

For Cochrane Liberary

#1 MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees

#2 ‘Renal Insufficiency, Chronic’ or ‘Chronic Renal Insufficiencies’ or ‘Renal Insufficiencies, Chronic’ or ‘Chronic Renal Insufficiency’ or ‘Kidney Insufficiency, Chronic’ or ‘Chronic Kidney Insufficiency’ or ‘Chronic Kidney Insufficiencies’ or ‘Kidney Insufficiencies, Chronic’ or ‘Chronic Kidney Diseases’ or ‘Chronic Kidney Disease’ or ‘Disease, Chronic Kidney’ or ‘Diseases, Chronic Kidney’ or ‘Kidney

Disease, Chronic' or 'Kidney Diseases, Chronic' or 'Chronic Renal Diseases' or 'Chronic Renal Disease' or 'Disease, Chronic Renal' or 'Diseases, Chronic Renal' or 'Renal Disease, Chronic' or 'Renal Diseases, Chronic'

#3 #1 OR #2

#4 MeSH descriptor: [Kidney Failure, Chronic] explode all trees

#5 'Kidney Failure, Chronic' or 'End-Stage Kidney Disease' or 'Disease, End-Stage Kidney' or 'End Stage Kidney Disease' or 'Kidney Disease, End-Stage' or 'Chronic Kidney Failure' or 'End-Stage Renal Disease' or 'Disease, End-Stage Renal' or 'End Stage Renal Disease' or 'Renal Disease, End-Stage' or 'Renal Disease, End Stage' or 'Renal Failure, End-Stage' or 'End-Stage Renal Failure' or 'Renal Failure, End Stage' or 'Renal Failure, Chronic' or 'Chronic Renal Failure' or 'ESRD'

#6 #4 OR #5

#7 #3 OR #6

#8 MeSH descriptor: [Probiotics] explode all trees

#9 probiotic

#10 #8 OR #9

#11 #7 AND #10

Supplementary Table S2. Risk of bias in each study.

Bias	Authors judgement	Evidence for judgement
Rangananthan 2010		
Random sequence generation	Unclear risk	It is unclear how were the random sequence generated. "The patients were randomized into two study arms: Group A and Group B".
Allocation concealment	Unclear risk	Not reported.
Blinding of participants and personnel	Unclear risk	Not reported.
Blinding of outcome assessment	Unclear risk	Not reported.
Incomplete outcome data	Low risk	Of the 62 subjects enrolled (all four sites combined), 46 completed the study, with the rest being lost to follow-up.
Selective reporting	High risk	Microbial counts were not reported in results.
Other bias	High risk	No wash out period.
Rangananthan 2014		
Random sequence generation	Unclear risk	Not reported.
Allocation concealment	Unclear risk	Not reported.

Blinding of participants and personnel	Unclear risk	Not reported.
Blinding of outcome assessment	Unclear risk	Not reported.
Incomplete outcome data	Low risks	Two patients withdrew consent after the baseline visit (T0). Four more dropped out after visit 1 (T1): 1 was transferred to a different facility, 2 withdrew consent, and 1 passed away of unrelated causes.
Selective reporting	High risk	NF-κB, free indoxyl sulfate, total and free indoxyl glucuronide, total and free indole acetic acid (IAA), total and free p-cresyl sulfate, total and free hippuric acid, pentosidine sulfate, β-2 microglobulin and 3-carboxyl-4-methyl-5-propyl-2-furan-propanoic acid (CMPF) were not reported
Other bias	Low risk	Other bias was not found.
Guida 2014		
Random sequence generation	Low risk	Patients were allocated to the two study groups

		by simple randomization using a computer-generated random binary list.
Allocation concealment	Unclear risk	Not reported.
Blinding of participants and personnel	Low risk	Neither the patients nor the medical doctors performing further patient evaluation were aware of group assignment.
Blinding of outcome assessment	Unclear risk	Not reported.
Incomplete outcome data	Low risk	All patients completed the study and no dropout was observed.
Selective reporting	Low risk	All the results were reported.
Other bias	Low risk	Other bias was not found.
Wang 2015		
Random sequence generation	Low risk	Randomization was performed using sequential numbers generated at computer center of China Medical University Hospital.
Allocation concealment	Low risk	The allocations were contained in opaque, sequentially numbered, sealed envelopes.

Blinding of participants and personnel	Low risk	Both investigators and patients were blind as to the assignment.
Blinding of outcome assessment	Unclear risk	Not reported.
Incomplete outcome data	Low risk	2/23 in probiotics, and 6/24 in placebos.
Selective reporting	Low risk	All the results were reported.
Other bias	Low risk	Other bias was not found.
Pavan 2015		
Random sequence generation	Unclear risk	Not reported.
Allocation concealment	Unclear risk	Not reported.
Blinding of participants and personnel	High risk	This was an open labeled study.
Blinding of outcome assessment	High risk	This was an open labeled study.
Incomplete outcome data	High risk	25 of 50 CKD patients were withdrawn.
Selective reporting	Low risk	All the results were reported.
Other bias	Low risk	Other bias was not found.
Rossi 2016		
Random sequence generation	Low risk	A computer–generated blocked randomization list with blocks of size 2 was produced by an

		external statistical consultant.
Allocation concealment	Low risk	Randomization list were maintained on a secure server not accessible to those recruiting for the trial. Random allocation was performed by telephoning the list custodian.
Blinding of participants and personnel	Low risk	This process of allocation will conceal the randomization order to researchers and participants.
Blinding of outcome assessment	Unclear risk	Not reported.
Incomplete outcome data	Low risk	Compliance to study medications was achieved by 90% of patients.
Selective reporting	Low risk	All the results were reported.
Other bias	Low risk	Other bias was not found.
Shariaty 2017		
Random sequence generation	Low risk	The patients were randomly allocated to Groups A and B using two sets of random numbers with codes 1–36.

Allocation concealment	Unclear risk	Not reported.
Blinding of participants and personnel	Low risk	Neither the patients nor the evaluators had any information about either of the two groups.
Blinding of outcome assessment	Low risk	One of the researchers' colleagues performed the assigning participants to intervention.
Incomplete outcome data	Low risk	1/18 in probiotics, and 1/18 in placebos.
Selective reporting	Low risk	All the results were reported.
Other bias	Low risk	Other bias was not found.
Borges 2018		
Random sequence generation	Low risk	The random sequence was manually generated for a simple randomization
Allocation concealment	Low risk	None of the subjects involved in the study had access to the allocation sequence until the end of the statistical analyses.
Blinding of participants and personnel	Low risk	The participants and the researchers were blinded to the contents of the bottles.
Blinding of outcome assessment	Low risk	All laboratory measurements were centralized

		and performed in a blinded manner.
Incomplete outcome data	Low risk	7/23 in probiotics, and 6/23 in placebos.
Selective reporting	Low risk	All the results were reported.
Other bias	Low risk	Other bias was not found.