Supplementary material

Supplemental Brief introduction of the Cohort

This study is based on a cohort study at the Third People's Hospital of Shenzhen, the only designated hospital for HIV care in Shenzhen, China. The hospital managed approximately 22,000 people living with HIV (PLWH) from 2009 to 2024. Antiretroviral therapy (ART) is provided free-of-charge according to national HIV treatment guidelines. PLWH visit the hospital every three months for continuous ART prescriptions and health monitoring. Before starting ART, comprehensive baseline assessments are conducted, including HIV viral load, T-cell subsets, common opportunistic infections, complete blood count, liver and kidney function, thyroid function, electrocardiogram, bone density, and co-infections (e.g., CMV, HBV, HCV, syphilis, HPV). Detailed patient histories and lifestyle information are also collected. After initiating ART, patients are regularly followed up every three months with routine HIV viral load and T-cell subset testing, and additional tests as needed. The high reimbursement rate of Shenzhen's health insurance policies contributes to a low loss-to-follow-up rate, providing a stable cohort and valuable clinical data for research.

The following are some studies we have conducted based on this cohort：

1. Li T, Sun L, He Y, et al. Increasing trends of overweight and obesity in treatment-naive people living with HIV in Shenzhen from 2014 to 2020: an emerging health concern. Front Public Health 2023; 11:1186838.
2. Sun L, He Y, Xu L, et al. Higher Risk of Dyslipidemia With Coformulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide than Efavirenz, Lamivudine, and Tenofovir Disoproxil Fumarate Among Antiretroviral-Naive People Living With HIV in China. J Acquir Immune Defic Syndr 2022; 91: S8-S15.
3. Liu J, Hou Y, Sun L, et al. High population-attributable fractions of traditional risk factors for non-AIDS-defining diseases among people living with HIV in China: a cohort study. Emerging Microbes & Infections 2021; 10:416-423.
4. Liu J, Sun L, Hou Y, et al. Barriers to early diagnosis and treatment of persistently high burden of severely immunosuppressed patients with HIV-1: a quantitative and qualitative study. HIV Medicine 2020; 21:708-717.
5. Sun LQ, Liu JY, He Y, et al. Evolution of blood lipids and risk factors of dyslipidemia among

people living with human immunodeficiency virus who had received first-line antiretroviral regimens for 3 years in Shenzhen. Chin Med J 2020; 133:2808-2815.

6. Li XR, Sun LQ, He Y, et al. HDL-C as a novel predictor of immune reconstitution in people living with HIV: insights from a baseline-to-dynamic change cohort study in China, 2005–2022. Frontiers in Immunology 2025; 16: 1520615.
7. Luo YS, Sun LQ, He Y, et al. The triglyceride-glucose index trajectories are associated with cardiovascular diseases in people living with HIV: evidence from a prospective cohort study in China, 2005–2022. BMC Public Health 2025; 25: 465.

Supplemental Table 1. Clinical and laboratory diagnostic criteria for 26 conditions in the study

Condition		Clinical and laboratory diagnostic criteria
1	Hypertension [1]	Blood pressure ≥140/90 mmHg
2	Diabetes Mellitus [2]	HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dL, or use of antidiabetic medications, or a self-reported history of diabetes
3	Dyslipidemia [3]	TC≥5.2 mmol/L, HDL-C≤1.0 mmol/L, LDL-C≥3.4 mmol/L, or TG ≥1.7 mmol/L
4	Cardiovascular Disease [4]	Confirmed by ECG, echocardiography, cardiac biomarkers, or coronary angiography
5	COPD (Chronic Obstructive Pulmonary Disease), Emphysema, Chronic Bronchitis [5]	FEV1/FVC < 0.70; use of anticholinergics
6	Diseases of Esophagus, Stomach, and Duodenum [6]	Diagnosis based on endoscopy, biopsy, or imaging
7	Hepatitis B (HBV) [7]	Persistent HBsAg positivity >6 months
8	Hepatitis C (HCV) [8]	Positive anti-HCV and HCV RNA
9	Chronic kidney disease (CKD) [9]	Glomerular filtration rate <60 mL/min/1.73 m^2 for ≥3 months(assessed using the CKD-EPI equation)
10	Non-AIDS-related cancers [10]	Histopathological confirmation
11	Osteoporosis [11]	Bone mineral density T-score ≤ -2.5
12	Mental health disorders [12]	Diagnosis per DSM-5
13	Sleep disorders [13]	Diagnosis per ICSD-3 and PSG
14	Syphilis [14]	Positive RPR/VDRL and TPPA/FTA-ABS
15	Human papillomavirus (HPV) infection [15]	Positive high-risk HPV DNA
16	Chronic liver disease (CLD) excluding viral hepatitis [16]	Abnormal liver function with imaging or pathology, excluding HBV/HCV
17	AIDS-defining cancers [17]	Kaposi sarcoma, cervical cancer, or aggressive

		B-cell lymphoma
18	HIV-associated encephalopathy [18]	Cognitive decline in HIV+ after excluding other causes
19	Pneumocystis jirovecii pneumonia (PJP) [19]	Radiologic findings and P. jirovecii in BAL or sputum
20	Nontuberculous mycobacterial infections [20]	≥2 positive sputum cultures and compatible imaging
21	Cytomegalovirus (CMV) infection [21]	CMV DNA PCR or inclusion bodies
22	Herpes simplex virus (HSV) infection [22]	Positive PCR or viral culture
23	Varicella-zoster virus (VZV) infection [23]	Clinical rash and positive PCR
24	Toxoplasmosis [24]	Positive IgM/IgG or CSF Toxoplasma DNA
25	Fungal infections [25]	Positive culture, microscopy, or serology (e.g., beta-D-glucan)
26	Tuberculosis (TB) [26]	AFB smear, culture, or PCR with radiographic evidence

Reference (ordered according to the 26 diseases)：

1. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension. J Hypertens. 2023;41(12):1874–2071. doi:10.1097/HJH.0000000000003480

2. American Diabetes Association. Standards of Medical Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S1–S350. doi:10.2337/dc24-S001

3. Joint Committee for the Revision of Guidelines for the Management of Blood Lipids in China. Chinese guidelines for the management of blood lipids (2023 edition). Chinese Circulation Journal. 2023;38(3):237–271. (In Chinese). doi: 10.3969/j.issn.1000-3614.2023.03.001

4. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. ACC/AHA Guideline on the Assessment of Cardiovascular Risk. J Am Coll Cardiol. 2014;63(25 Pt B):2935–2959. doi:10.1016/j.jacc.2013.11.005

5. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of COPD – 2023 Report. Available at: https://goldcopd.org

6. Katz PO, Dunbar KB, Schnoll-Sussman FH, et al. ACG Clinical Guideline for the Diagnosis and Management of GERD. Am J Gastroenterol. 2022;117(1):27–56. doi:10.14309/ajg.0000000000001538

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8. Centers for Disease Control and Prevention (CDC). Hepatitis C Guidance: Testing, Management, and Treatment. Updated 2023. Available at: https://www.cdc.gov/hepatitis/hcv/index.htm

9. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105(4S):S117-S314. doi:10.1016/j.kint.2023.10.018

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12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). American Psychiatric Publishing; 2013. Available at: https://www.psychiatry.org/psychiatrists/practice/dsm

13. American Academy of Sleep Medicine. International Classification of Sleep Disorders—Third Edition (ICSD-3). 2014. Available at: https://aasm.org/clinical-resources/international-classification-sleep-disorders/

14. Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1–187. doi:10.15585/mmwr.rr7004a1

15. World Health Organization. WHO Guidelines for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention. 2nd edition. 2021. Available at: https://www.who.int/publications/i/item/9789240030824

16. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328–357. doi:10.1002/hep.29367

17. Centers for Disease Control and Prevention. AIDS-Defining Conditions. Available at: https://www.cdc.gov/hiv/library/reports/hiv-surveillance/vol-32/content/appendix-c.html

18. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. U.S. Department of Health and Human Services. Updated May 13, 2025. Available at: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv.

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21. Kotton CN, Kumar D, Caliendo AM, et al. The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid Organ Transplantation. Transplantation. 2018;102(6):900–931. doi:10.1097/TP.0000000000002191

22. Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1–187. doi:10.15585/mmwr.rr7004a1

23. Centers for Disease Control and Prevention. Varicella-Zoster Virus Infection. Available at: https://www.cdc.gov/chickenpox

24. Centers for Disease Control and Prevention. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. Updated 2022.

25. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1–e50. doi:10.1093/cid/civ933

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Supplemental Table 2. Included ICD-10 codes in each condition

	Condition	ICD-10
1	Hypertension	I10-I15
2	Diabetes Mellitus	E10-E14
3	Dyslipidemia	E78
4	Cardiovascular Disease	I20-I25, I63-I69, I10-I15
5	COPD (Chronic Obstructive Pulmonary Disease), Emphysema, Chronic Bronchitis	J41-J44, J47
6	Diseases of Esophagus, Stomach, and Duodenum	I85, K21-K22, K224-K227, K230-K231, K254-K257, K264-K267, K274-K277, K284-K287, K293-K299, K311-K315, Q39-Q40, Z903
7	Chronic Hepatitis B	B15, B17.2, B18 (exclude B18.2)
8	Chronic Hepatitis C	B18.2
9	Chronic kidney disease (CKD)	K70-K74, K76.0
10	Non-AIDS-related cancers	I120-I139, N01-N05, N07-N08, N11, N183-N189, Q60-Q61, Q618-Q619, Z905, Z940
11	Osteoporosis	C00-C45, C47-C82, C83.1-C83.9, C84-C85.8, C86-C96
12	Mental health disorders	M80-M82
13	Sleep disorders	F20-F48
14	Syphilis	F51.0-F51.3, G47
15	Human papillomavirus (HPV) infection	A50-A53
16	Chronic liver disease excluding viral hepatitis	A63.0, B07, B97.7, D06, D10.5, D14.1, N87.1-N87.9, N89.0-N89.1, N90.0-N90.1, K62.8
17	AIDS-defining cancers	C46, C53, C83.0, C85.9
18	HIV-associated encephalopathy	B22
19	Pneumocystis jirovecii pneumonia (PJP)	B59

20	Nontuberculous mycobacterial infections	A31
21	Cytomegalovirus (CMV) infection	B25
22	Herpes simplex virus (HSV) infection	B00
23	Varicella-zoster virus (VZV) infection	B01, B02
24	Toxoplasmosis	B58
25	Fungal infections	B37, B45, B48
26	Tuberculosis	A15-A19

Supplemental Table 3. Classification of the 26 conditions by curability, metabolic status, and infectious status

Category	Classification	Condition number*
Curability	Curable condition	8, 13, 14, 15, 19, 21, 22, 23, 24, 25, 26
	Non-curable condition	1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 16, 17, 18, 20
Metabolic status	Metabolic condition	1, 2, 3, 11, 16
	Non-metabolic condition	4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26
Infectious status	Infectious condition	7, 8, 14, 15, 19, 20, 21, 22, 23, 24, 25, 26
	Non-infectious condition	1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 16, 17, 18

* Condition number refers to the numbered disease entities listed in Supplemental Table 1.

Supplemental Table 4. Distribution of six multimorbidity patterns and dropout across three waves

Category	Total, N	Proportion, %	Category (Baseline to 4-year)	Total, N	Proportion, %	Category (4-year to 8-year)	Total, N	Proportion, %
Incurable multimorbidity pattern	456	7.66	Incurable multimorbidity pattern	1120	18.82	Incurable multimorbidity pattern	1517	25.50
Curable multimorbidity pattern	46	0.77	Curable multimorbidity pattern	7	0.12	Curable multimorbidity pattern	4	0.07
Mixed curable multimorbidity pattern	1037	17.43	Mixed curable multimorbidity pattern	1042	17.51	Mixed curable multimorbidity pattern	1007	16.92
Single incurable disease	2739	46.03	Single incurable disease	3086	51.87	Single incurable disease	2665	44.79
Single curable disease	208	3.50	Single curable disease	60	1.01	Single curable disease	16	0.27
No disease	1464	24.61	No disease	493	8.29	No disease	192	3.23
Dropout	0	0.00	Dropout	142	2.39	Dropout	549	9.23

Counts (N) and proportions (%) are shown for Baseline, Baseline to 4-year (Wave1), and 4-year to 8-year (Wave2). “Incurable/Curable/Mixed curable” multimorbidity patterns follow the classification in Supplemental Table 3; “Dropout” denotes participants without follow-up data in the specified interval.

Supplemental Table 5. Multimorbidity patterns distribution and sex difference in different waves

Category	Male		Female		Test type	P-value
	Counts	Proportion, %	Counts	Proportion, %		
Baseline						
Incurable multimorbidity pattern	411	7.95	45	5.78	Chi-square	<0.05
Curable multimorbidity pattern	44	0.85	2	0.26	Fisher	0.08
Mixed curable multimorbidity pattern	938	18.14	99	12.71	Chi-square	<0.01
Single incurable disease	2385	46.12	354	45.44	Chi-square	0.75
Single curable disease	196	3.79	12	1.54	Chi-square	<0.01
No disease	1197	23.15	267	34.27	Chi-square	<0.01
Dropout	0	0.00	0	0.00	Fisher	1.00
Baseline to 4-year						
Incurable multimorbidity pattern	987	19.09	133	17.07	Chi-square	0.20
Curable multimorbidity pattern	5	0.10	2	0.26	Fisher	0.23
Mixed curable multimorbidity pattern	956	18.49	86	11.04	Chi-square	<0.01
Single incurable disease	2640	51.05	446	57.25	Chi-square	<0.01
Single curable disease	59	1.14	1	0.13	Fisher	<0.01

No disease	401	7.75	92	11.81	Chi-square	<0.01
Dropout	123	2.38	19	2.44	Chi-square	1.00
4-year to 8-year						
Incurable multimorbidity pattern	1340	25.91	177	22.72	Chi-square	0.06
Curable multimorbidity pattern	3	0.10	1	0.13	Fisher	0.43
Mixed curable multimorbidity pattern	928	17.95	79	10.14	Chi-square	<0.01
Single incurable disease	2275	44.00	390	50.06	Chi-square	<0.01
Single curable disease	14	0.27	2	0.26	Fisher	1.00
No disease	158	3.06	34	4.36	Chi-square	0.07
Dropout	453	8.76	96	12.32	Chi-square	<0.01

Counts and proportions by sex across Baseline, Wave1, and Wave2; P-values from chi-square or Fisher's exact tests.

Supplemental Table 6. Multimorbidity patterns change over time among male participants

Wave comparison	Category	Test type	P- value
Baseline vs Wave1	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Chi-square	<0.01
	Mixed curable multimorbidity pattern	Chi-square	0.67
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01
Wave1 vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	0.73
	Mixed curable multimorbidity pattern	Chi-square	0.49
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Chi-square	<0.01
Baseline vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	<0.01
	Mixed curable multimorbidity pattern	Chi-square	0.82
	Single incurable disease	Chi-square	<0.05
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01

P-values are from chi-square tests (or Fisher's exact tests where appropriate) comparing Baseline vs Wave1 (Baseline to 4-year), Wave1 vs Wave2 (4-year to 8-year), and Baseline vs Wave2.

Supplemental Table 7. Multimorbidity patterns change over time among female participants

Wave comparison	Category	Test type	P- value
Baseline vs Wave1	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	1.00
	Mixed curable multimorbidity pattern	Chi-square	0.35
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Fisher	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01
Wave1 vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	1.00
	Mixed curable multimorbidity pattern	Chi-square	0.62
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Fisher	1.00
	No disease	Chi-square	<0.01
	Dropout	Chi-square	<0.01
Baseline vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	1.00
	Mixed curable multimorbidity pattern	Chi-square	0.13
	Single incurable disease	Chi-square	0.08
	Single curable disease	Fisher	<0.05
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01

P-values are from chi-square tests (or Fisher's exact tests where appropriate) for Baseline vs Wave1, Wave1 vs Wave2, and Baseline vs Wave2. Wave definitions as above.

Supplemental Table 8. Multimorbidity patterns distribution and diagnostic age difference in different waves

Category	≤32 years		>32 years		Test type	P-value
	Counts	Proportion, %	Counts	Proportion, %		
Baseline						
Incurable multimorbidity pattern	159	5.18	297	10.30	Chi-square	<0.01
Curable multimorbidity pattern	24	0.78	22	0.76	Chi-square	1.00
Mixed curable multimorbidity pattern	452	14.74	585	20.29	Chi-square	<0.01
Single incurable disease	1414	46.10	1325	45.96	Chi-square	<0.01
Single curable disease	139	4.53	69	2.39	Chi-square	0.93
No disease	879	28.66	585	20.29	Chi-square	<0.01
Dropout	0	0.00	0	0.00	Fisher	1.00
Baseline to 4-year						
Incurable multimorbidity pattern	394	12.85	726	25.18	Chi-square	<0.01
Curable multimorbidity pattern	4	0.13	3	0.10	Fisher	1.00
Mixed curable multimorbidity pattern	580	18.91	462	16.02	Chi-square	<0.01
Single incurable disease	1659	54.09	1427	49.50	Chi-square	<0.01
Single curable disease	43	1.40	17	0.59	Chi-square	<0.01

No disease	317	10.34	176	6.10	Chi-square	<0.01
Dropout	70	2.28	72	2.50	Chi-square	0.65
4 to 8-year						
Incurable multimorbidity pattern	606	19.76	911	31.60	Chi-square	<0.01
Curable multimorbidity pattern	2	0.07	2	0.07	Fisher	1.00
Mixed curable multimorbidity pattern	540	17.61	467	16.20	Chi-square	0.16
Single incurable disease	1501	48.94	1164	40.37	Chi-square	<0.01
Single curable disease	11	0.36	5	0.17	Chi-square	0.26
No disease	134	4.37	58	2.01	Chi-square	<0.01
Dropout	273	8.90	276	9.57	Chi-square	0.40

Counts and proportions are presented at Baseline, Wave1, and Wave2 with P-values from chi-square or Fisher's exact tests as indicated.

Supplemental Table 9. Multimorbidity patterns change over time among younger (≤ 32 years) participants

Wave comparison	Category	Test type	P- value
Baseline vs Wave1	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	<0.01
	Mixed curable multimorbidity pattern	Chi-square	<0.01
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01
Wave1 vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	0.69
	Mixed curable multimorbidity pattern	Chi-square	0.20
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Chi-square	<0.01
Baseline vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	<0.01
	Mixed curable multimorbidity pattern	Chi-square	<0.01
	Single incurable disease	Chi-square	<0.05
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01

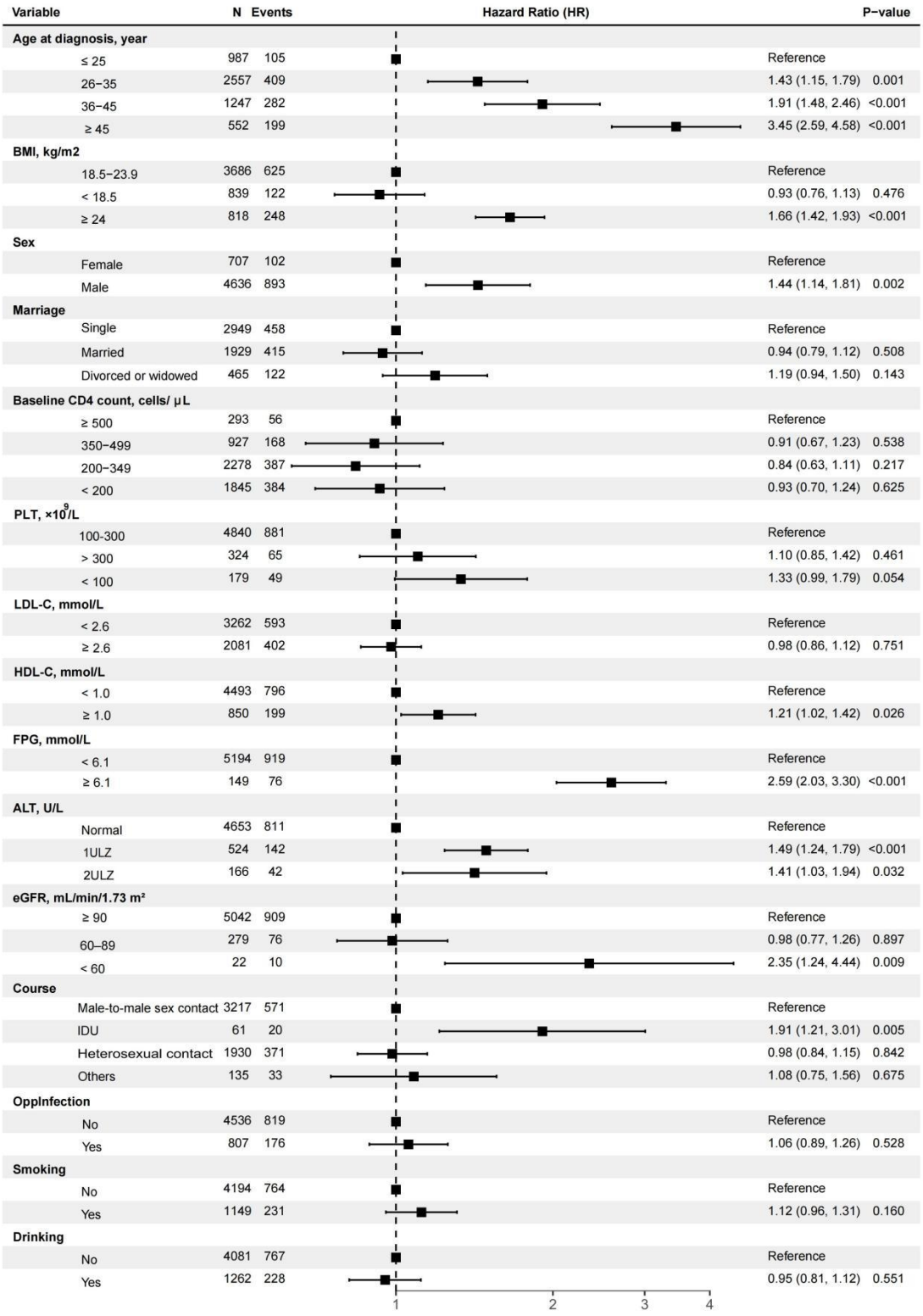
P-values are from chi-square tests (or Fisher's exact tests where appropriate) comparing Baseline vs Wave1, Wave1 vs Wave2, and Baseline vs Wave2.

Supplemental Table 10. Multimorbidity patterns change over time among older (>32 years) participants

Wave comparison	Category	Test type	P- value
Baseline vs Wave1	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	<0.01
	Mixed curable multimorbidity pattern	Chi-square	<0.01
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01
Wave1 vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	1.00
	Mixed curable multimorbidity pattern	Chi-square	0.89
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.05
	No disease	Chi-square	<0.01
	Dropout	Chi-square	<0.01
Baseline vs Wave2	Incurable multimorbidity pattern	Chi-square	<0.01
	Curable multimorbidity pattern	Fisher	<0.01
	Mixed curable multimorbidity pattern	Chi-square	<0.01
	Single incurable disease	Chi-square	<0.01
	Single curable disease	Chi-square	<0.01
	No disease	Chi-square	<0.01
	Dropout	Fisher	<0.01

P-values are from chi-square tests (or Fisher's exact tests where appropriate) comparing Baseline vs Wave1, Wave1 vs Wave2, and Baseline vs Wave2.

Supplemental Figure 1. Sensitivity analysis of Cox regression on metabolic multimorbidity using an extended 6-month ART initiation window



Forest plot from the sensitivity analysis using Cox regression. ART initiation within 6 months was used as the baseline definition for metabolic multimorbidity outcomes.