HIV/AIDS患者心血管疾病风险因素调查及评估

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2019-10-17 杭州

中华内科杂志

• 标准与讨论 •

中国艾滋病诊疗指南（2018年版）

中华医学会感染病学分会艾滋病丙型肝炎学组　中国疾病预防控制中心

中华内科杂志, 2018,57(12)：867-884. DOI: 10.3760/cma.j.issn.0578-1426.2018.12.002

Zhonghua Nei Ke Za Zhi. 2018 Dec 1;57(12):867-884. doi: 10.3760/cma.j.issn.0578-1426.2018.12.002.

[Chinese guidelines for diagnosis and treatment of HIV/AIDS (2018)].

[Article in Chinese]

AIDS and Hepatitis C Professional Group, Society of Infectious Diseases, Chinese Medical Association; Chinese Center for Disease Control and Prevention.

Abstract

(AIDS) is an important public health problem in China. In 2005, the first edition of the guidelines for the diagnosis and treatment of AIDS was formulated by the AIDS Professional Group of Society of Infectious Diseases of Chinese Medical Association, which was updated twice in 2011 and 2015. The fourth edition of the guidelines in 2018 is revised on the basis of national clinical practice and the latest research studies. The new research progress in opportunistic infections and human immunodeficency virus(HIV) associated cancers, antiretroviral therapy, HIV post-exposure prophylaxis, and prevention of mother to child transmission were updated in these guidelines. In the 2018 edition, pre-exposure prophylaxis is mentioned for the first time. The strategy of whole course management of HIV infection is put forward in the current version, which needs the participation of multidisciplinary team in prophylaxis, early diagnosis, individualized treatment and humanistic care.

KEYWORDS: Acquired immunodeficiency syndrome; Diagnosis; Treatment

PMID: 30486555 DOI: 10.3760/cma.j.issn.0578-1426.2018.12.002

[Indexed for MEDLINE]

·导向与述评·

《中国艾滋病诊疗指南（2018版）》解读

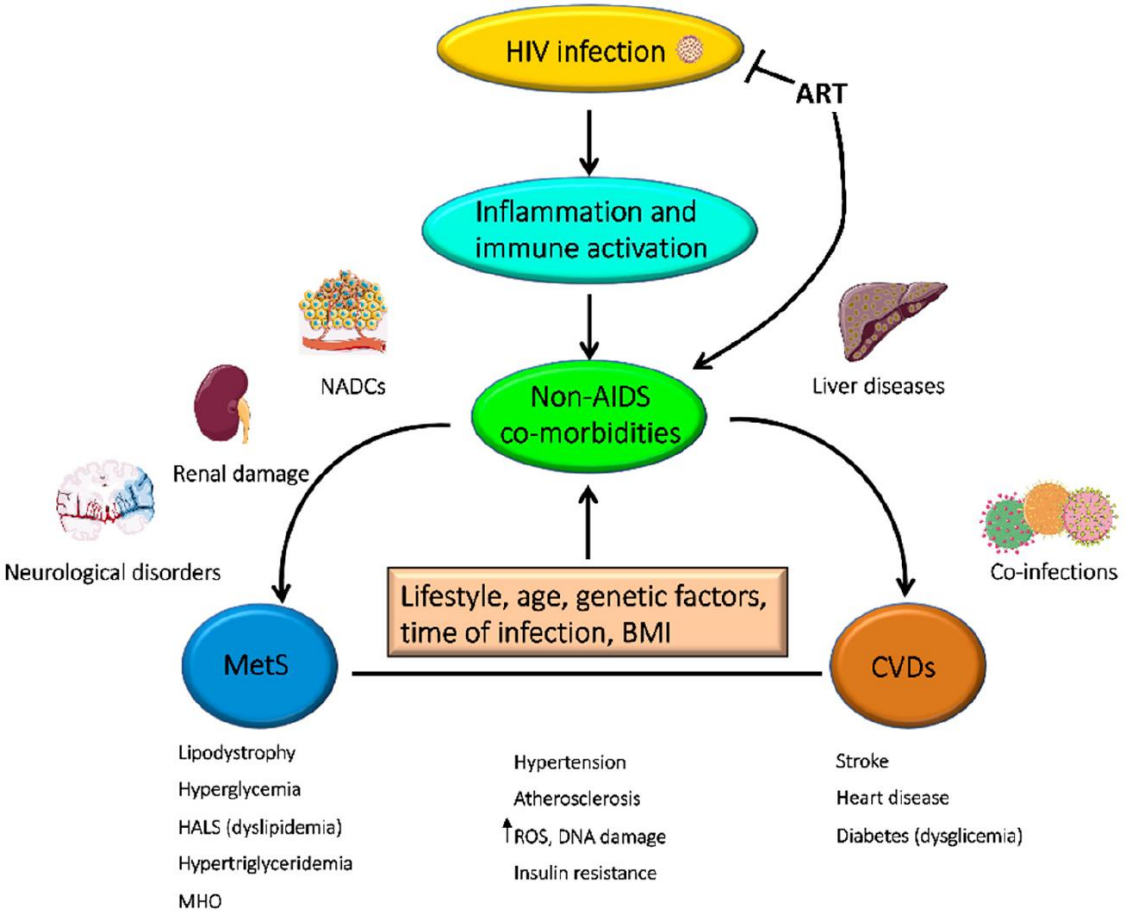
沈银忠

- 强化了艾滋病预防的理念
- 突出了核酸检测在诊断和治疗中的价值
- 艾滋病合并结核病和隐球菌脑膜炎治疗方案更新幅度大，突出了中国研究者的贡献
- 抗病毒治疗推荐方案向便捷、高效、低毒的方向发展
- 更新抗病毒治疗失败的定义及其处理规范
- 首次规范了HIV单阳家庭的生育问题
- **首次提出HIV感染的全程管理理念**

HIV感染的全程管理

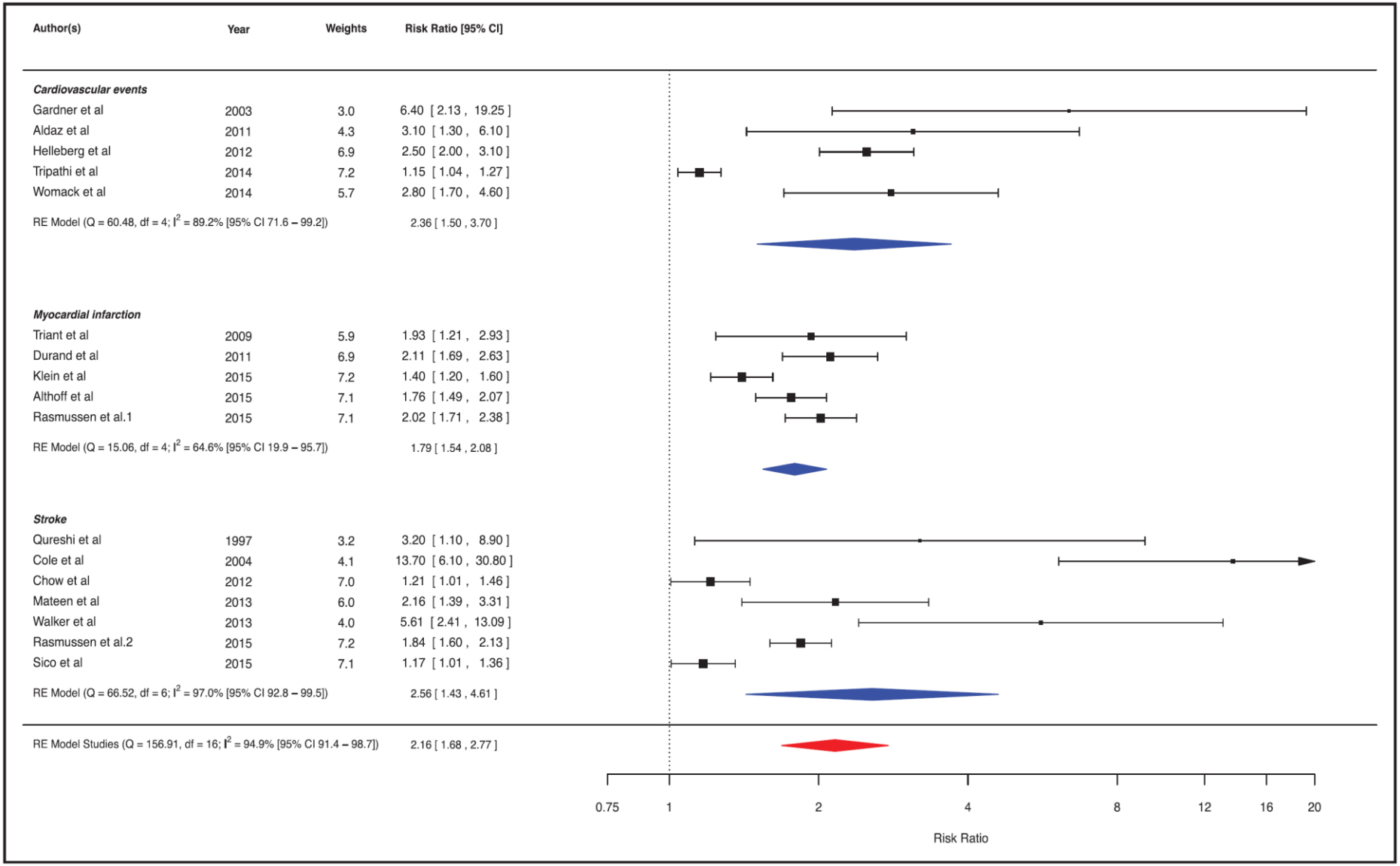
- HIV感染者在确诊后多学科合作团队为其提供的一种全程综合诊治和服务关怀管理模式。
- 全程管理的诊治模式是一种以感染科医生参与的多学科协作诊治模式。
- **全程管理的关注环节：**
  - HIV感染的预防和早期诊断
  - 机会性感染的诊治和预防
  - 个体化抗病毒治疗的启动和随访
  - **非HIV定义性疾病的筛查与处理**
  - 社会心理综合关怀
- **国内外首次提出此概念**

非HIV定义性疾病的筛查与处理



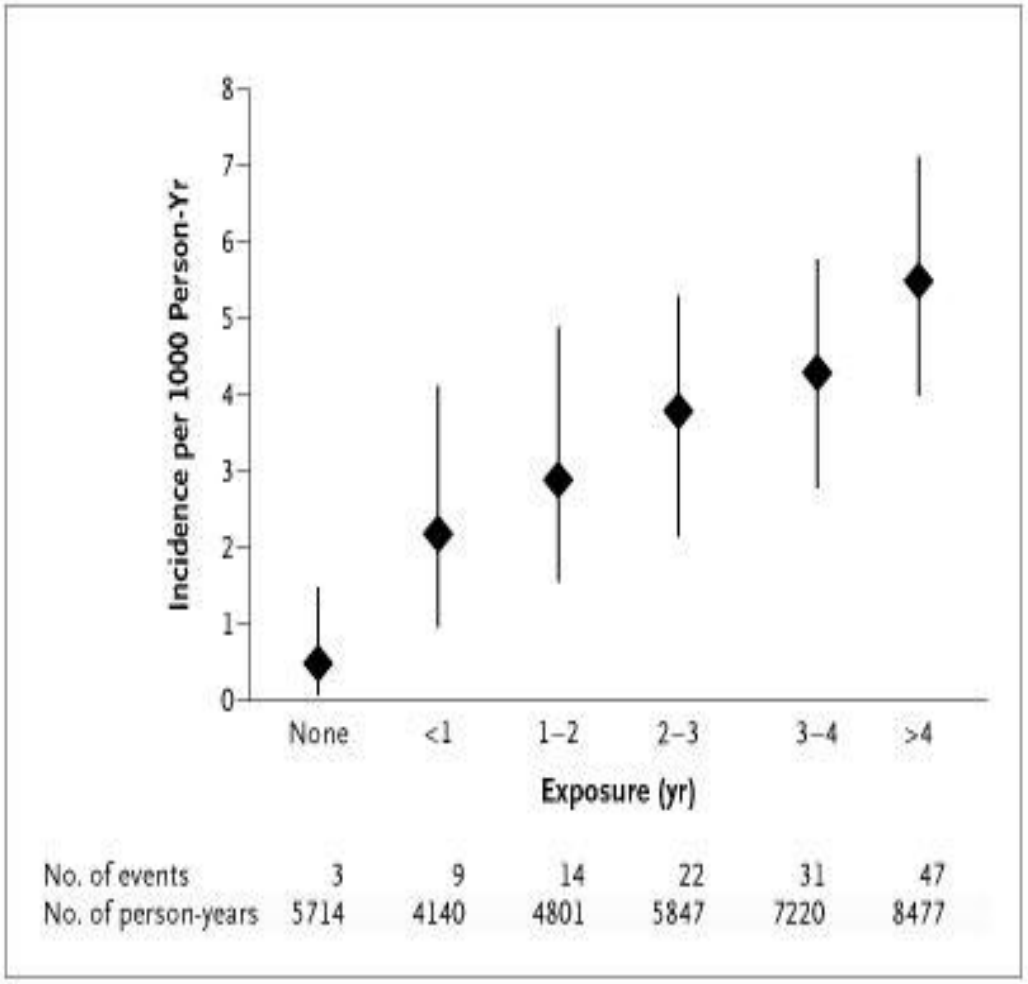
- Routine metabolic screenings should become an essential part of routine HIV care.
- Measuring personal patients' risks at every visit, starting immediately from the time of HIV diagnosis, will help to improve quality of life.

Zicari S, et al. Viruses. 2019 Feb 27;11(3). pii: E200.



Circulation. 2018;138:1100–1112. DOI: 10.1161/CIRCULATIONAHA.117.033369

Incidence of Myocardial Infarction According to the Duration of Exposure to Combination Antiretroviral Therapy



The DAD Study Group, N Engl J Med 2003;349:1993-2003

HIV and Noncommunicable Cardiovascular and Pulmonary Diseases in Low- and Middle-Income Countries in the ART Era: What We Know and Best Directions for Future Research

Gerald S. Bloomfield, MD, MPH,† Prateeti Khazanie, MD, MPH,* Alison Morris, MD, MS,‡ Cristina Rabadán-Diehl, PhD, MPH,§ Laura A. Benjamin, MD, PhD,‖¶ David Murdoch, MD, MPH,# Virginia S. Radcliff, MD,# Eric J. Velazquez, MD,*† and Charles Hicks, MD***

Abstract: With the advent of effective antiretroviral therapy (ART), HIV is becoming a chronic disease. HIV-seropositive (+) patients on ART can expect to live longer and, as a result, they are at risk of developing chronic noncommunicable diseases related to factors, such as aging, lifestyle, long-term HIV infection, and the potential adverse effects of ART. Although data are incomplete, evidence suggests that even in low- and middle-income countries (LMICs), chronic cardiovascular and pulmonary diseases are increasing in HIV-positive patients. This review summarizes evidence-linking HIV infection to the most commonly cited chronic cardiovascular and pulmonary conditions in LMICs: heart failure, hypertension, coronary artery disease/myocardial infarction, stroke, obstructive lung diseases, and pulmonary arterial hypertension. We describe the observed epidemiology of these conditions, factors affecting expression in LMICs, and key populations that may be at higher risk (ie, illicit drug users and children), and finally, we suggest that strategic areas of research and training intended to counter these conditions effectively. As access to ART in LMICs increases, long-term outcomes among HIV-positive persons will increasingly be determined by a range of associated chronic cardiovascular and pulmonary complications. Actions taken now to identify those conditions that contribute to long-term morbidity and mortality optimize early recognition and diagnosis and implement effective prevention strategies and/or disease interventions are likely to have the greatest impact on limiting cardiovascular and pulmonary disease comorbidity and improving population health among HIV-positive patients in LMICs.

Key Words: HIV, cardiovascular disease, pulmonary disease, global health, developing countries, sub-Saharan Africa

(*J Acquir Immune Defic Syndr* 2014;67:S40–S53)

INTRODUCTION

The risk of developing chronic cardiovascular and pulmonary diseases is increasingly recognized as a major public health problem in patients infected with HIV,[1–3] perhaps related to long-term exposure to the virus, the effects of ongoing inflammatory responses, progressive immunologic dysfunction, and/or long-term adverse effects associated with antiretroviral therapy (ART). The inevitable consequences of aging, the development of age-related chronic conditions, and other factors affecting cardiopulmonary health are likely to compound any HIV viral or treatment effect. The overall impact of chronic noncommunicable cardiovascular and pulmonary diseases occurring among HIV-positive people in low- and middle-income countries (LMICs) (defined according to

Abstracts of the HIV Drug Therapy Glasgow Congress 2014
Begovac J et al. *Journal of the International AIDS Society* 2014, **17(Suppl 3)**:19549
http://www.jiasociety.org/index.php/jias/article/view/19549 | http://dx.doi.org/10.7448/IAS.17.4.19549

JIAS Journal of the International AIDS Society

Poster Sessions – Abstract P017

Prevalence and concordance of high cardiovascular disease scores in HIV/AIDS patients from Croatia and Serbia with four international algorithms

Begovac, Josip[1]; Dragovic, Gordana[2]; Viskovic, Klaudija[1]; Kusic, Jovana[3]; Perovic Mihanovic , Marta[1]; Lukas, Davorka[1] and Jevtovic, Djordje[3]

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Introduction: We evaluated cardiovascular risks in HIV-infected patients from Croatia and Serbia and the eligibility for statin therapy as recommended by the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines, European AIDS Clinical Society (EACS) Guidelines and European Society of Cardiology and the European Atherosclerosis Society (ESC/EAS) guidelines for cardiovascular disease (CVD) prevention [1–3].
Materials and Methods: A cross-sectional analysis of consecutive patients between 40 and 79 years old who had received antiretroviral therapy for at least 12 months was performed.
Results: Of 254 (132 from Croatia and 122 from Serbia) persons included in the study, 76% were male; median age was 49 years. Up to 51.6% of persons had a high CVD risk. The prevalence of current smoking was 42.9%, hypertension 31.5% and hypercholesterolaemia (>6.2 mmol/L) 35.4%. Statins would be recommended to 21.3% (95% CI, 16.3% to 27.4%) of persons by the EACS, 25.6% (95% CI, 20.2% to 31.9%) by ESC/EAS and 37.9% (95% CI, 31.6 to 44.6%) by the ACC/AHA guidelines. A high 5-year data collection on adverse effects of anti-HIV drugs study risk score ($>5\%$) had a moderate agreement with the high ($\geq 20\%$) 10-year CVD Framingham risk score (kappa $=0.47$) and high ($\geq 5\%$) 10-year European systematic coronary risk evaluation score algorithm (kappa $=0.47$), and substantial agreement with the elevated ($\geq 7.5\%$) 10-year Pooled Cohort Atherosclerotic CVD risk equation score (kappa $=0.63$).
Conclusion: We found a high prevalence of CVD risks in patients from Croatia and Serbia. The ACC/AHA guideline would recommend statins more often than ESC/EAS and EACS guidelines.

References

Original Article

DOI: 10.5582/bst.2016.01195

Trends and characteristics of all-cause mortality among HIV-infected inpatients during the HAART era (2006-2015) in Shanghai, China

Yongjia Ji[1,§], Zhenyan Wang[1,§], Jiayin Shen[1,§], Jun Chen[1], Junyang Yang[1], Tangkai Qi[1], Wei Song[1], Yang Tang[1], Li Liu[1], Yinzhong Shen[1], Renfang Zhang[1], Hongzhou Lu[1,2,3,*]

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[2] *Department of Infectious Diseases, Huashan Hospital Affiliated to Fudan University, Shanghai, China;*
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Table 2. Causes of death among HIV-infected inpatients from 2006 to 2015

Cause of death	Number of patients $n = 303$ (%)
AIDS-related death	233 (76.9)
Pneumocystis jirovecii pneumonia	80 (26.4)
NTM/MTB infection[a]	56 (18.5)
AIDS-related encephalopathy[b]	47 (15.5)
Recurrent bacterial pneumonia	31 (10.2)
AIDS-related malignancy[c]	18 (5.9)
Wasting syndrome	1 (0.4)
Non-AIDS-related death	70 (23.1)
Sepsis	18 (5.9)
Liver disease	11 (3.6)
Non-recurrent bacterial pneumonia	9 (3.0)
Gastrointestinal hemorrhage	8 (2.6)
Non-AIDS-related malignancy	7 (2.3)
Cardiovascular disease	6 (2.0)
Renal disease	5 (1.7)
Trauma	2 (0.7)
Other[d]	4 (1.3)

非HIV定义性疾病的筛查与处理

- HAART的应用把艾滋病变成一种慢性病，应该按照慢性管理模式来进行随访和管理，随访中应注意评估和筛查NAD（非HIV定义性疾病），并根据评估结果给予相应预防或治疗措施。
- 随着患者生存期的延长，随访中应特别注意评估患者心血管疾病的风险并给予相应的预防措施。
- HIV患者中各种慢性疾病如高血压、糖尿病、血脂紊乱、冠心病、脑血管疾病、非HIV相关肿瘤（尤其是肝癌、肺癌、乳腺癌、前列腺癌、结肠直肠癌等）、COPD、非酒精性脂肪肝、骨骼疾病等均需按照HIV阴性者一样建立慢病管理档案并按照相关指南进行筛查和预防处理。
- 随着HIV患者生存期的延长，年龄对HIV患者关怀的影响需要特别关注，应把对老年综合征的评估纳入HIV综合关怀之中。在每次随访中，应该对患者是否存在老年综合征进行评估，尤其应该对其心理精神状况、肾功能、心功能、骨骼、社会适应能等进行综合评估。
- 应根据这些慢性疾病特点和分级诊疗要求来进行诊治，鼓励患者在综合医院相应专科门诊接受诊治。

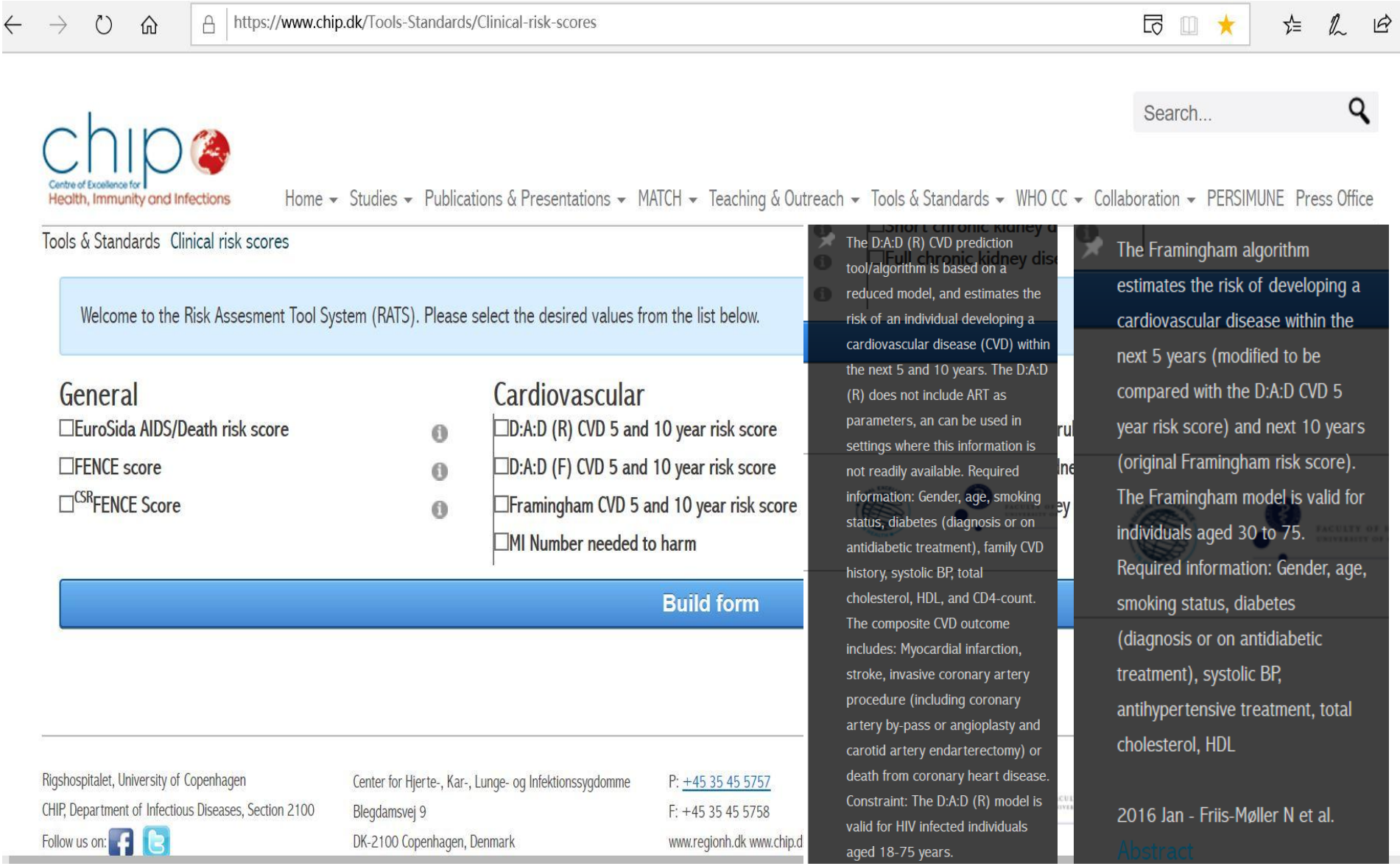
中国艾滋病诊疗指南（2018年版）. 中华内科杂志,2018,57(12): 867-884

研究目的

- 抗反转录病毒治疗 (ART)广泛深入地实施，大大延长了人类免疫缺陷病毒 (HIV) 感染者的生存期，但同时该人群的心血管疾病（CVD）患病率也逐步升高。
- 本研究调查在未接收ART的艾滋病患者中CVD风险因素并进行风险评估，旨在为患者后续ART方案选择及CVD的监测和管理提供参考。

研究方法

- 对上海市公共卫生临床中心感染与免疫科门诊2018年11月～2019年6月间199例新确诊HIV感染者进行横断面调查。
- 使用结构化问卷收集研究对象的社会人口学特征。
- 通过问诊收集患者CVD的传统危险因素包括高血压、血脂异常、糖尿病、生活方式、吸烟等资料，同时收集CD4+T淋巴细胞计数、高密度脂蛋白胆固醇 (HDL-C) 、低密度脂蛋白胆固醇 (LDL-C)、甘油三酯 (TG) 及总胆固醇 (TC)的检测值。
- 分别使用D:A:D(RF)CVD 5 and 10 year risk score , Framingham CVD 5 and 10 year risk score进行风险评估。
- 使用Stata13.0来输入和分析数据。


https://www.chip.dk/Tools-Standards/Clinical-risk-scores
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Tools & Standards Clinical risk scores
Welcome to the Risk Assesment Tool System (RATS). Please select the desired values from the list below.
General
EuroSida AIDS/Death risk score
FENCE score
CSRFENCE Score
Cardiovascular
D:A:D (R) CVD 5 and 10 year risk score
D:A:D (F) CVD 5 and 10 year risk score
Framingham CVD 5 and 10 year risk score
MI Number needed to harm
Build form
The D:A:D (R) CVD prediction tool/algorithm is based on a reduced model, and estimates the risk of an individual developing a cardiovascular disease (CVD) within the next 5 and 10 years. The D:A:D (R) does not include ART as parameters, an can be used in settings where this information is not readily available. Required information: Gender, age, smoking status, diabetes (diagnosis or on antidiabetic treatment), family CVD history, systolic BP, total cholesterol, HDL, and CD4-count. The composite CVD outcome includes: Myocardial infarction, stroke, invasive coronary artery procedure (including coronary artery by-pass or angioplasty and carotid artery endarterectomy) or death from coronary heart disease. Constraint: The D:A:D (R) model is valid for HIV infected individuals aged 18-75 years.
The Framingham algorithm estimates the risk of developing a cardiovascular disease within the next 5 years (modified to be compared with the D:A:D CVD 5 year risk score) and next 10 years (original Framingham risk score). The Framingham model is valid for individuals aged 30 to 75. Required information: Gender, age, smoking status, diabetes (diagnosis or on antidiabetic treatment), systolic BP, antihypertensive treatment, total cholesterol, HDL
2016 Jan - Friis-Møller N et al.
Abstract
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D:A:D (R) CVD 5 and 10 year risk score

1. Age: [ ] yr
2. Gender: ○Male ○Female
3. Previous smoker? ○Yes ○No
4. Smoker? ○Yes ○No
5. Family CVD history? ○Yes ○No
6. Diabetes? ○Yes ○No
7. CD4 cell count: [ ] Cells/μL
8. Systolic blood pressure: [ ] mmHg
9. Total cholesterol: [ ] mmol/L
10. HDL: [ ] mmol/L

Framingham CVD 5 and 10 year risk score

1. Age: [ ] yr
2. Gender: ○Male ○Female
3. Smoker? ○Yes ○No
4. Diabetes? ○Yes ○No
5. BP lowering treatment? ○Yes ○No
6. Systolic blood pressure: [ ] mmHg
7. Total cholesterol: [ ] mmol/L
8. HDL: [ ] mmol/L

研究结果

项目	数值（百分比）
年龄（岁）	
中位数	34（18- 74）
18-24	31（15.58%）
25-34	72（36.18%）
35-44	36（18.09%）
45-54	24（12.06%）
≥55	36（18.09%）
性别	
男	182（91.46%）
女	17 （8.54%）

研究结果

项目	数值（百分比）
CD4+T淋巴细胞计数（/μL）	
中位数	269（2-815）
<50	11（6.25%）
50-200	43（36.75%）
200-350	59（33.52%）
≥350	63（35.80%）

研究结果

项目	数值（百分比）
高血压	17（8.54%）
治疗	12（70.59%）
未治疗	5（29.41%）
糖尿病	12（6.03%）
治疗	11（91.67%）
未治疗	1（8.33%）
冠心病 (CHD) 病史	2（1%）
脑梗死	8（6.72%）
扩展型心脏病	1（0.50%）
室间隔缺损	1（0.50%）
房间隔缺损	1（0.50%）
心脏瓣膜病变	1（0.50%）

研究结果

项目	数值（百分比）
HDL-C 降低	99（54.96%）
TG 升高	62（33.70%）
TC升高	23（12.5%）
LDL-C 升高	6（3.31%）

研究结果

项目	数值（百分比）
饮食习惯	
喜好清淡	39（34.51%）
喜好脂肪饮食	39（34.51%）
无明显偏好	37（32.74%）
吸烟	45（22.61%）
服用心血管药物	4（3.36%）
服用他汀类药物	2（1%）
合并HCV感染	3（2.52%）
每周运动30min*3次	86（43.22%）

研究结果

风险评估方法	风险评估
D:A:D(R)CVD 5 year risk score	0.04%-50.24%
D:A:D(R)CVD 10 year risk score	0.09%-76.54%
低危组[10年内发生CVD风险<10%]	**81.67%**
中危组[10年内发生CVD风险10%-20%]	**5.83%**
高危组[10年内发生CVD风险大于20%]	**12.5%**

研究结果

风险评估方法	风险评估
Framingham CVD 5 year risk score	0.21%- 54.7%
Framingham CVD 10year risk score	1.0%- >30%
低危组[10年内发生CVD风险<10%]	**66.23%**
中危组[10年内发生CVD风险10%-20%]	**10.39%**
高危组[10年内发生CVD风险大于20%]	**23.38%**

结果解读

- 新确诊患者CVD存在的传统高危因素多见：高血压、血脂紊乱、高血糖、胰岛素抵抗、CVD、吸烟、饮食习惯、缺乏运动等。
- 确诊时CD4+T淋巴细胞计数低。
- 传统高危因素干预：干预率低。
- 抗病毒治疗方案的选择。

Shen et al. BMC Infectious Diseases 2013, 13:79
http://www.biomedcentral.com/1471-2334/13/79

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Prevalence of hyperglycemia among adults with newly diagnosed HIV/AIDS in China

Yinzhong Shen, Zhenyan Wang, Li Liu, Renfang Zhang, Yufang Zheng and Hongzhou Lu*

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Prevalence of Dyslipidemia Among Antiretroviral-Naive HIV-Infected Individuals in China

Yinzhong Shen, MD, Jiangrong Wang, MS, Zhenyan Wang, MS, Tangkai Qi, MS, Wei Song, MS, Yang Tang, MS, Li Liu, MD, Renfang Zhang, MS, and Hongzhou Lu, MD

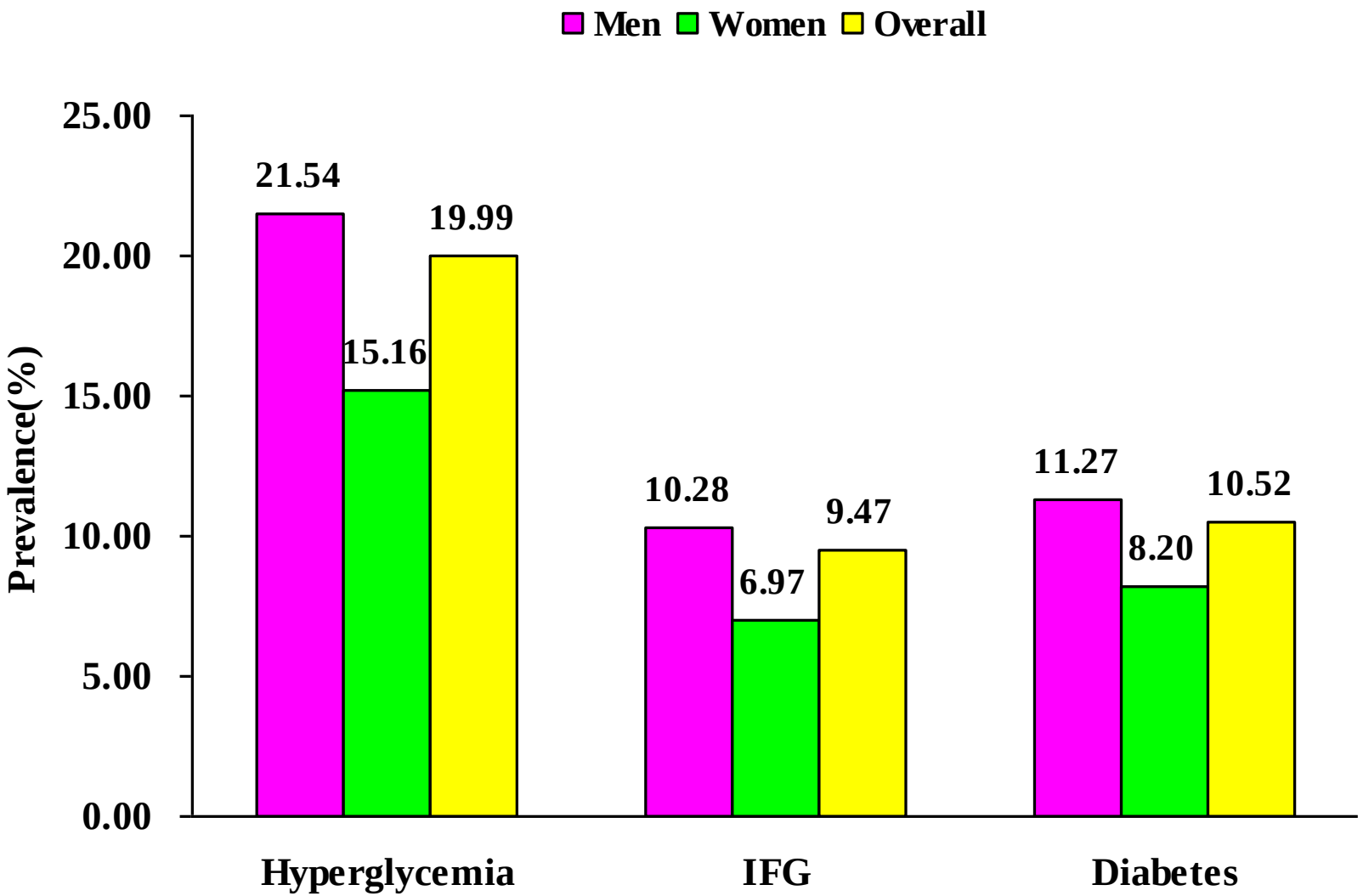


Figure 1 Prevalence of hyperglycemia, IFG and diabetes among men and women with newly diagnosed HIV/AIDS

TABLE 2. Prevalence of Dyslipidemia Among All Study Subjects

Cohort	High TC	High TG	High LDL	Low HDL
Number	1865	1865	1697	1697
Overall	12.1%	30.7%	14.2%	54.4%
Sex				
Male	9.3%	33.0%	10.9%	61.5%
Female	17.5%	26.4%	22.3%	37.1%
P-value for difference	<0.001	0.004	<0.001	<0.001
Ethnicity				
Han	14.1%	31.7%	15.7%	50.9%
Other (minority)	4.3%	26.9%	9.0%	66.8%
P-value for difference	<0.001	0.07	0.001	<0.001
Age, years				
18–24	12.0%	29.3%	23.3%	44.4%
25–34	8.9%	28.5%	13.3%	54.6%
35–44	10.7%	32.2%	12.5%	56.4%
45–54	17.4%	36.3%	14.4%	56.3%
≥55	16.8%	25.4%	16.5%	50.9%
P-value for difference	<0.001	0.04	0.07	0.19
HIV status				
HIV positivity	8.4%	33.9%	8.5%	59.6%
HIV negativity	28.2%	17.0%	62.6%	11.2%
P-value for difference	<0.001	<0.001	<0.001	<0.001
HCV serostatus				
HCVAb positivity	9.3%	30.4%	8.4%	61.2%
HCVAb negativity	12.5%	30.8%	15.1%	53.4%
P-value for difference	0.16	0.91	0.007	0.027

未接受ART的HIV患者血脂紊乱发生率为75.6%

Shen et al. BMC Infectious Diseases 2013, 13:429
http://www.biomedcentral.com/1471-2334/13/429

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Analysis of the immunologic status of a newly diagnosed HIV positive population in China

Yinzhong Shen, Hongzhou Lu*, Zhenyan Wang, Tangkai Qi and Jiangrong Wang

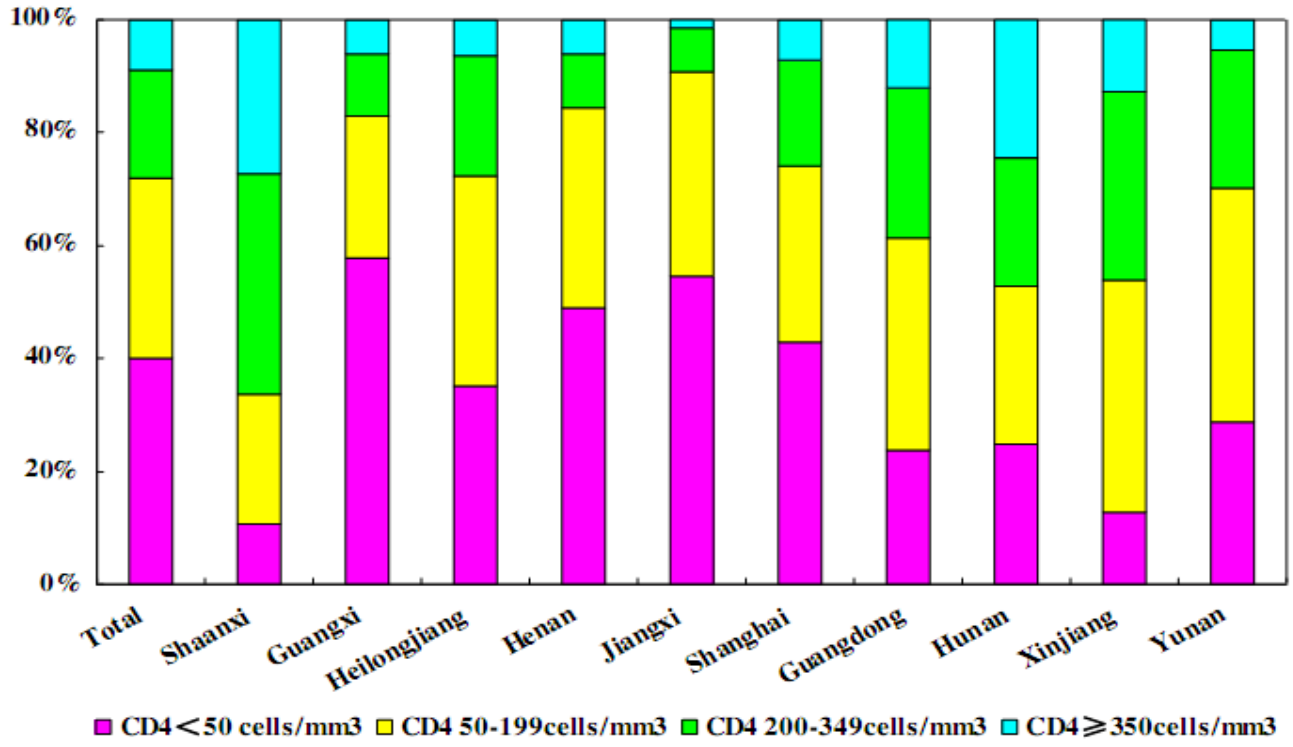


Figure 1 The distribution of CD4 counts in newly diagnosed HIV-infected patients in China by province.

Initial Characteristics to Consider in All Persons with HIV:

- Pretreatment HIV RNA level (viral load)
- Pretreatment CD4 count
- HIV genotypic drug resistance testing results (based on current rates of transmitted drug resistance to different ARV medications, standard genotypic drug-resistance testing in ARV-naive persons should focus on testing for mutations in the reverse transcriptase [RT] and protease [PR] genes. If transmitted INSTI resistance is a concern, providers should consider also testing for resistance mutations to this class of drugs).
- HLA-B*5701 status
- Individual preferences
- Anticipated adherence to the regimen

Specific Comorbidities or Other Conditions:

- Cardiovascular disease, hyperlipidemia, renal disease, liver disease, osteopenia/osteoporosis or conditions associated with BMD loss, psychiatric illness, neurologic disease, drug abuse or dependency requiring narcotic replacement therapy
- Pregnancy or pregnancy potential. Clinicians should refer to the latest Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in The United States (Perinatal Guidelines) for more detailed recommendations on the safety and effectiveness of ARV drugs during pregnancy.
- Coinfections: HBV, hepatitis C virus (HCV), TB

Regimen-Specific Considerations:

- Regimen's genetic barrier to resistance
- Potential adverse effects
- Known or potential drug interactions with other medications (see Drug Interactions)
- Convenience (e.g., pill burden, dosing frequency, availability of fixed-dose combination formulations, food requirements)
- Cost (see Cost Considerations and Antiretroviral Therapy)

FDA Approval of HIV Medicines

1981: First AIDS cases are reported in the United States.

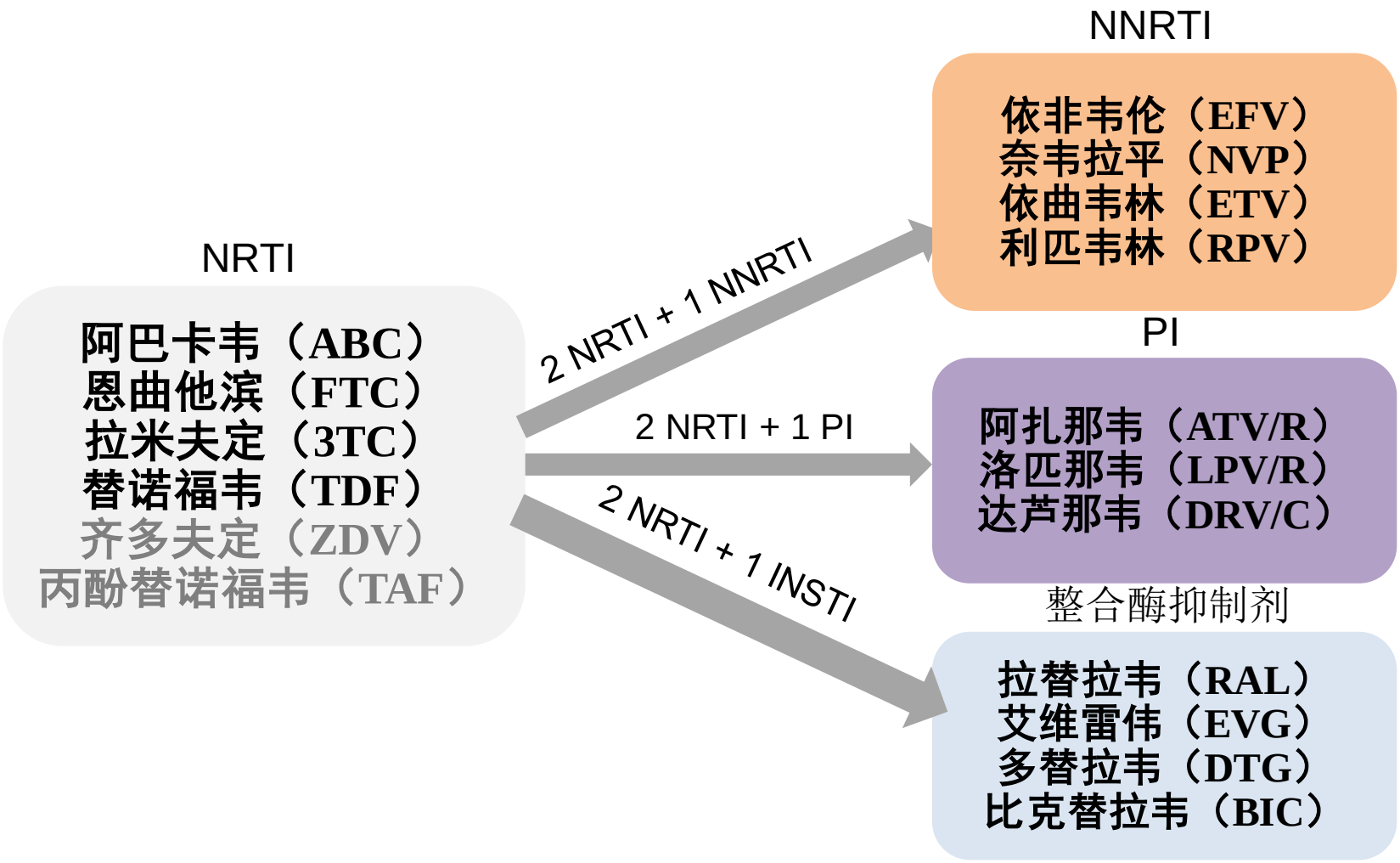
'85-'89	**1987** Zidovudine (NRTI)				
'90-'94	**1991** Didanosine (NRTI)	**1992** Zalcitabine (NRTI)	**1994** Stavudine (NRTI)		
'95-'99	**1995** Lamivudine (NRTI) Saquinavir (PI)	**1996** Indinavir (PI) Nevirapine (NNRTI) Ritonavir (PI)	**1997** Combivir (FDC) Delavirdine (NNRTI) Nelfinavir (PI)	**1998** Abacavir (NRTI) Efavirenz (NNRTI)	**1999** Amprenavir (PI)
'00-'04	**2000** Didanosine EC (NRTI) Kaletra (FDC) Trizivir (FDC)	**2001** Tenofovir DF (NRTI)	**2003** Atazanavir (PI) Emtricitabine (NRTI) Enfuvirtide (FI) Fosamprenavir (PI)	**2004** Epzicom (FDC) Truvada (FDC)	
'05-'09	**2005** Tipranavir (PI)	**2006** Atripla (FDC) Darunavir (PI)	**2007** Maraviroc (CA) Raltegravir (INSTI)	**2008** Etravirine (NNRTI)	
'10-'14	**2011** Complera (FDC) Nevirapine XR (NNRTI) Rilpivirine (NNRTI)	**2012** Stribild (FDC)	**2013** Dolutegravir (INSTI)	**2014** Cobicistat (PE) Elvitegravir (INSTI) Triumeq (FDC)	
'15-'19	**2015** Evotaz (FDC) Genvoya (FDC) Prezcobix (FDC)	**2016** Descovy (FDC) Odefsey (FDC)	**2017** Juluca (FDC)	**2018** Biktarvy (FDC) Cimduo (FDC) Delstrigo (FDC) Doravirine (NNRTI) Ibalizumab-uiyk (PAI) Symfi (FDC) Symfi Lo (FDC) Symtuza (FDC) Temixys (FDC)	**2019** Dovato (FDC)

Drug Class Abbreviations:
CA: CCR5 Antagonist; **FDC:** Fixed-Dose Combination; **FI:** Fusion Inhibitor; **INSTI:** Integrase Inhibitor; **NNRTI:** Non-Nucleoside Reverse Transcriptase Inhibitor; **NRTI:** Nucleoside Reverse Transcriptase Inhibitor; **PE:** Pharmacokinetic Enhancer; **PI:** Protease Inhibitor; **PAI:** Post-Attachment Inhibitor

Note: Drugs in gray are no longer available and/or are no longer recommended for use in the United States by the HHS HIV/AIDS medical practice guidelines. These drugs may still be used in fixed-dose combination formulations.

AIDSinfo

初始治疗方案如何选择


NNRTI
依非韦伦（EFV）
奈韦拉平（NVP）
依曲韦林（ETV）
利匹韦林（RPV）
NRTI
阿巴卡韦（ABC）
恩曲他滨（FTC）
拉米夫定（3TC）
替诺福韦（TDF）
齐多夫定（ZDV）
丙酚替诺福韦（TAF）
2 NRTI + 1 NNRTI
2 NRTI + 1 PI
2 NRTI + 1 INSTI
PI
阿扎那韦（ATV/R）
洛匹那韦（LPV/R）
达芦那韦（DRV/C）
整合酶抑制剂
拉替拉韦（RAL）
艾维雷伟（EVG）
多替拉韦（DTG）
比克替拉韦（BIC）

结果解读

- HIV患者CVD风险评估的方法： **traditional risk scores perform poorly because they consistently underestimate the risk in HIV populations.**
  - **the Framingham CVD Risk Score (FRS)**
  - **Data Collectionon Adverse events of Anti-HIV Drugs (D:A:D) risk scores**
  - **the American College of Cardiology/American Heart Association (ACC/AHA) Atherosclerotic Cardiovascular Disease Risk Score (ASCVD)**
- 未接受ART患者CVD风险高。
- 未接受ART患者CVD的预防与干预？

Whether patients living with HIV should be considered high risk and started on primary prevention, such as statin therapy, remains unclear. A recent randomized controlled trial of rosuvastatin in patients with HIV demonstrated a reduction in carotid artery intima-media thickness despite these individuals having low low-density lipoprotein cholesterol concentrations at baseline.[58] Although the latest international guide-

Guo et al. BMC Infectious Diseases (2017) 17:287
DOI 10.1186/s12879-017-2358-0

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Cardiovascular disease risk among Chinese antiretroviral-naïve adults with advanced HIV disease

Fuping Guo[1†], Evelyn Hsieh[1,2†], Wei Lv[1], Yang Han[1], Jing Xie[1], Yanling Li[1], Xiaojing Song[1] and Taisheng Li[1*]

Abstract

Background: Cardiovascular disease (CVD) is an important cause of mortality among HIV-infected patients, however little is known about the burden of CVD among this population in Asia. We sought to quantify prevalence of CVD risk factors, 10-year CVD risk, and patterns of CVD risk factor treatment in a group of individuals with HIV in China.

Methods: We retrospectively analyzed baseline data from treatment-naïve HIV-infected adults enrolled in two multicenter clinical trials in China. Data regarding CVD risk factors such as smoking, hypertension, diabetes, dyslipidemia and obesity were assessed. The Framingham Risk Score (FRS) and Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) risk scores were calculated to estimate 10-year CVD risk. The American College of Cardiology/American Heart Association Atherosclerotic Cardiovascular Disease (ASCVD) Risk Score was used to identify individuals meeting criteria for lipid-lowering therapy.

Results: In total, 973 patients were included in the analysis. Mean age was 36.0 ± 10.2 years and 74.2% were men. The most common CVD risk factors were dyslipidemia (51.7%) and smoking (23.7%). Prevalence of hypertension, diabetes and obesity were 8.4%, 4.6% and 1.0%, respectively. Over 65% of patients had at least one CVD risk factor. The prevalence of 10-year risk of CVD ≥10% was 4.5% based upon FRS and was 3.3% based upon D:A:D risk score. Few patients with dyslipidemia, hypertension or diabetes were on treatment.

Conclusions: CVD risk factors are common but under-treated among Chinese treatment-naïve individuals with HIV. Future interventions should focus on training HIV providers to appropriately recognize and manage CVD risk factors during routine clinical assessments.

Keywords: HIV, Cardiovascular disease risk, Framingham risk score, Data collection on adverse events of anti-HIV drugs (D:A:D) risk score, Atherosclerotic cardiovascular disease risk score

Table 2 Estimated 10-year cardiovascular risk among Chinese antiretroviral-naïve HIV-infected patients

Characteristics	All *n/N* (%)	Male *n/N* (%)	Female *n/N* (%)	*p*-value
FRS				NA
< 10%	921/965 (95.5%)	671/715 (93.8%)	250/250 (100%)	
10–20%	39/965 (4.0%)	39/715 (5.5%)	0/250 (0%)	
> 20%	5/965 (0.5%)	5/715 (0.7%)	0/250 (0%)	
D:A:D Risk Score				NA
< 10%	941/973 (96.7%)	692/722 (95.8%)	249/251 (99.2%)	
10–20%	20/973 (2.1%)	18/722 (2.5%)	2/251 (0.8%)	
> 20%	12 /973 (1.2%)	12/722 (1.7%)	0/251 (0%)	
Favorable Cardiovascular Risk Profile	364/973 (37.4%)	257/722 (35.6%)	107/251 (42.6%)	0.047

NA, not applicable; FRS, the Framingham Risk Score; (D:A:D) Risk Score, Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) Risk Scores; Favorable cardiovascular risk profile was defined on the basis of a number of modifiable risk factors as follows: total cholesterol <5.17 mmol/l, systolic blood pressure ≤ 120 mmHg, diastolic blood pressure ≤ 80 mmHg, no current smoking, no diabetes and no prior CVD

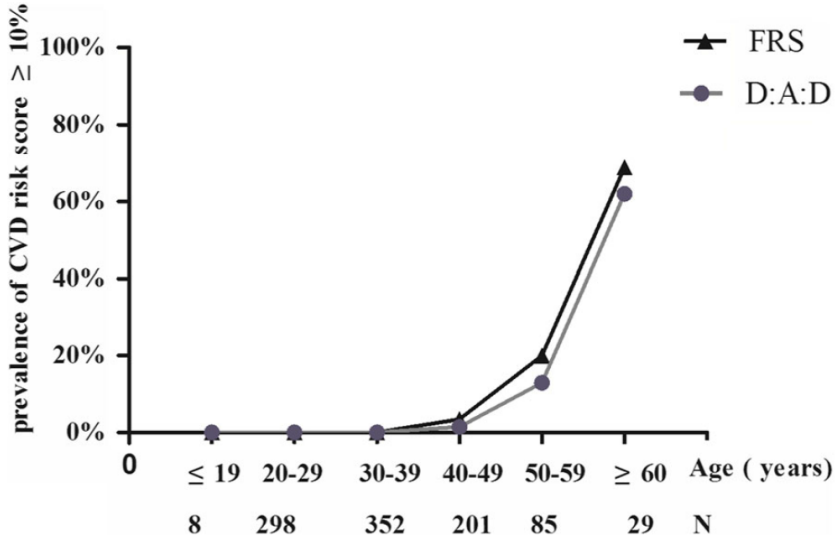


Fig. 1 Prevalence of individuals with 10-year risk of CHD ≥ 10% according to the FRS and D:A:D Risk Score. FRS: the Framingham risk score; D:A:D: Data Collection on Adverse Events of Anti-HIV Drugs Risk Score

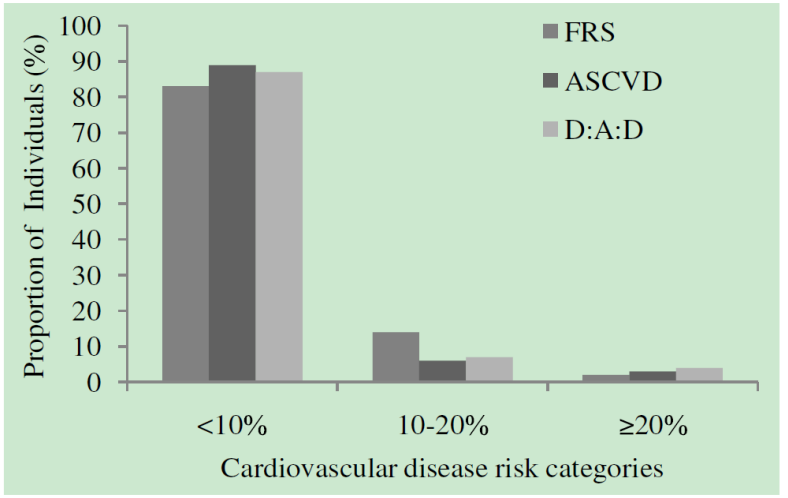
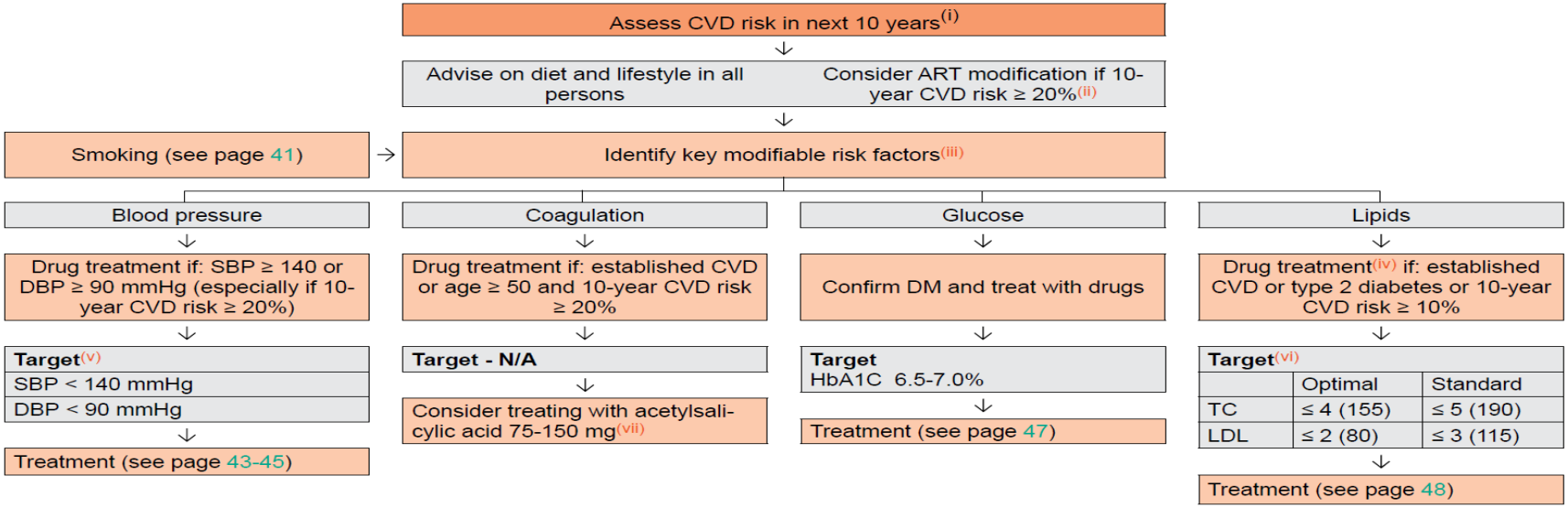


Fig. 2 Cardiovascular disease (CVD) risk categories, by risk score. Ten-year CVD risk is depicted in three categories: <10%, 10–20% and >20%, for each of the three CVD risk prediction models. ASCVD: atherosclerotic cardiovascular disease risk score; FRS: the Framingham risk score; D:A:D: Data Collection on Adverse Events of Anti-HIV Drugs Risk Score

Prevention of CVD

Principles: The intensity of efforts to prevent CVD depends on the underlying risk of CVD, which can be estimated[i]. The preventive efforts are diverse in nature and require involvement of a relevant specialist, in particular if the risk of CVD is high and always in persons with a history of CVD.



i Use the Framingham equation or whatever system local National Guidance recommends; a risk equation developed from HIV populations is available: see https://www.chip.dk/Tools-Standards/Clinical-risk-scores. This assessment and the associated considerations outlined in this figure should be repeated annually in all persons under care, see pages 6-8, to ensure that the various interventions are initiated in a timely way.

ii Options for ART modification include:
(1) Replace with NNRTI, INSTI or another PI/r known to cause less metabolic disturbances and/or lower CVD risks, see pages 21-22
(2) Consider replacing ZDV or ABC with TDF or use an NRTI-sparing regimen

iii Of the modifiable risk factors outlined, drug treatment is reserved for certain subgroups where benefits are considered to outweigh potential harm. Of note, there is a combined benefit of various interventions in target groups identified. Per 10 mmHg reduction in systolic blood pressure, per 1 mmol/L (39 mg/dL) reduction in TC and with use of acetylsalicylic acid, each reduces risk of IHD by 20-25%; the effect is additive. Observational studies suggest that smoking cessation results in about 50% less risk of IHD – and this is additive to other interventions.

iv See discussion on drug treatment of persons with lower CVD risk at https://www.nhlbi.nih.gov/files/docs/guidelines/atp3xsum.pdf

v For higher risk individuals (e.g. diabetes) where resources allow target SBP < 130 and DBP < 80 mmHg.

vi Target levels are to be used as guidance and are not definitive – expressed as mmol/L with mg/dL in parenthesis. In case LDL cannot be calculated because of high triglyceride levels, the non-HDL-c (TC minus HDL-c) target should be used which is 0.8 mmol/L (30 mg/dL) higher than the corresponding LDL-c target. Target levels for TG are not listed because an independent contribution from TG to CVD risk is uncertain, and hence whether this condition should be treated, see page 48.

vii Evidence for benefit when used in persons without a history of CVD (including diabetics) is less compelling. BP should be reasonably controlled before aspirin use in such a setting.

See online video lecture CVD, CKD, Endocrinology from the EACS online course Clinical Management of HIV.

Hypertension: Diagnosis, Grading and Management

Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)	Blood pressure (mmHg)	Blood pressure (mmHg)	Blood pressure (mmHg)
	High normal SBP 130-139 or DBP 85-89	Grade 1 hypertension SBP 140-159 or DBP 90-99	Grade 2 hypertension SBP 160-179 or DBP 100-109	Grade 3 hypertension SBP ≥ 180 or DBP ≥ 110
No other risk factors	• Lifestyle changes[i] • No BP drug intervention	• Lifestyle changes[i] for several months • Then add BP drugs targeting < 140/90	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 140/90	• Lifestyle changes[i] • Immediate BP drugs targeting < 140/90
1-2 risk factors	• Lifestyle changes[i] • No BP drug intervention	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 140/90	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 140/90	• Lifestyle changes[i] • Immediate BP drugs targeting < 140/90
≥ 3 risk factors	• Lifestyle changes[i] • i.e. no BP drug intervention	• Lifestyle changes[i] for several weeks • Then add BP drugs targeting < 140/90	• Lifestyle changes[i] • BP drugs targeting < 140/90	• Lifestyle changes[i] • Immediate BP drugs targeting < 140/90
Organ damage, CKD stage 3 or diabetes	• Lifestyle changes[i] • Consider blood pressure drugs targeting < 130/80	• Lifestyle changes[i] • BP drugs targeting < 140/90[ii]	• Lifestyle changes[i] • BP drugs targeting < 140/90[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 140/90[ii]
Symptomatic CVD, CKD stage ≥ 4 or diabetes with organ damage/risk factors	• Lifestyle changes[i] • Consider blood pressure drugs targeting < 130/80	• Lifestyle changes[i] • BP drugs targeting < 140/90[ii]	• Lifestyle changes[i] • BP drugs targeting < 140/90[ii]	• Lifestyle changes[i] • Immediate BP drugs targeting < 140/90[ii]

Drug-drug Interactions between Antihypertensives and ARVs

Type 2 Diabetes[i]: Management

If modification of lifestyle measures is insufficient

↓

Metformin[ii] start dose (500-850 mg qd), increase to maximum tolerated dose of 2(-3) g/day over 4-6 weeks[iii]

↓

HbA1c > 6.5-7% (> 48-53 mmol/mol)

↓

Metformin[ii] + sulfonylureas or thiazolidinedione or DPP-4 inhibitor or SGLT-2 inhibitor or GLP-1 agonist or insulin

↓

HbA1c > 6.5-7% (> 48-53 mmol/mol)

↓

Refer to specialist for triple therapy – use insulin

Treatment goals:

Prevention of hyper-/hypoglycaemia, glucose control (HbA1c < 6.5-7% without hypoglycaemia, fasting plasma glucose 4-6 mmol/L (73-110 mg/dL), prevention of long-term complications.

- Normal blood lipids, see pages 42 and 48, and blood pressure < 130/80 mmHg, see page 43.
- Acetylsalicylic acid (75-150 mg qd) considered in diabetics with elevated underlying CVD risk, see page 42.
- Nephropathy, polyneuropathy and retinopathy screening should be performed as in diabetic persons without HIV
- Consultation with a specialist in diabetology is recommended

i Type 1 diabetes should be treated according to national guidelines.

ii Metformin may worsen lipoatrophy.
No data for any oral antidiabetic agents in terms of CVD prevention in HIV-positive persons. Incretins (DDP-4 inhibitors [e.g. linagliptin, saxagliptin (reduce dose when given with a booster), sitagliptin and vildagliptin], GLP-1 agonists [liraglutide, exenatide], and SGLT-2 inhibitors [e.g. dapagliflozin, canagliflozin, empagliflozin] have not been evaluated in HIV-positive persons, but some (e.g empagliflozin, liraglutide) have shown to reduce mortality from CVD; choice of drugs dependent on a variety of individual- & disease-specific factors; no clinically significant drug-drug-interaction or adverse effects on CD4 counts expected; clinical use of pioglitazone questioned by its side effects; HbA1c targets up to 7.5% can be considered for older persons with long-standing type 2 diabetes and evidence of CVD.

iii Consider lower dose in individuals with mild to moderate CKD or individuals receiving DTG.

Dyslipidaemia

Principles: Higher LDL-c levels increase risk of CVD and reduction diminishes this risk (see table below for drugs used on this indication); the reverse is probably true for HDL-c but trial data are less compelling. The CVD risk implications from higher than normal TG levels are even less clear, as TG has not consistently been shown to independently predict the risk of CVD. Furthermore, the clinical benefit of treating moderate hypertriglyceridaemia is uncertain; very high TG (> 10 mmol/L or > 900 mg/dL) increase risk of pancreatitis.

Less calories, more exercise, reducing bodyweight, and stopping smoking tend to improve (increase) HDL. Eating fish, reducing calories, saturated fat and alcohol intake reduce triglyceride levels. Reducing dietary saturated fat intake improves LDL-levels; if not effective, consider change of ART, then consider lipid-lowering medicine, see page 42. Statins should be used by all those with established vascular disease and among those with type 2 diabetes or at high risk of CVD, irrespective of lipid levels.

Drugs used to lower LDL-c

Drug class	Drug	Dose	Side effects	Advise on use of statin together with ART	
				use with PI/r	use with NNRTIs
Statin[i,ix]	atorvastatin[ii]	10-80 mg qd	Gastrointestinal symptoms, headache, insomnia, rhabdomyolysis (rare) and toxic hepatitis	Start with low dose[v] (max: 40 mg)	Consider higher dose[vi]
	fluvastatin[iii]	20-80 mg qd		Consider higher dose[vi]	Consider higher dose[vi]
	pravastatin[iii]	20-80 mg qd		Consider higher dose[vi,vii]	Consider higher dose[vi]
	rosuvastatin[ii]	5-40 mg qd		Start with low dose[v] (max: 20 mg)	Start with low dose[v]
	simvastatin[ii]	10-40 mg qd		Contraindicated	
Intestinal cholesterol absorption inhibitor↓[i,viii]	ezetimibe[iv]	10 mg qd	Gastrointestinal symptoms	No known drug-drug interactions with ART	
PCSK9-inhibitor[x]	evolocumab	140 mg 2 weekly or 420 mg monthly	Nil	No drug-drug interactions anticipated	

如何管理这位患者？

- 男，31岁，确诊HIV感染，未曾接受ART
- 体重90.0kg，身高178cm
- CD4细胞计数：358/μL
- 病毒载量：66800拷贝/mL
- 耐药检测：均敏感
- 父母均有糖尿病和高血压病
- 吸烟
- 需上夜班

临检

上海市公共卫生临床中心
复旦大学附属中山医院南院
Report in Dept. of Clinical Laboratory

检验报告单
Shanghai Public Health Clinical Center
zhongshan hospital(s) affiliated to fudan university

姓名 Patient	[redacted]	性别 Sex	男	年龄 Age	31 岁	病员号 Patient No.	[redacted]
病人类别 Patient type	门诊						
科室 Department	[redacted]	病区 Ward		床号 Bed		申请医生 Ordering physician	沈银忠
临床诊断 Clinical Indication							
条码号 Specimen No.	[redacted]	标本种类 Specimen Type	尿液	采样日期 Date Collected	2018-09-25 11:58:11	接收日期 Date Received	2018-09-25 12:27:18

代码 Code	项目 Test name	结果 Result	生物参考区间 Reference intervals
YS	颜色	淡黄色	
CLA	浊度	透明	
UPH	尿酸碱度	5.00	4.8-7.4
SG	比重	↑1.043	1.003～1.030
LEU	尿白细胞	阴性	阴性
NIT	亚硝酸盐	阴性	阴性
PRO	尿蛋白	1+	阴性
UGLU	尿葡萄糖	4+	阴性
KET	酮体	阴性	阴性
UBG	尿胆元	阴性	阴性
BIL	尿胆红素	阴性	阴性
ERY	尿隐血试验	阴性	阴性
UWBC	尿白细胞定量	<1.14	0-5 /HPF
URBC	尿红细胞定量	<1.14	0-3 /HPF
SEC	鳞状上皮细胞	0	0-15 /HPF
NEC	非鳞状上皮细胞	0	0-2 /HPF
BAC	细菌	0	0-30 /HPF
HYA	透明管型	0	0-2 /HPF
PAT	病理管型	阴性	阴性
CRY	结晶	阴性	阴性
MUC	粘液	阴性	阴性
YEA	酵母菌	阴性	阴性
	精子	阴性	阴性

检测仪器(方法) Instrument(Method) cobas65　样本号 Sample No. [redacted]　报告日期 Date of Report 2018-09-25 12:45:31　检验员 Technician [redacted]　签发人 Reporter [redacted]

报告地址 Report Address 上海市金山区漕廊公路2901号
No.2901 CaoLang Rd., JinShan District, Shanghai

备注 Comment

※本报告仅对所检测的标本负责!

生化

上海市公共卫生临床中心
复旦大学附属中山医院南院

Report in Dept. of Clinical Laboratory

检验报告单

Shanghai Public Health Clinical Center
zhongshan hospital(s) affiliated to fudan university

姓名 Patient	[redacted]	性别 Sex	男	年龄 Age	31 岁	病员号 Patient No.	[redacted]
病人类别 Patient type	门诊						
科室 Department	[redacted]	病区 Ward		床号 Bed		申请医生 Ordering physician	沈银忠
临床诊断 Clinical Indication							
条码号 Specimen No.	[redacted]	标本种类 Specimen Type	血清	采样日期 Date Collected	2018-09-25 11:58:11	接收日期 Date Received	2018-09-25 13:10:38

代码 Code	项目 Test name	结果 Result	生物参考区间 Reference intervals
ALT	丙氨酸氨基转移酶	↑ 69.00	9.00～50.00 U/L
AST	天门冬氨酸氨基转移酶	↑ 48.00	15.00～40.00 U/L
ALP	碱性磷酸酶	66.00	45.00～125.00 U/L
GGT	L-γ-谷氨酰基转移酶	↑ 72.00	10.00～60.00 U/L
LDH	乳酸脱氢酶	↑ 300.00	109.00～245.00 U/L
AMS	淀粉酶	45.00	25.00～125.00 U/L
TC	总胆固醇	↑ 5.47	0.00～5.17 mmol/L
TG	三酰甘油	↑ 2.91	0.00～1.69 mmol/L
TP	总蛋白	↑ 97.76	65.00～85.00 g/L
ALB	白蛋白	45.84	40.00～55.00 g/L
GLB	球蛋白	↑ 51.92	20.00～40.00 g/L
A/G	白球比例	↓ 0.88	1.50～2.50 %
GLU	葡萄糖	↑ 29.42	3.90～6.10 mmol/L
UREA	尿素	4.48	3.20～7.40 mmol/L
Cr	肌酐	64.00	57.00～104.00 umol/L
UA	尿酸	↑ 514.59	210.00～420.00 umol/L
TBIL	总胆红素	↑ 25.05	3.40～20.50 umol/L
DBIL	直接胆红素	↑ 9.03	0.00～8.60 umol/L
eGFR	eGFR	134.493	ml/(min*1.73㎡) >=90肾功能正常 60-89肾功能轻度下降 30-59肾功能中度下降 15-29肾功能重度下降

检测仪器(方法) Instrument(Method) c16000　样本号 Sample No. [redacted]　报告日期 Date of Report 2018-09-25 14:53:20　检验员 Technician [redacted]　签发人 Reporter [redacted]

报告地址 Report Address 上海市金山区漕廊公路2901号 No.2901 CaoLang Rd., JinShan District, Shanghai

备注 Comment

※本报告仅对所检测的标本负责!

CVD风险评估

风险评估方法	风险评估
D:A:D(R)CVD 5 year risk score	**4.48%**
D:A:D(R)CVD 10 year risk score	**7.1%**
Framingham CVD 5 year risk score	**1.27%**
Framingham CVD 10 year risk score	**6.7%**

结　论

- 新确诊艾滋病患者中存在CVD风险因素者比例高，发生CVD的风险高。
- 新确诊HIV/AIDS患者CVD的筛查、评估与管理应纳入HIV感染者管理和关怀常规中。
- CVD的预防、评估与管理是HIV全程管理的重要内容，围绕CVD的相关研究是今后关注的方向之一。

The End


Thank You!