

Supplementary Materials

Table S1. Quality assessment of included studies based on the Newcastle-Ottawa Scale for case-control and cohort studies.

Study	Year	Selection				Comparability	Exposure			Score
		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	
Kang <i>et al.</i>	2013	*	-	-	-	**	-	*	*	5
De Angelis <i>et al.</i>	2013	*	*	*	-	**	-	*	-	6
Son <i>et al.</i>	2015	*	*	*	*	*	-	*	-	6
Lee <i>et al.</i>	2017	*	*	-	*	**	-	-	-	5
Strati <i>et al.</i>	2017	*	*	-	-	**	-	*	-	5
Liu <i>et al.</i>	2017	-	-	*	*	-	*	*	*	5
Luna <i>et al.</i>	2017	*	*	*	*	**	-	*	*	8
Berding & Donovan	2018	*	*	*	*	**	-	*	-	7
Coretti <i>et al.</i>	2018	*	*	*	-	*	-	*	-	5
Rose <i>et al.</i>	2018	*	*	-	*	**	-	*	-	6
Zhang <i>et al.</i>	2018	*	*	*	*	*	-	*	-	6
Berding & Donovan	2019	*	*	*	*	**	-	*	-	7
Kong <i>et al.</i>	2019	*	*	*	*	**	-	*	-	7
Li <i>et al.</i>	2019	*	*	*	-	-	-	*	-	4
Niu <i>et al.</i>	2019	*	*	*	*	*	-	*	-	6
Sun <i>et al.</i>	2019	*	*	*	*	*	-	*	-	6
Plaza-Días <i>et al.</i>	2019	*	*	*	*	**	-	*	-	7
Ma <i>et al.</i>	2019	*	*	*	*	**	-	*	-	7
Liu <i>et al.</i>	2019	*	*	*	*	**	-	*	-	7
Wang <i>et al.</i>	2019	-	*	*	-	-	-	*	-	3
Tomova <i>et al.</i>	2020	*	*	*	*	-	-	*	-	5
Hazan <i>et al.</i>	2020	*	-	*	*	*	-	*	-	5
Ding <i>et al.</i>	2020	*	*	-	*	**	-	*	-	6
Chen <i>et al.</i>	2020	*	*	-	*	-	-	*	-	4
Zurita <i>et al.</i>	2020	*	*	*	*	**	-	*	-	7

Low quality studies (score < 4), Moderate quality (5 < score < 7), High quality (7 < score < 9)

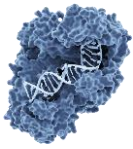


Table S2. Summary of Risk of Bias Assessment for five Included Studies in a Systematic Review.

Study ID	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias	Overall Judgement
Grimaldi <i>et al.</i> 2018	Low	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Arnold <i>et al.</i> 2019	Low	Unclear	Low	Unclear	Unclear	Unclear	Low	Unclear
Inoue <i>et al.</i> 2019	High	High	Unclear	Low	Unclear	Unclear	Unclear	High
Kang <i>et al.</i> 2019	Unclear	NA	Unclear	Unclear/Low	Low	Unclear	Unclear	Unclear
Kong <i>et al.</i> 2021	Low	Low	Low	Low	Unclear	Low/Unclear	Low	Low

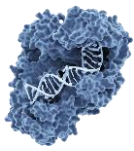
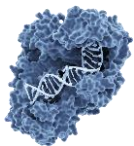


Table S3. Details of sample handling and analysis approach for the study.

Study	Sample type	Sample Storage	DNA/RNA extraction	Sequencing technique/target
Kang <i>et al.</i> , 2013	Stool	stored at -80 °C	QIAamp DNA Stool Mini Kit	454 FLX pyrosequencing/ V2-V3 regions of bacterial 16S rDNA
De Angelis <i>et al.</i> , 2013	Stool	stored at -80 °C	FastDNA Pro Soil-Direct Kit	bTEFAP / V1-V3 region of the 16 S rRNA gene
Son <i>et al.</i> , 2015	Stool	stored at -80 °C	ZR Fecal DNA MiniPre	Illumina MiSeq / V1V2 and V1V3 of the 16S rRNA gene
Lee <i>et al.</i> , 2017	Urine	stored at -20 °C	PowerSoil DNA Isolation Kit	Illumina MiSeq / V3-V4 of the 16S rRNA gene
Strati <i>et al.</i> , 2017	Stool	stored at -80 °C	FastDNA SPIN Kit for Feces	454 FLX pyrosequencing/ V3-V5 region of 16S rRNA
Liu <i>et al.</i> , 2017	Venous blood/Stool	stored at -80 °C	QIAamp Fast DNA Stool Mini Kit	Illumina MiSeq / V3-V4 of the bacterial 16S rRNA gene
Luna <i>et al.</i> , 2017	Blood/Rectum.biopsie	stored at -80 °C	No information	Illumina Miseq/ V1-V3 and V4 regions of the 16S rRNA gene
Berding et Donovan, 2018	Stool	stored at -80 °C	QIAamp Fast DNA Stool Mini Kit	Illumina Miseq / V3-V4 regions of the 16S rRNA gene
Coretti <i>et al.</i> , 2018	Stool	stored at -20 °C	QIAamp DNA Stool Mini Kit	Illumina Miseq / V3-V4 regions of the 16S rRNA gene
Rose <i>et al.</i> , 2018	Stool/Peripheral blood	stored at -20 °C	PowerSoil DNA isolation kit	Illumina MiSeq / V3-V4 regions of the 16S rRNA
Zhang <i>et al.</i> , 2018	Stool	stored at -80 °C	NEXTflex Rapid DNA-Seq kit for Illumina	Illumina HiSeq / V3-V4 regions of the 16S rRNA gene
Grimaldi <i>et al.</i> , 2018	Stool	stored at -80 °C	QIAamp DNA stool mini kit	Illumina MiSeq / V3-V4 region of the 16S rRNA
Arnold <i>et al.</i> , 2019	Stool	No information	No information	Illumina / V1-V3 and V4 regions of the 16S rRNA gene
Berding et Donovan, 2019	Stool	stored at -80 °C	Bead beating QIAamp Fast DNA Stool Mini Kit	Illumina Miseq / V3-V4 regions of the 16S rRNA gene
Inoue <i>et al.</i> , 2019	Stool/Peripheral blood	No information	No information	Illumina Miseq
Kong <i>et al.</i> , 2019	Saliva/Stool	frozen at -20 °C stored at room °T	HR-Easy Fecal DNA Kit	Illumina MiSeq / V3-V4 regions of the 16S rRNA gene
Kang <i>et al.</i> , 2019	Stool	No information	PowerSoil DNA Isolation Kit	MiSeq Illumina/ V4 region of the 16S rRNA gene



Li <i>et al.</i> , 2019	Stool	stored at -80°C	FastDNA SPIN Kit for Feces	Illumina HiSeq / V1–V2 regions of the 16S rRNA gene
Niu <i>et al.</i> , 2019	Stool	No information	OMEGA E.Z.N.A Stool DNA Kit	Illumina MiSeq
Sun <i>et al.</i> , 2019	Stool	stored at -80°C	QIAamp DNA Stool Mini Kit	Illumina MiSeq / V3–V4 region of the 16S ribosomal RNA
Plaza-Días <i>et al.</i> , 2019	Stool	stored at -80°C	QIAamp DNA Stool Mini Kit Exception : pretreatment in lysis buffer at 95°C	Illumina MiSeq / V3–V4 regions of the 16S rRNA gene
Ma <i>et al.</i> , 2019	Stool	stored at -80°C	QIAamp Fast DNA Stool Mini kit	Illumina HiSeq / V3–V4 regions of the 16S rRNA gene
Liu <i>et al.</i> , 2019	Stool	stored at -80°C	QIAamp Fast DNA Stool Mini Kit	Illumina MiSeq / V3–V4 region of the bacterial 16S rRNA gene
Wang <i>et al.</i> , 2019	Stool	stored at -80°C	StoolGen fecal DNA extraction kit	Illumina Hiseq shotgun sequencing / V3–V4 regions of the 16S rRNA gene
Tomova <i>et al.</i> , 2020	Stool	stored at -80°C	QIAamp Fast DNA Stool Mini Kit	Illumina MiSeq / V1–V9 region of 16S rRNA
Hazan <i>et al.</i> , 2020	Stool	No information	QIAamp PowerFecal Pro DNA Kit	Illumina NextSeq 550 System
Ding <i>et al.</i> , 2020	Stool	stored at -80°C	Cetyltrimethylammonium bromide (CTAB)-based method	Illumina HiSeq / V4 region of the 16S rRNA genes
Chen <i>et al.</i> , 2020	Stool	stored at -80°C	No information	Illumina MiSeq / V3–V4 regions of the 16S rRNA gene
Zurita <i>et al.</i> , 2020	Blood/Blood	stored at -80°C	FastDNA SPIN Kit for Soil	Illumina MiSeq / V4 region of the 16S rRNA genes
Kong <i>et al.</i> , 2021	Stool/Blood	stored at -80°C	No information	Illumina MiSeq / V4 region of the 16S rRNA genes