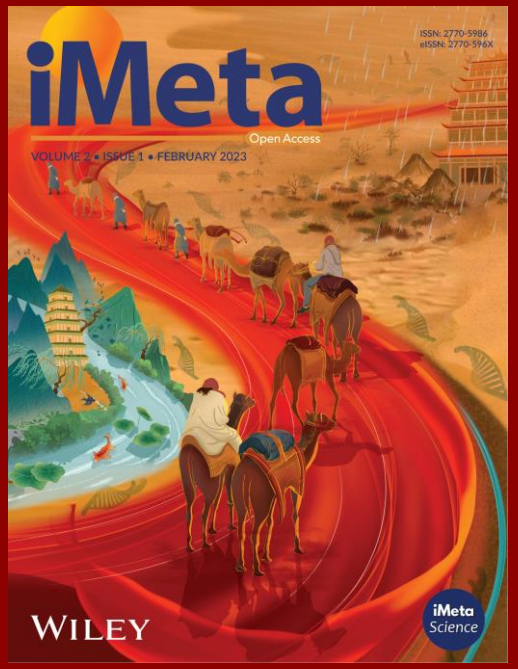
肠道微生物介导的免疫与代谢失调在冠状动脉粥样硬化性心脏病进展及预后中的研究

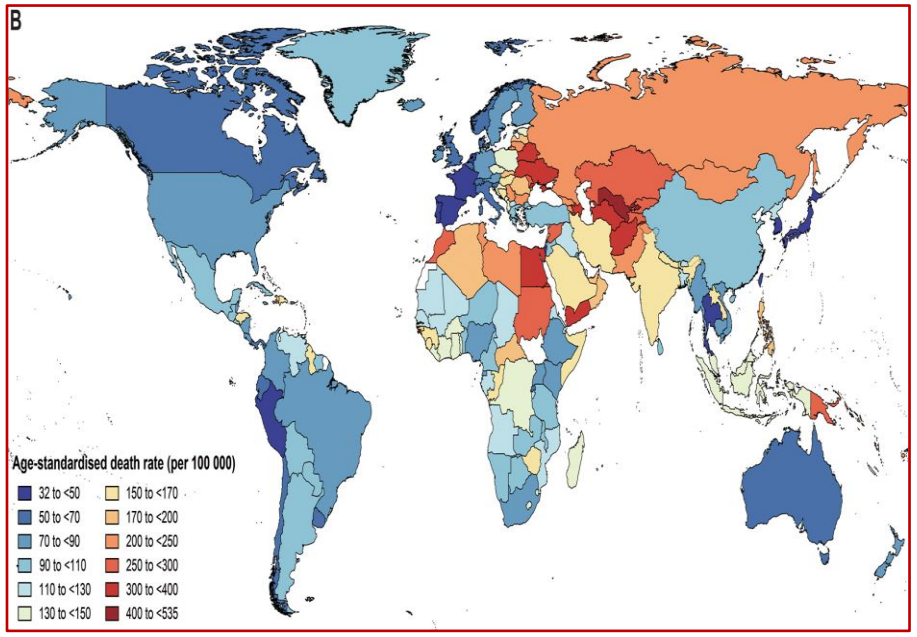
刘红宏 [1,2,3#]，封思琴 [1,3#]，梁丽凤 [4#]，唐牧云 [2,3]，王一斐 [2]，王一阳 [2]，张志宇 [2]，邢海平 [1,2]，张晨虹 [5,6*]，田然 [2*]，张抒扬 [2,3*]

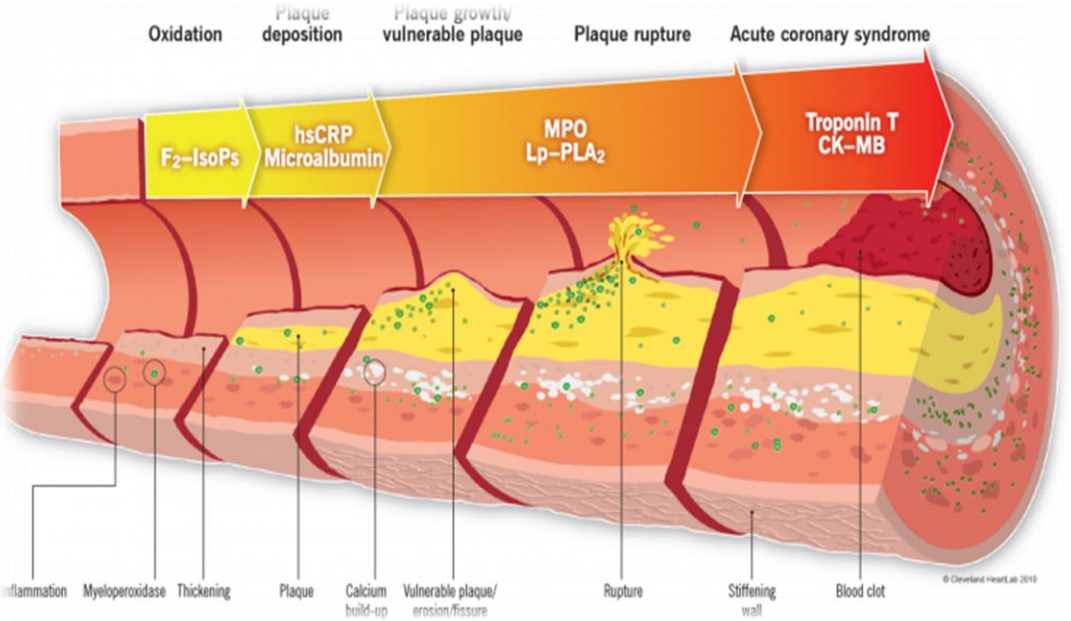
1.中国医学科学院北京协和医学院北京协和医院，内科，北京 100730
2.中国医学科学院北京协和医学院北京协和医院，心内科，北京 100730
3.中国医学科学院北京协和医学院北京协和医院，疑难重症及罕见病国家重点实验室，北京 100730
4.零一生命研究院，深圳 518000
5.上海交通大学，生命科学技术学院微生物代谢国家重点实验室，上海 200240
6.上海交通大学，代谢与发育科学国际合作联合实验室，上海 200240



Honghong Liu, Siqin Feng, Lifeng Liang, Muyun Tang, Yifei Wang, Yiyang Wang, Zhiyu Zhang, et al. 2026. Gut microbiota-mediated immune and metabolic dysregulation in coronary artery disease progression and prognosis. ***iMeta*** 5: e70147. https://doi.org/10.1002/imt2.70147

研究背景





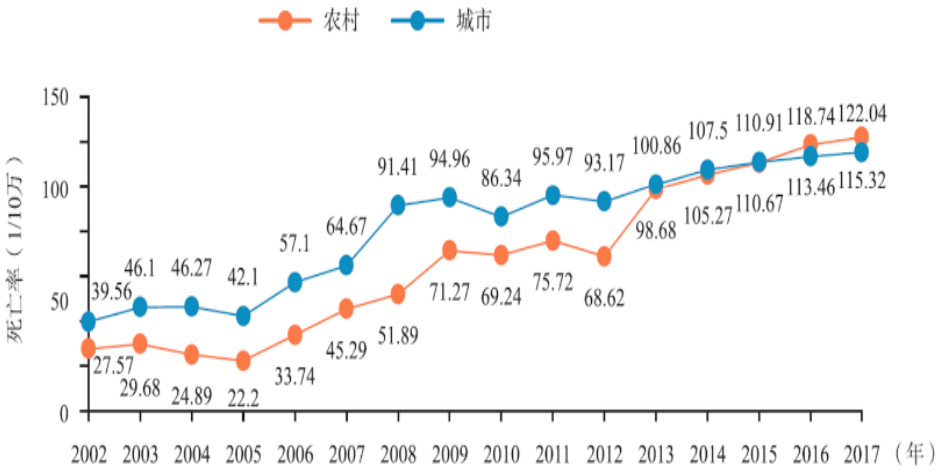
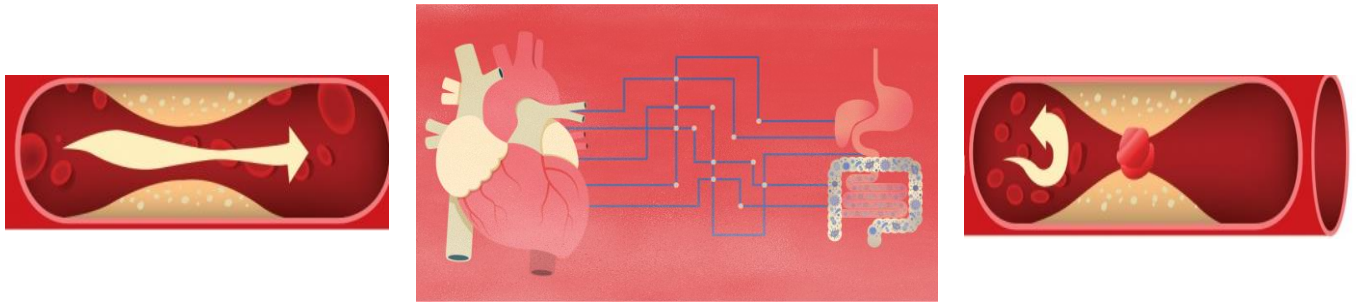


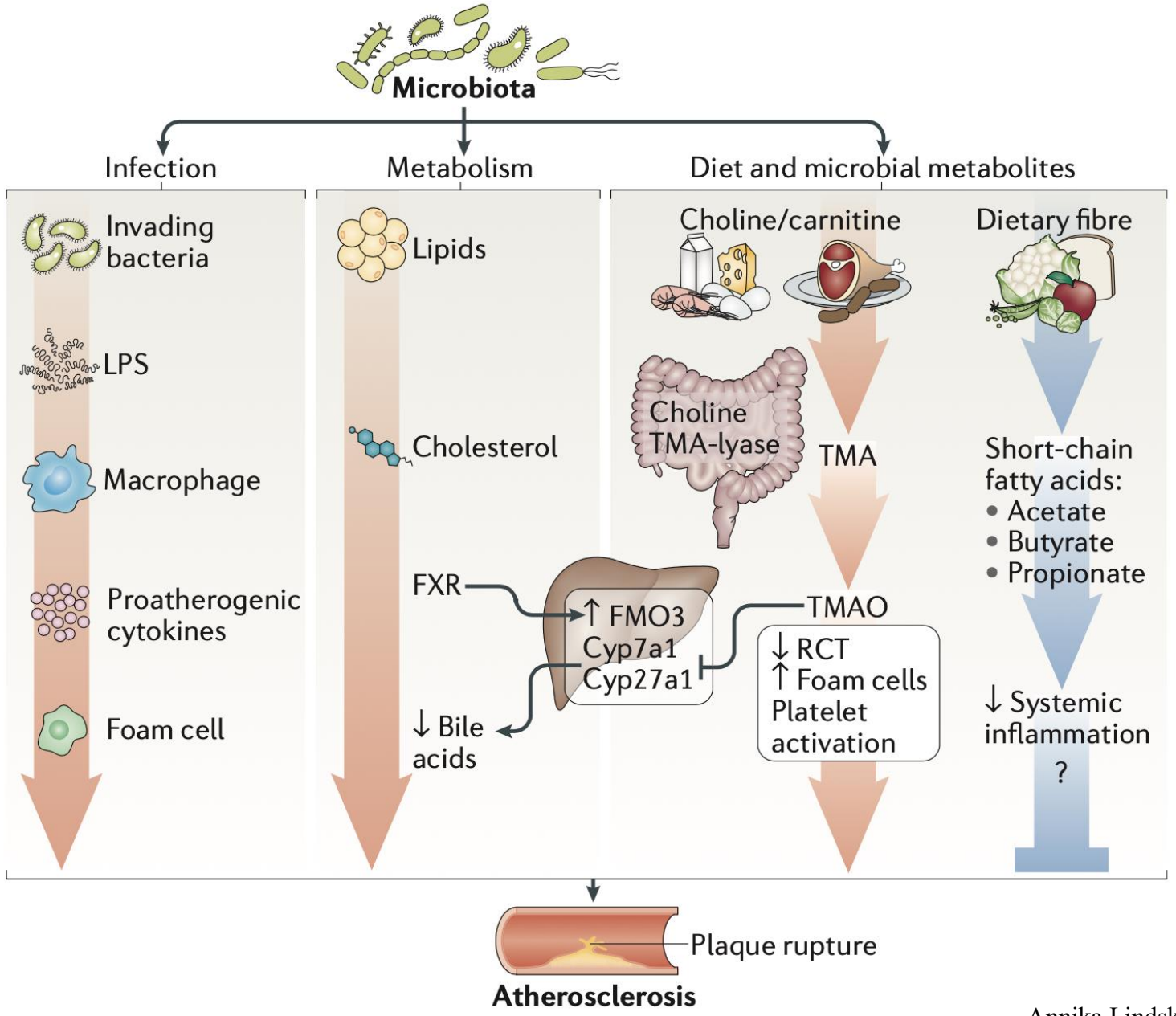
图 4-2-2　2002~2017 年中国城乡地区冠心病病死率变化趋势



Angina → **Heart attack**

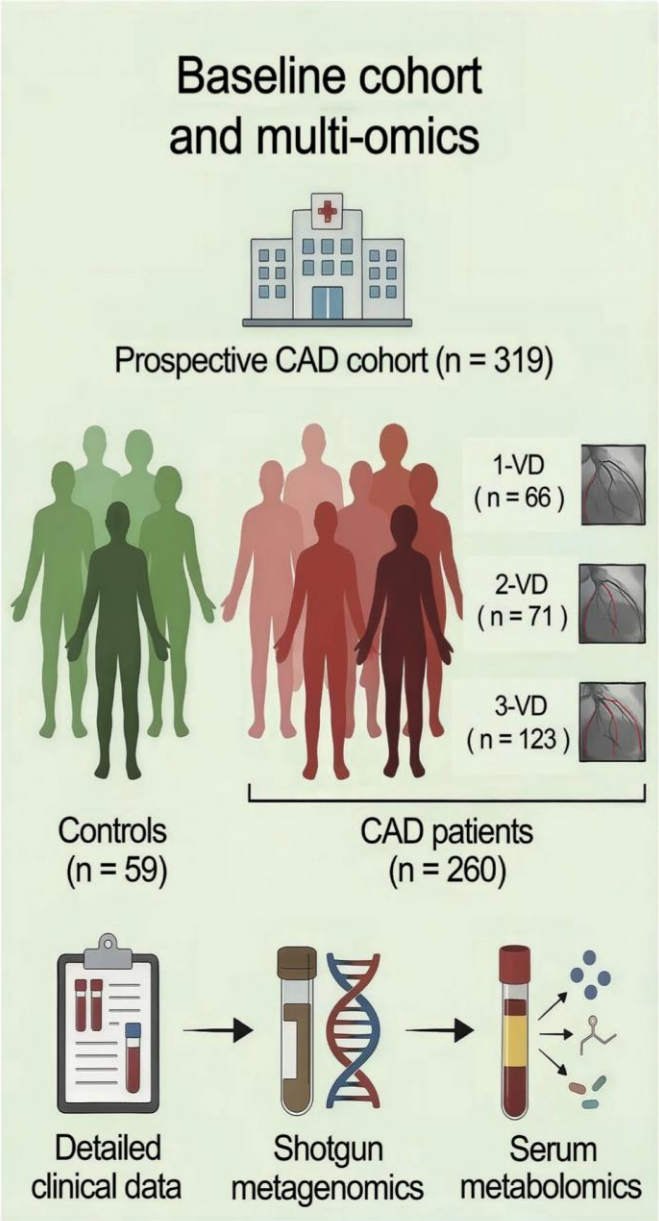
- Roth, Gregory A. et al. *Journal of the American College of Cardiology* , 2020
- 《中国心血管健康与疾病报告》2019

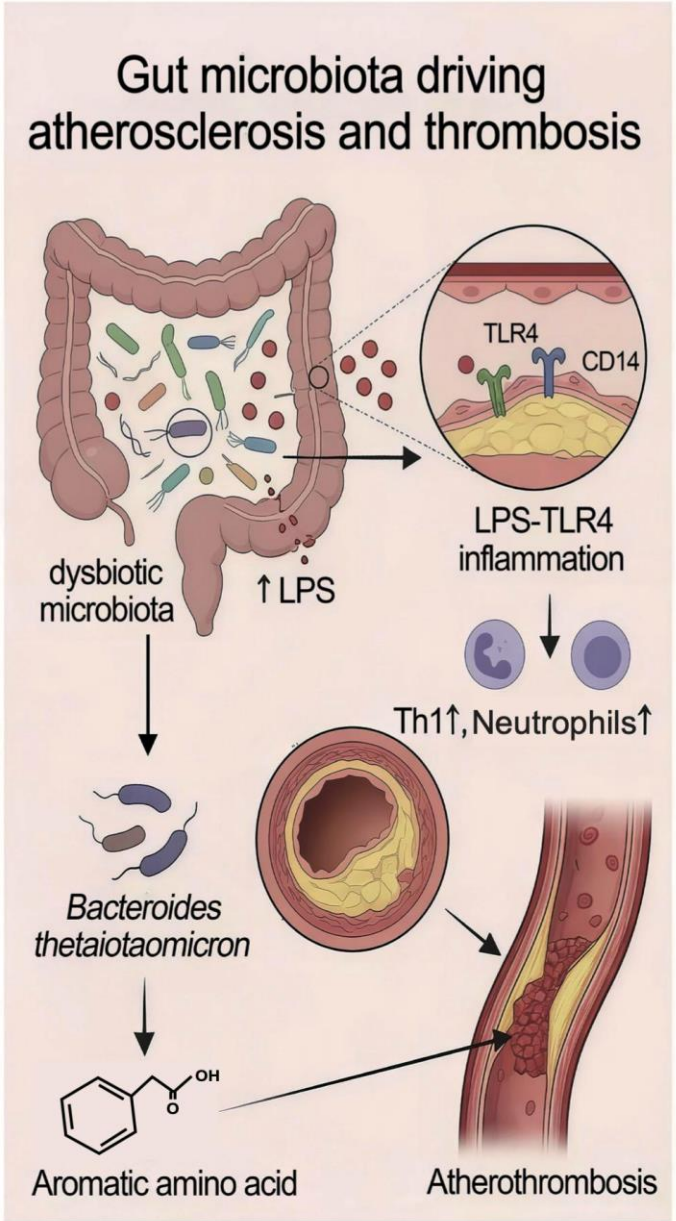
研究背景

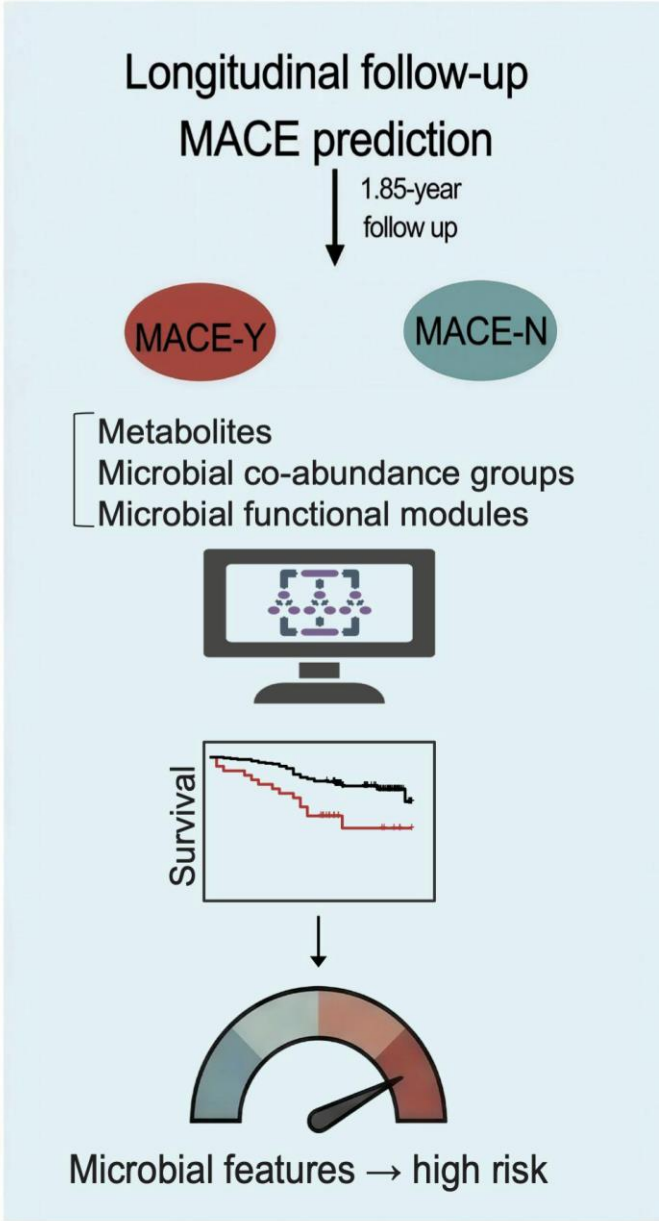


Annika Lindskog Jonsson et al. *Nat Rev Cardiol,* 2017

亮点


Baseline cohort
and multi-omics
Prospective CAD cohort (n = 319)
1-VD
(n = 66)
2-VD
(n = 71)
3-VD
(n = 123)
Controls
(n = 59)
CAD patients
(n = 260)
Detailed
clinical data
Shotgun
metagenomics
Serum
metabolomics

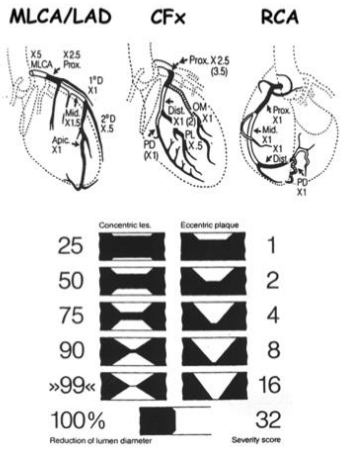

Gut microbiota driving
atherosclerosis and thrombosis
TLR4
CD14
LPS-TLR4
inflammation
dysbiotic
microbiota
↑LPS
Th1↑, Neutrophils↑
Bacteroides
thetaiotaomicron
OH
Aromatic amino acid
Atherothrombosis

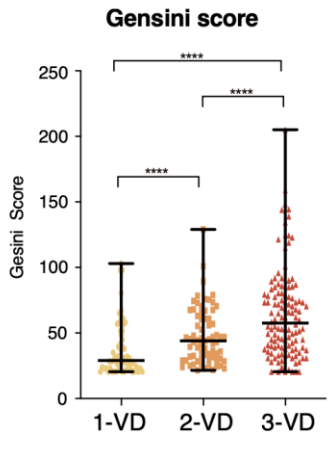

Longitudinal follow-up
MACE prediction
1.85-year
follow up
MACE-Y
MACE-N
Metabolites
Microbial co-abundance groups
Microbial functional modules
Survival
Microbial features → high risk

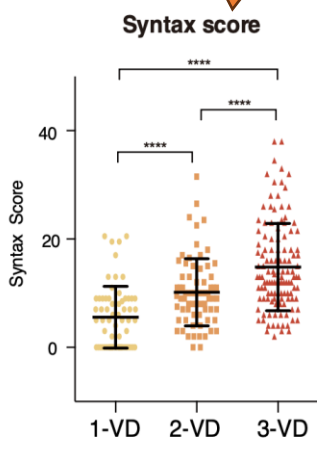
冠心病队列的临床基线特征

斑块负荷↑

		CAD (n= 260)			
	Control (n= 59)	1-Vessel Disease (n= 66)	2-Vessel Disease (n= 71)	3-Vessel Disease (n= 123)	*P* Value
Sex, M/F, n	29/30	41/25	51/20	89/34	<0.001[abc]
Age, y	51.5±10.2	62.2±9.1	61.4±10.8	62.4±7	0.013[abcdef]
Gensini score		**29 (23, 45.9)**	**44 (30.5, 63)**	**57.5 (38, 79.1)**	<0.001[def]
Syntax score		**5 (0, 9)**	**10 (6, 13)**	**13 (9, 20)**	<0.001[def]
Myocardial Infarction		**8 (12.1)**	**20 (28.2)**	**32 (26)**	<0.001[de]
SBP, mmHg	118.8±20.0	131.1±15.2	131.6±15.3	128.6±10.8	0.011[abcdef]
BMI, kg/m^2*	24±3.1	25.1±3.7	26.4±3.7	25.8±3.2	0.296[abc]
Current smoker	8 (13.6)	20 (31.3)	38 (54.3)	60 (49.2)	<0.001[abcde]
Hypertension	8 (13.6)	32 (48.5)	47 (66.2)	89 (72.4)	<0.001[abcde]
DM	0	14 (21.2)	26 (36.6)	48 (39)	<0.001[abcde]
PAD	1 (1.7)	17 (25.8)	12 (16.9)	39 (31.7)	<0.001[abcf]
Drugs					
Aspirin	0	55 (83.3)	68 (95.8)	120 (97.6)	<0.001[abcde]
b-blocker	0	41 (62.1)	57 (80.3)	103 (83.7)	<0.001[abcde]
ACEI/ARB	0	33 (50)	38 (53.5)	64 (52)	<0.001[abc]
CCB	0	18 (27.3)	28 (39.4)	53 (43.1)	<0.001[abce]
Statin	1 (1.7)	62 (93.9)	67 (94.4)	123 (100)	<0.001[abc]
Metformin	0	6 (9.1)	11 (15.5)	22 (17.9)	<0.001[abc]
PPI	0	14 (21.2)	11 (15.5)	41 (33.3)	<0.001[abcf]
Laboratory data					
WBC	5.6±2.9	6.9±1.8	7.2±2.4	7.3±1.3	<0.001[abcd]
TC	4.6 (4.1, 5.4)	3.9 (3.2, 4.8)	3.8 (3.3, 4.3)	4.0 (3.4, 4.9)	<0.001[abc]
TG	1.2 (0.8, 1.6)	1.4 (1.0, 1.9)	1.3 (1.0, 1.9)	1.5 (1.0, 2.1)	0.051[abc]
HDL-C	1.2 (1.0, 1.4)	1.0 (0.8, 1.2)	1.0 (0.8, 1.1)	0.9 (0.8, 1.1)	<0.001[abce]
LDL-C	2.8 (2.3, 3.3)	2.1 (1.7, 2.7)	2.2 (1.8, 2.6)	2.3 (1.8, 2.9)	<0.001[abc]
hs-CRP	0.7 (0.4, 1.1)	1.0 (0.5, 2.5)	1.6 (0.7, 3.9)	1.8 (0.7, 4.4)	<0.001[abce]
Glucose	5.7 (5.2, 7.2)	6.3 (5.4, 8.0)	6.9 (5.5, 8.7)	6.9 (5.9, 8.5)	0.011[abc]
cTnI	**0 (0, 0)**	**0.004 (0, 0.0223)**	**0.004 (0, 0.143)**	**0.009 (0, 0.072)**	<0.001[abce]
TNF-a	9.7 (4.4, 15.8)	20.9 (15.8, 35.2)	19.9 (15.0, 47.6)	20.5 (15.8, 55.3)	<0.001[abc]

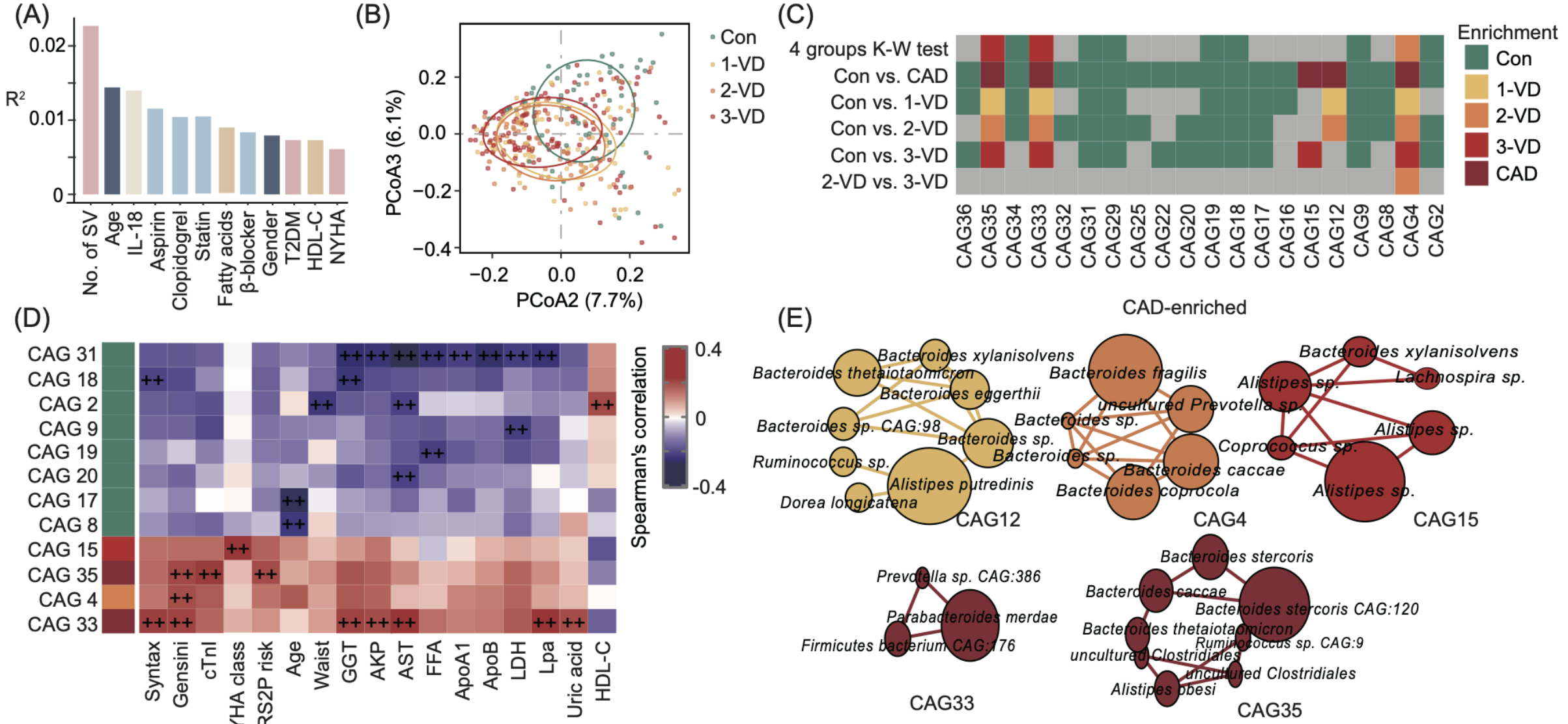




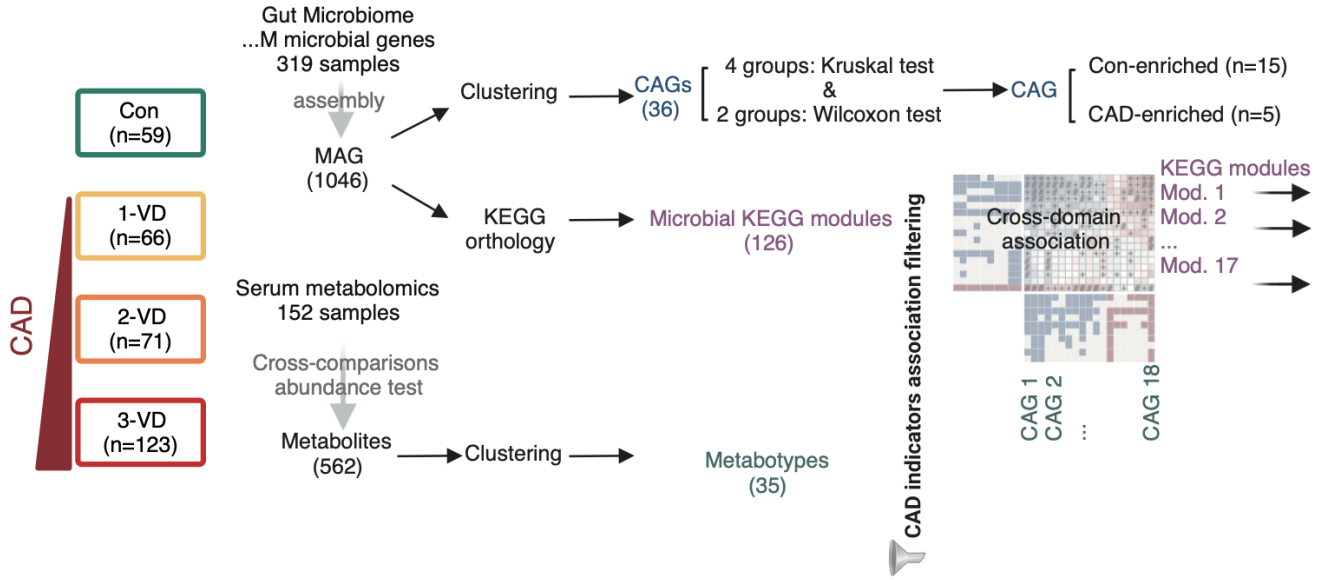


	HC (N=45)	1-VD (N=42)	2-VD (N=45)	3-VD (N=82)	P value
Physical situation (h/per week)					
Heavy intensity	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.5544
Moderate intensity	1.8 (0, 7)	0 (0, 3.5)	0 (0, 0)	0 (0, 0)	0.0048 [bc]
Light intensity	14 (7,21)	13 (5.5, 21)	7 (1.5, 14)	10 (3.5, 14)	0.2211
Walk	7 (3.5, 14)	7 (3.96, 14)	7 (3.5, 14)	7 (4.05, 14)	0.9507
Sit	35 (21, 42)	35 (28, 49)	42 (35, 63)	42 (28, 56)	0.0895 [bc]
Body weight situation					
1. lose weight	17 (37.8%)	7 (16.7%)	7 (15.6%)	9 (11%)	0.002 [abc]
2. gain weight	1 (2.2%)	1 (2.4%)	0	0	0.399
3. none	27 (60%)	34 (81%)	38 (84.4%)	73 (89%)	0.001[abc]
Bristol score					
Type 1, very constipated	0	2 (4.8%)	1 (2.2%)	0	0.141[e]
Type 2, slightly constipated	2 (4.4%)	3 (7.1%)	5 (11.1%)	9 (11%)	0.578
Type 3, sausage shape with cracks	6 (13.3%)	13 (31%)	11 (24.4%)	25 (30.5%)	0.156 [ac]
Type 4, smooth, soft	27 (60%)	17 (40.5%)	20 (44.4%)	35 (42.7%)	0.216
Type 5, lacking fiber	8 (17.8%)	4 (9.5%)	5 (11.1%)	5 (6.1%)	0.225 [c]
Type 6, mild diarrhea	2 (4.4%)	2 (4.8%)	3 (6.7%)	7 (8.5%)	0.783
Type 7, severe diarrhea	0	1 (2.4%)	0	1 (1.2%)	0.6
Dietary intake					
Protein	598.2 (103.4, 1834.4)	108.9 (81.4, 164.2)	100.5 (78.9, 140.8)	101.3 (82.7, 137.5)	<0.0001[abc]
Fat	224.3 (127.5, 560.2)	98.4 (73.9, 139)	105.9 (67.5, 147.6)	103.5 (82.8, 145.5)	<0.0001[abc]
Fiber	37.8 (22.3, 96)	25.8 (16.6, 37.7)	26.5 (19.4, 38)	24.2 (17.5, 33.6)	0.0612 [c]
Carbohydrate	160.1 (83.9, 342.8)	360.6 (265.9, 544.4)	309.8 (251.7, 501.7)	341.9 (254.2, 511.9)	<0.0001[abc]

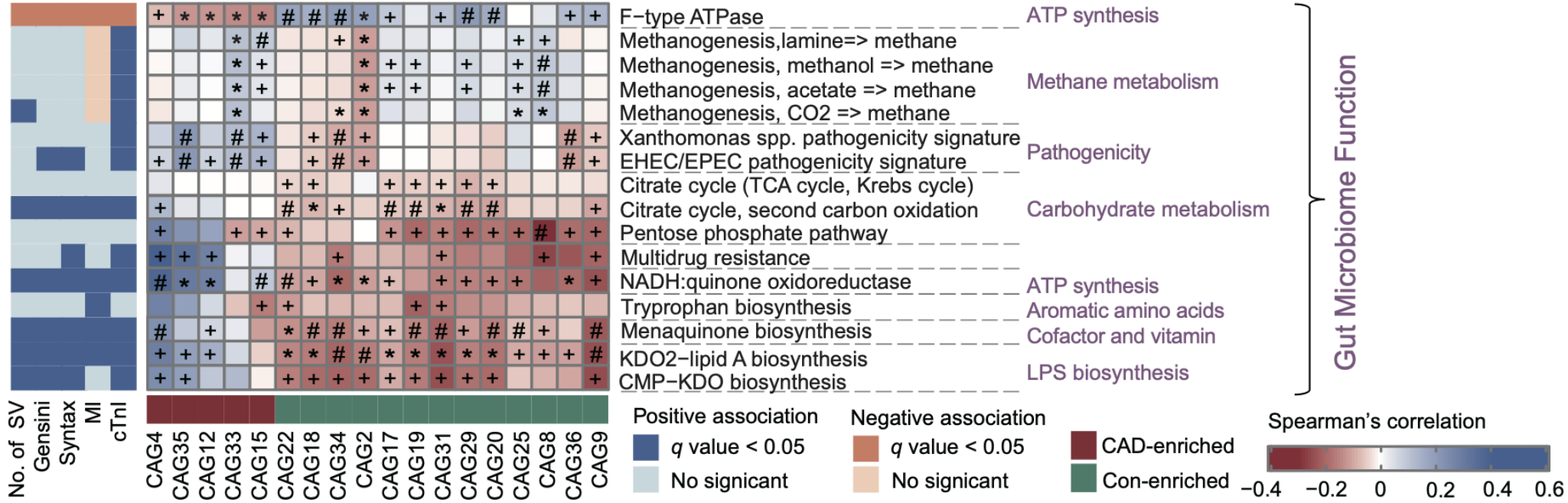
肠道菌群以CAG形式随冠心病严重程度发生改变



多组学分析证实肠道菌群参与冠心病发生发展



(F)



肠道微生物预后标记物与主要不良心血管事件的关联

Follow-up Study

Variable	CAD participants			P-value
	1-VD (N=66)	2-VD (N=71)	3-VD (N=123)	
Study follow-up				
Missing – no. (%)	11 (16.7%)	8 (11.3%)	15 (12.2%)	
Median duration (IQR) -yrs	1.84 (1.49-2.11)	1.94 (1.52-2.17)	1.708 (1.48-2.10)	
Primary endpoint– no. (%)	2 (3.64%)	5 (7.94%)	8 (7.41%)	0.5844
All cause death	0 (0%)	2 (3.17%)	3 (2.78%)	0.434
Nonfatal myocardial infarction	1 (1.82%)	2 (3.17%)	4 (3.7%)	0.81
Nonfatal stroke	1 (1.82%)	1 (1.59%)	1 (0.93%)	0.872
Secondary endpoint	6 (10.91%)	9 (14.29%)	23 (21.3)	0.2009
Hospitalization – no. (%)	6 (10.91%)	9 (14.29%)	22 (20.37)	0.2644
Unstable angina	5 (9.09%)	7 (11.11%)	18 (16.67%)	0.351
Heart failure	0 (0%)	1 (1.59%)	3 (2.78%)	0.446
Arrhythmia	1 (1.82%)	2 (3.17%)	2 (1.85%)	0.826
Other reasons	0 (0%)	1 (1.59%)	2 (1.85%)	0.609
Procedures – no. (%)	2 (3.64%)	2 (3.17%)	14 (12.96%)	0.0293[f]
Coronary angiography	3 (5.45%)	8 (12.7%)	14 (12.96%)	0.318
Revascularization PCI	2 (3.64%)	2 (3.17%)	12 (11.11%)	0.081
Revascularization CABG	0 (0%)	0 (0%	2 (1.85%)	0.335

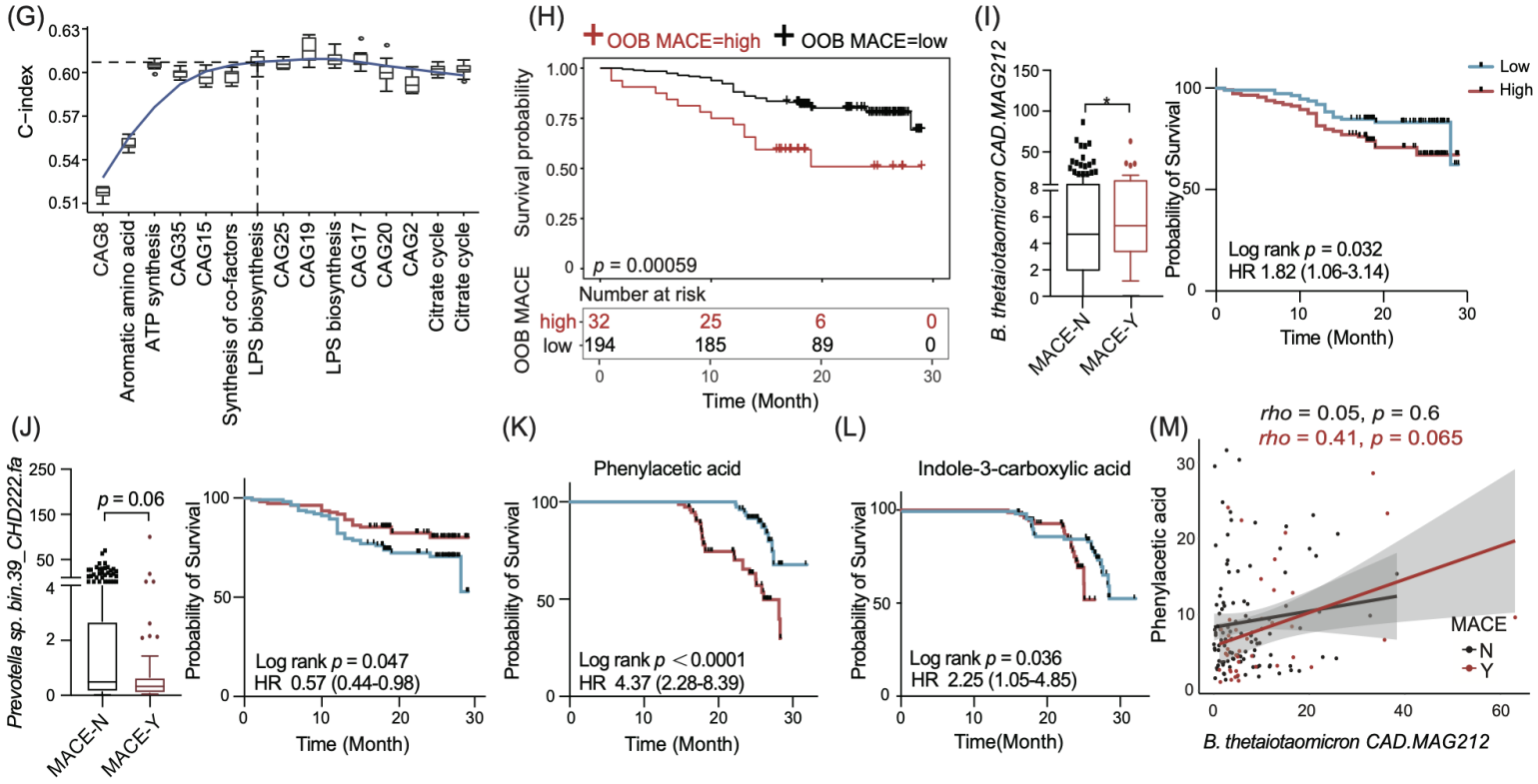
MACE

随访人数：CAD 226人

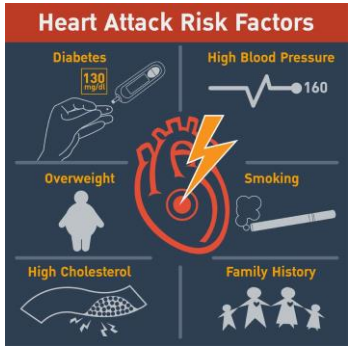
随访时间：1.85 年（四分位数：1.5-2.15年）

失访率：13.1%

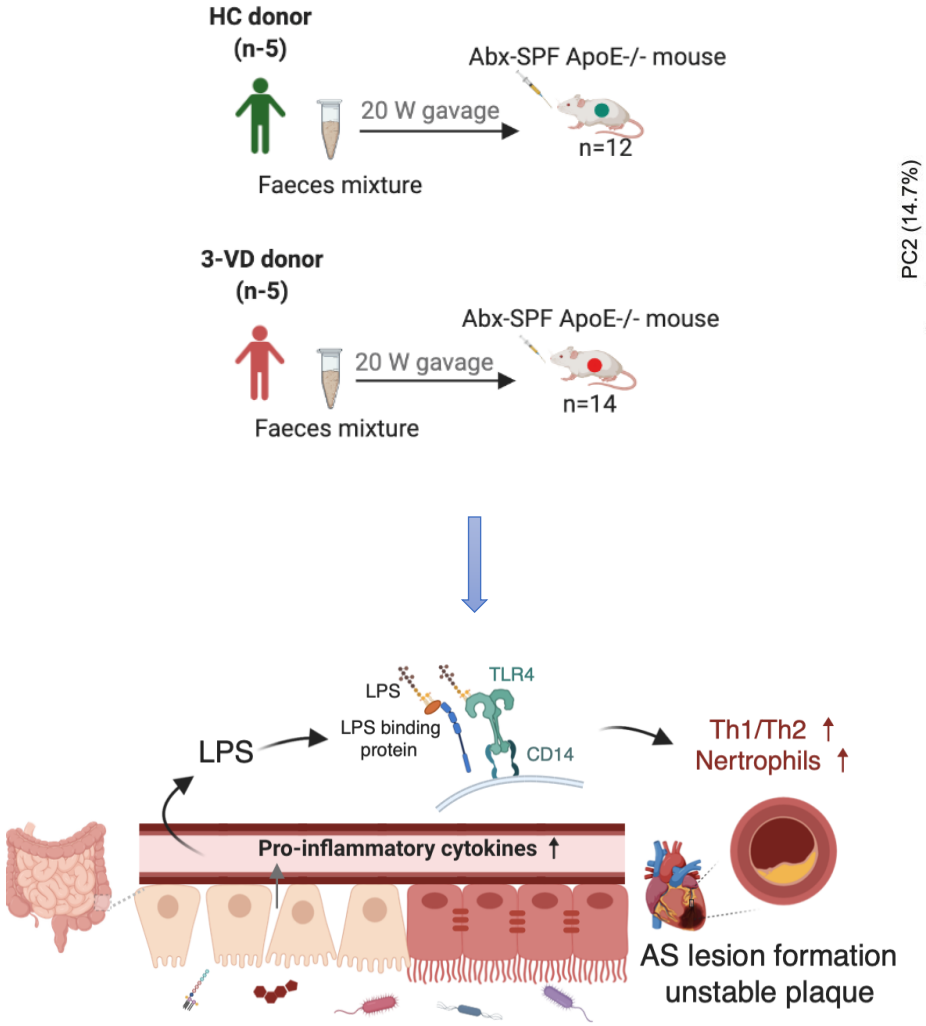
Total MACE = 43

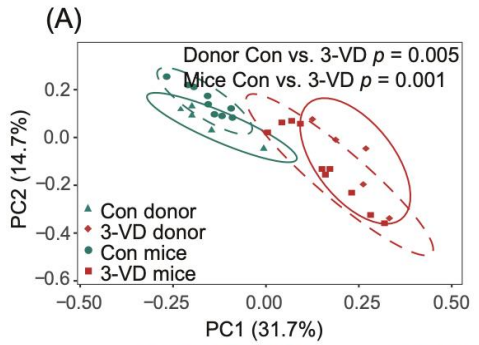


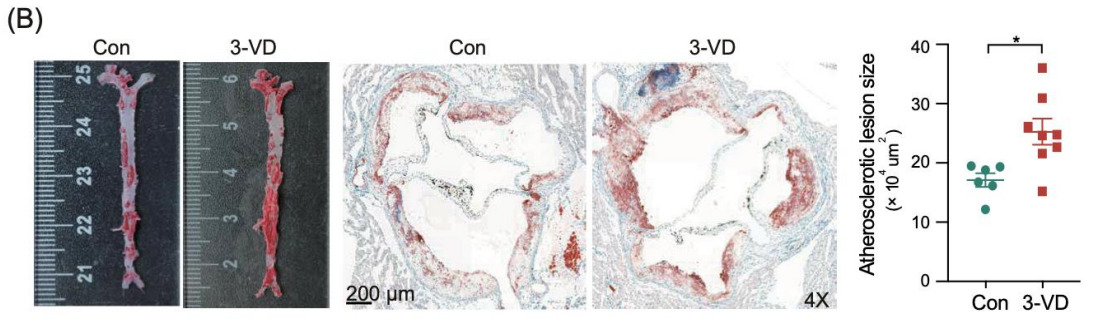
传统心血管危险因素 ✚ 肠道菌群 ⟶ 提升疾病早期预防

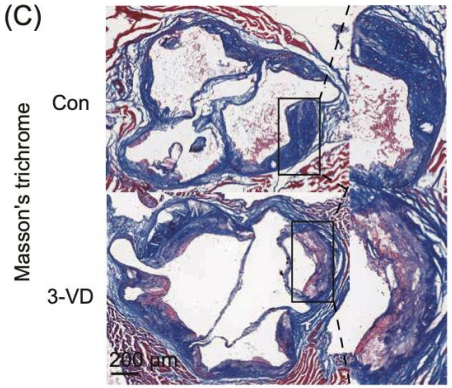


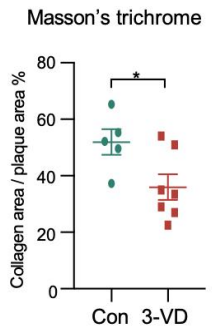
冠心病相关微生物定植引起动脉粥样硬化斑块形成

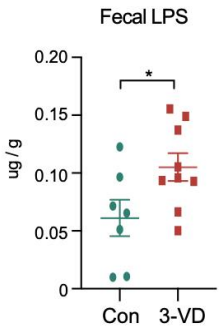


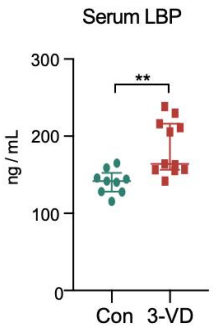


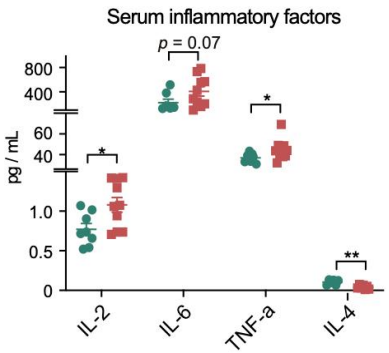


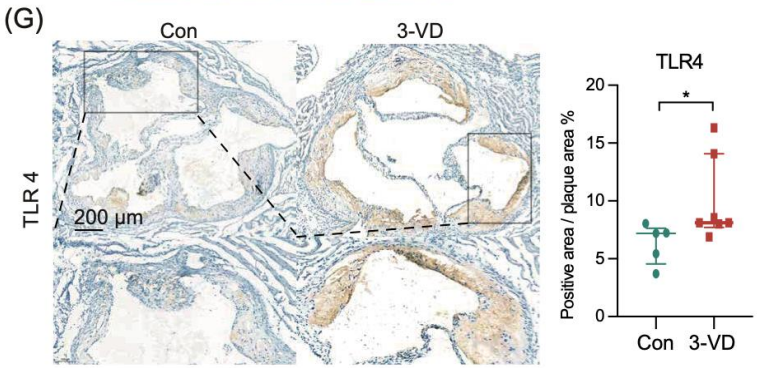


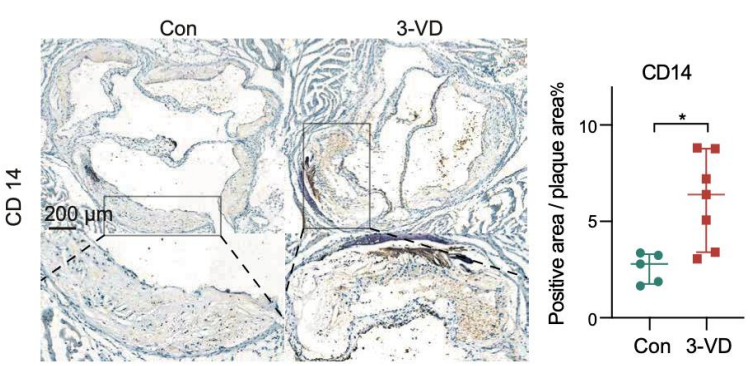




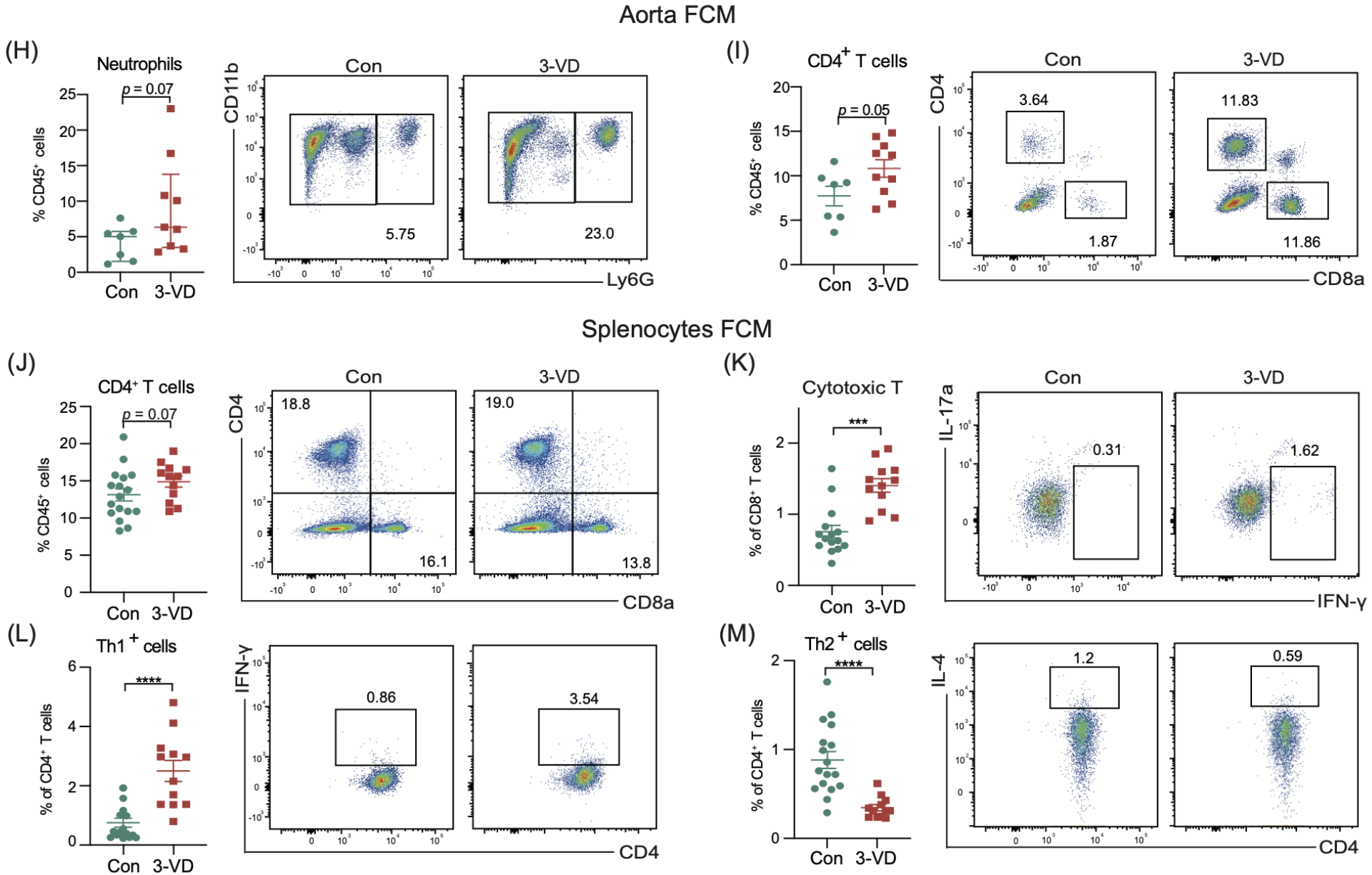








冠心病相关微生物定植引起系统性和血管性炎症



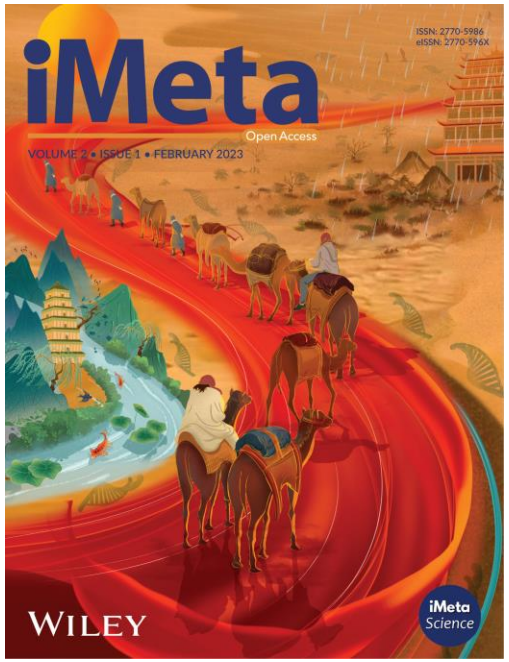
总结

- 基于 319 人前瞻性冠心病队列，整合宏基因组学 + 代谢组学 + 实验机制验证 + 预测建模的多组学研究范式，识别从冠心病早期到晚期进展过程中的动态菌群变化。
- 粪菌移植实验证实，冠心病相关肠道菌群通过LPS-TLR4 信号通路诱导血管炎症，加剧动脉粥样硬化。
- 通过动态随访+机器学习风险预测模型，将微生物特征与传统临床危险因素整合，提升主要不良心血管事件（MACE）的预测效能。

Honghong Liu, Siqin Feng, Lifeng Liang, Muyun Tang, Yifei Wang, Yiyang Wang, Zhiyu Zhang, et al. 2026. Gut microbiota-mediated immune and metabolic dysregulation in coronary artery disease progression and prognosis. ***iMeta*** 5: e70147. https://doi.org/10.1002/imt2.70147

iMeta(宏): 生物和医学顶级成果发表平台

iMeta WILEY



iMeta(宏)期刊由宏科学创办，对标***Cell***的生物/医学综合期刊，SCIE、PubMed收录，影响因子(IF)44.4，位列全球第47，中国第4，分区表生物学1区Top，外审平均21天，投稿至发表中位数87天(比同水平期刊快3倍)，欢迎高影响力的研究、方法和综述投稿，CNS外审稿件可带意见和回复转投。

iMetaOmics (宏组学)，定位IF>15对标***NC/SA***的生物/医学综合期刊，已被ESCI、PubMed等收录。

iMetaMed (宏医学)定位IF>15的医学综合期刊，欢迎投稿!

主页: http://www.imeta.science

出版社: https://wileyonlinelibrary.com/journal/imeta

投稿: iMeta: https://wiley.atyponrex.com/journal/IMT2
iMetaOmics: https://wiley.atyponrex.com/journal/IMO2
iMetaMed: https://wiley.atyponrex.com/journal/IMM3

office@imeta.science
imetaomics@imeta.science

宣传片

iMeta

更新日期
2026/6/17