Address the health checks in medical care

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Overview

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Agenda

- **PART 1: General overview on mandatory screening**
- PART 2: Standard of care / Cascade of care
- PART 3: How to measure patient's satisfaction of care?

Current guidelines

- **European AIDS Clinical Society**: EACS Guidelines 8.1 3 (2016)

- **Centers for Disease Control and Prevention, the National Institutes of Health and the Infectious Diseases Society of America:** Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents (2016)

- **Infectious Diseases Society of America:** Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update.

- **HHS Panel on Antiretroviral Guidelines for Adults and Adolescents:** Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents (2014)

- **Società Italiana Malattie Infettive e Tropicali:** Italian guidelines for the use of antiretroviral agents and the diagnostic-clinical management of HIV-1 infected persons (2016)

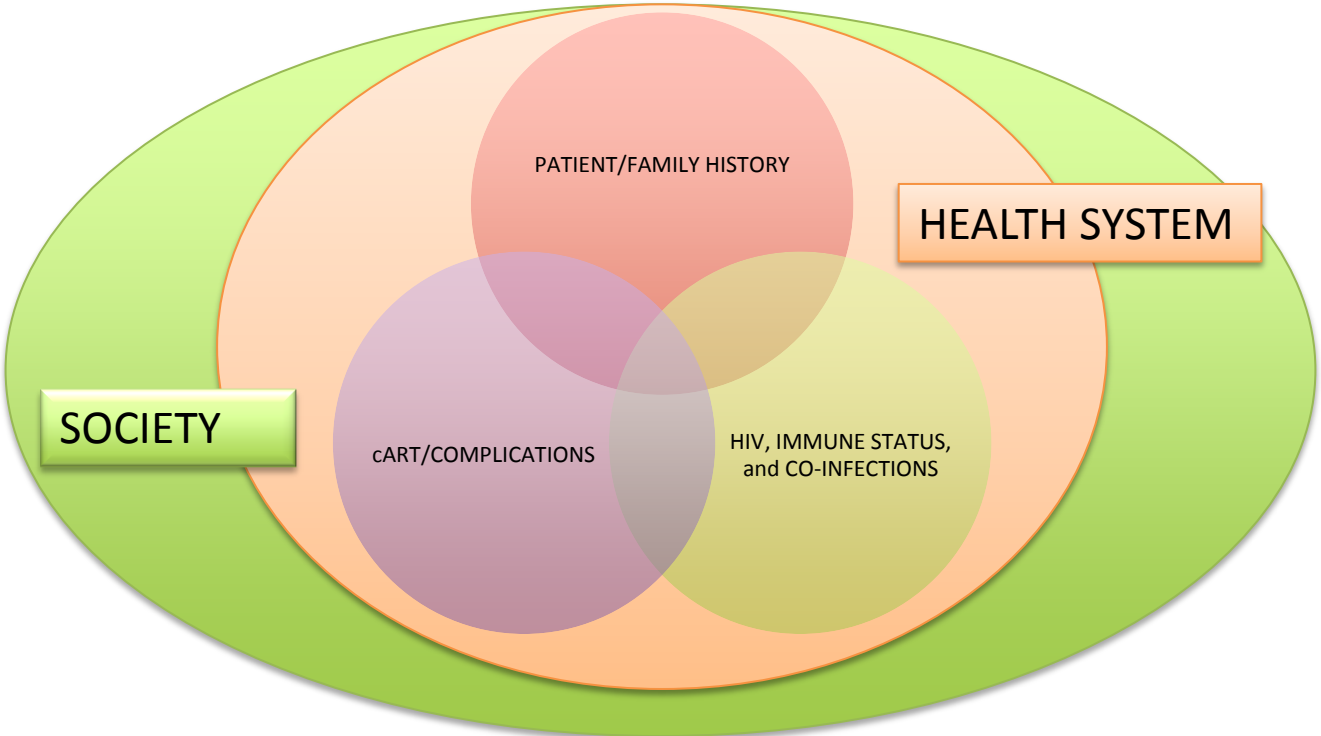
Structure of guidelines

Part I: Assessment of HIV-positive Persons at Initial & Subsequent Visits
Part II: ARV Treatment of HIV-positive Persons
Part III: Prevention and Management of Co-morbidities in HIV-positive Persons
Part IV: Clinical Management and Treatment of Chronic HBV and HCV Co-infection in HIV-positive Persons
Part V: Opportunistic Infections

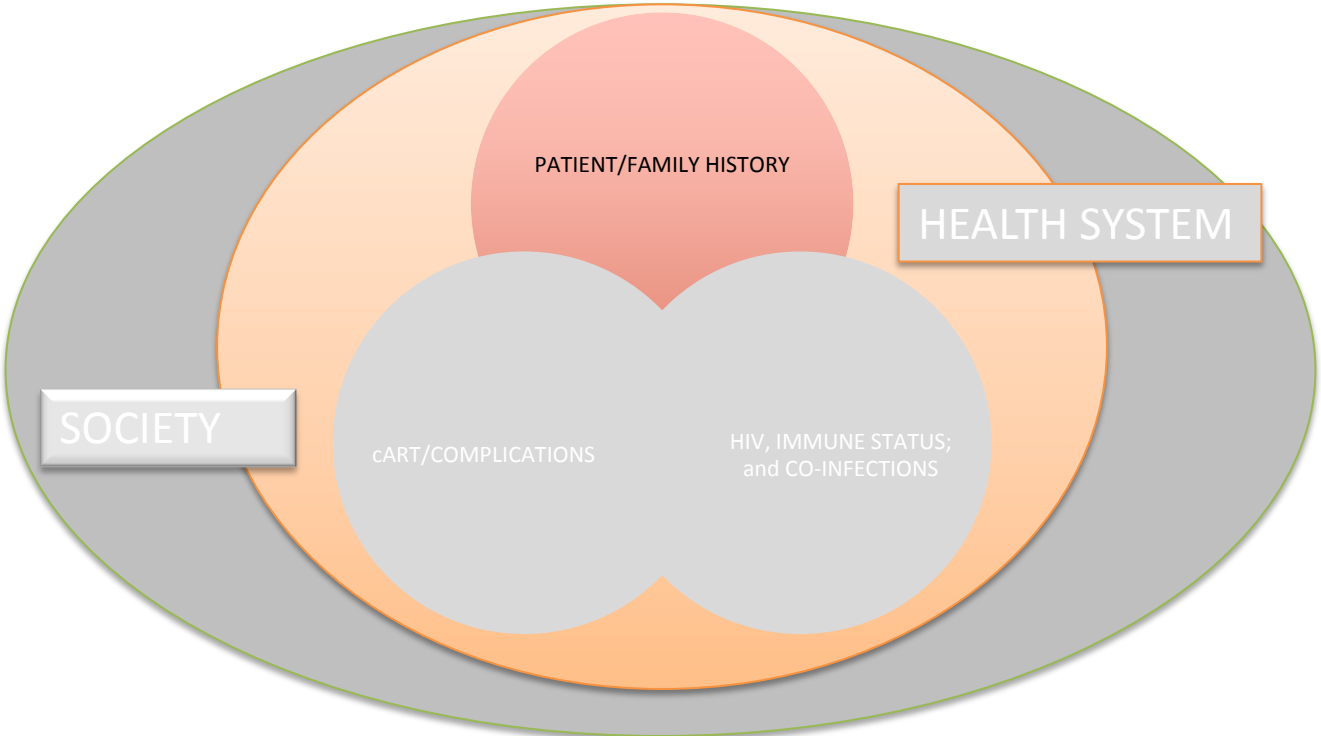
I: What initial evaluation and immediate follow-up should be performed for HIV-infected patients?
II: What are the special considerations for women and the prevention of mother-to-child transmission? Contraception and Preconception Care
III. What are the special considerations for children?
IV: What are the special considerations for adolescents?
V: What are the metabolic comorbidities associated with HIV and antiretroviral therapy?
VI: How can patient adherence to HIV care be optimized?

Section 1: Adults and adolescents
Section 2: HIV related diseases
Section 3: Special populations
Section 4: Special conditions
Section 5: Prophylaxis

Not only medicine in the checks for health care



Patient/family history



	Assessment	At HIV diagnosis	Prior to starting ART	Follow-up frequency	Comment
HISTORY					
Medical	Complete medical history including:	+	+	First visit	On transfer of care repeat assessment
	• Family history (e.g. premature CVD, diabetes, hypertension, CKD)	+		First visit	Premature CVD: cardiovascular events in a first degree relative (male < 55, female < 65 years)
	• Concomitant medicines(i)	+	+	Every visit	
	• Past and current co-morbidities	+	+	Every visit	
	• Vaccination history	+		Annual	Measure antibody titres and offer vaccinations where indicated, see Vaccination
Psychosocial	Current lifestyle (alcohol use, smoking, diet, exercise, drug use)	+	+	6-12 months	Adverse lifestyle habits should be addressed more frequently
	Employment	+	+	Every visit	Provide advice and support if needed
	Social and welfare	+	+		Provide counselling if needed
	Psychological morbidity	+	+		
	Partner and children	+			Test partner and children if at risk
Sexual and Reproductive Health	Sexual history	+		6-12 months	Address issues concerning sexual dysfunction
	Safe sex	+			Risk of sexual transmission should be addressed
	Partner status and disclosure	+			Recommend starting ART in serodifferent couples
	Conception issues	+	+		

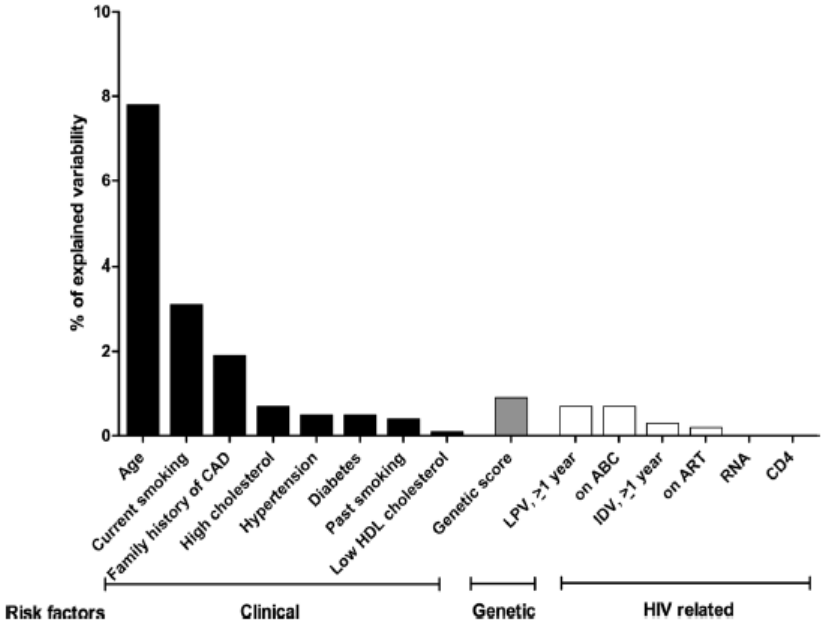
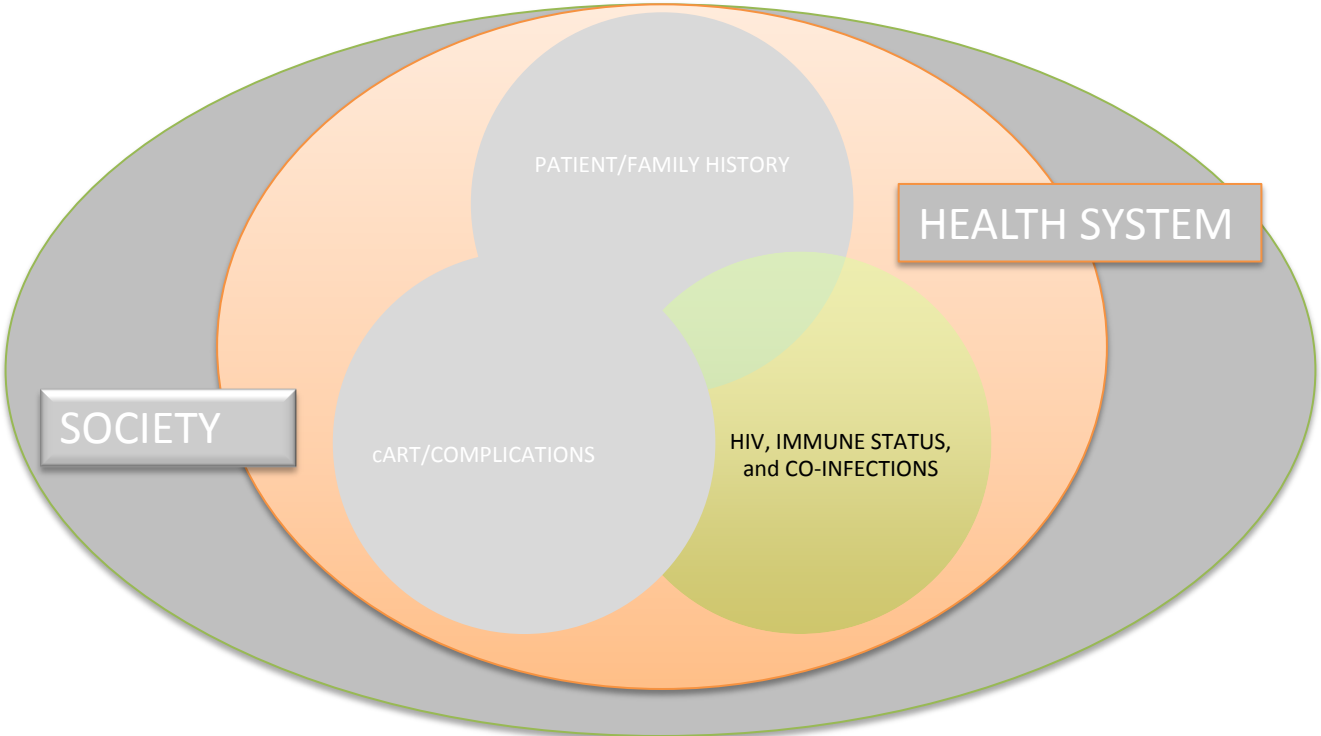


Figure 4. Coronary artery disease (CAD) variability explained by traditional risk factors, human immunodeficiency virus–related factors and genetic background. Variability in the CAD odds ratio explained by the final model: 21.1%. Of this, age: 7.5%, current smoking: 3.1%, past smoking: 0.4%, high total cholesterol: 0.7%, hypertension: 0.5%, diabetes: 0.5%, low high-density lipoprotein cholesterol: 0.1%, family history of CAD: 1.9%, genetic risk score: 0.9%, current antiretroviral therapy: 0.2%, current abacavir: 0.7%, lopinavir (≥1 year): 0.7%, indinavir (≥1 year): 0.3%, HIV load: 0%, $CD4^+$ count: 0%. Abbreviations: ABC, abacavir; CAD, coronary artery disease; HDL, high-density lipoprotein; IDV, indinavir; LPV, lopinavir.

Tarr P *et al. Clin Infect Dis*. 2013 Jul;57(1):112-21

HIV and co-infections



Resistance testing

- All patients should be assessed for transmitted drug resistance with an HIV genotype test upon initiation of care (strong recommendation, high quality evidence)
- Resistance testing is also indicated for patients who are experiencing virologic failure to guide modification of ART (strong recommendation, high quality evidence)
- In persons failing integrase strand transfer inhibitor (INSTI)–based regimens, genotypic testing for INSTI resistance should be ordered (strong recommendation, high quality evidence)

Resistance testing (new technologies)

- Use of ultradeep resistance test is currently not extensively used in standard of care, but it could be useful in case of suspected transmitted resistance or in case of HIV-RNA undetectability (proviral HIV-DNA)

- Proviral HIV-DNA analysis can be requested in particular conditions (switch for simplification, prospect of cART efficacy)

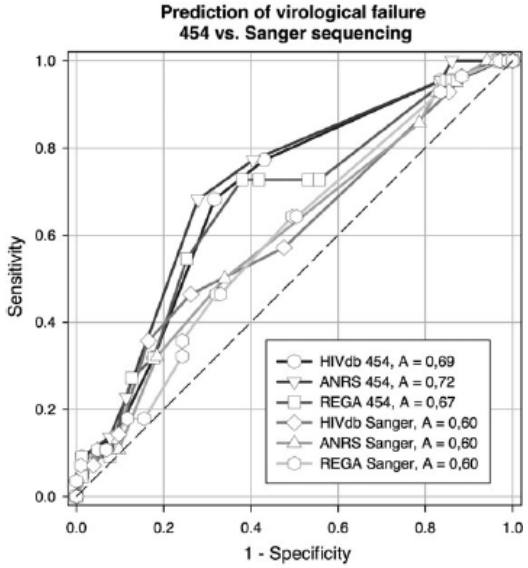


Figure 3. Improved prediction of virological failure with 454 relative t Sanger sequencing. Receiver operating characteristic curves of the abilit of HIVdb, ANRS, and REGA algorithms to predict virological failure whe genotypic sensitivity scores are calculated using 454 sequencing (HIVdl 454, ANRS 454, REGA 454 groups) or Sanger sequencing (HIVdb Sange ANRS Sanger, REGA Sanger groups). The legend shows the area under th curve values (*A*) for each category. Pairwise differences in area under th curve between 454 and Sanger categories were statistically significan using the method of Delong, Delong, and Clarke-Pearson [27], ie $P = .029$ for HIVdb; $P = .005$ for ANRS, and $P = .008$ for REGA.

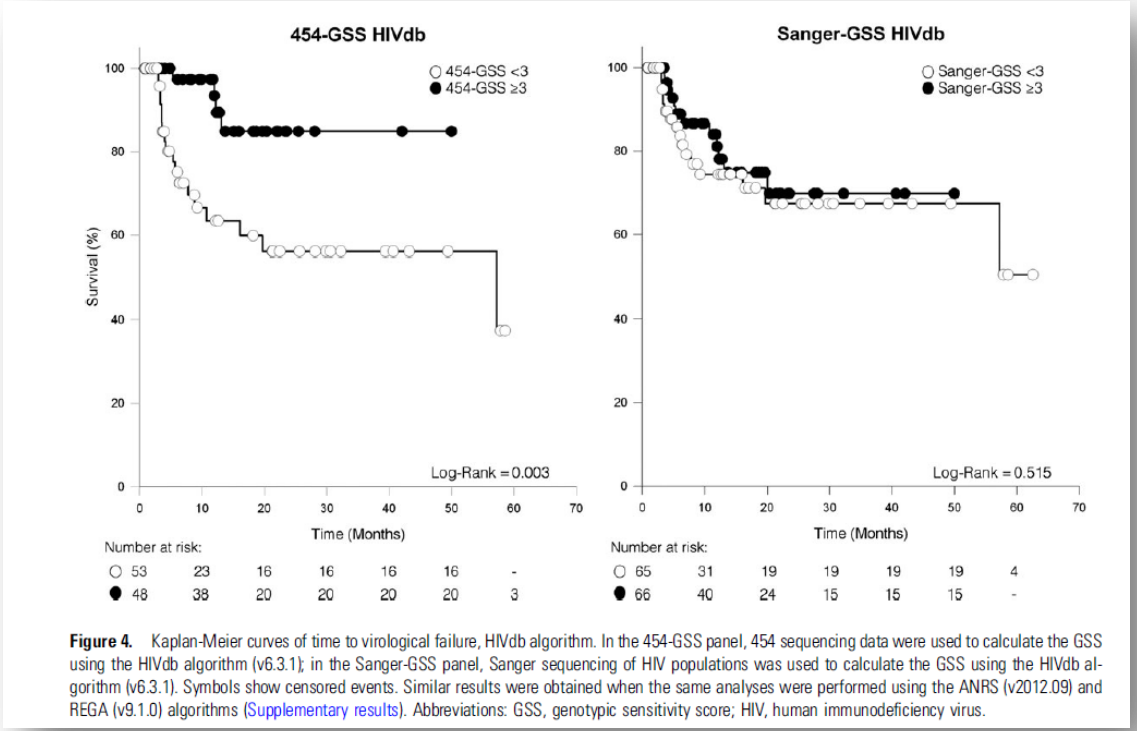
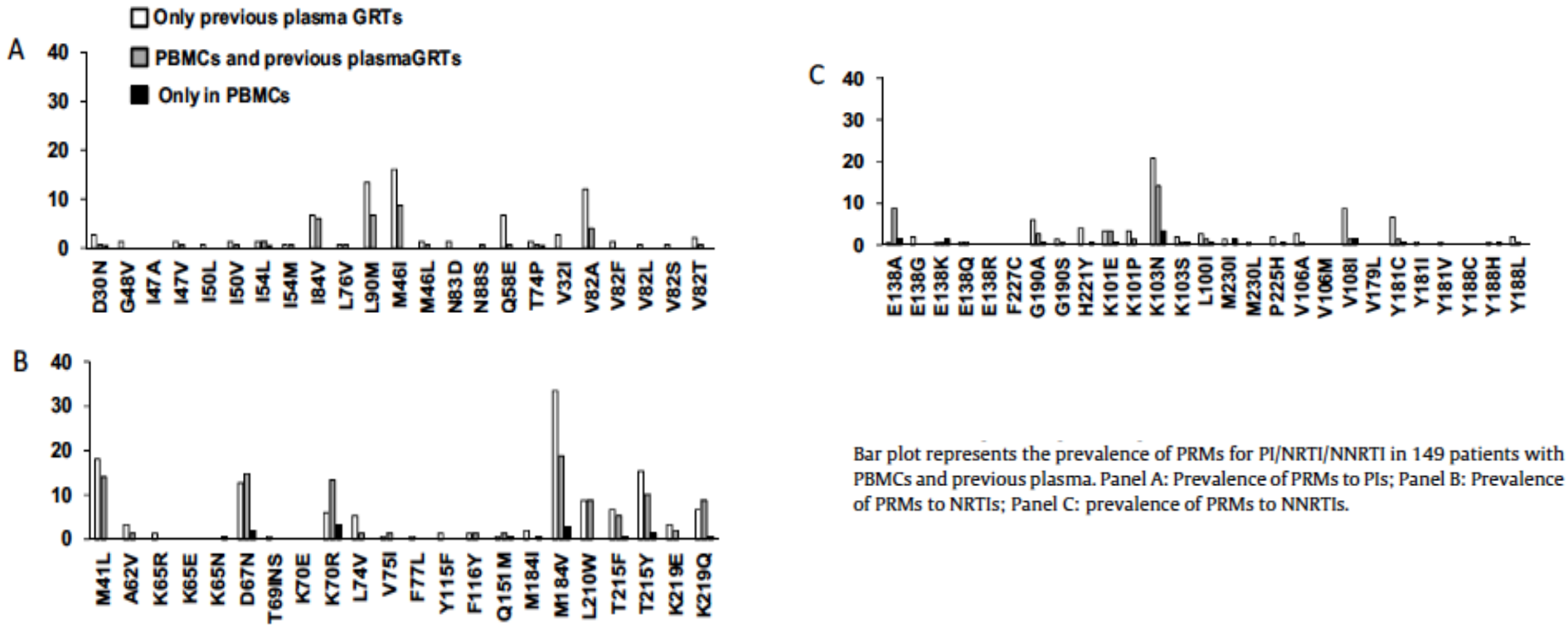


Figure 4. Kaplan-Meier curves of time to virological failure, HIVdb algorithm. In the 454-GSS panel, 454 sequencing data were used to calculate the GSS using the HIVdb algorithm (v6.3.1); in the Sanger-GSS panel, Sanger sequencing of HIV populations was used to calculate the GSS using the HIVdb algorithm (v6.3.1). Symbols show censored events. Similar results were obtained when the same analyses were performed using the ANRS (v2012.09) and REGA (v9.1.0) algorithms (Supplementary results). Abbreviations: GSS, genotypic sensitivity score; HIV, human immunodeficiency virus.

Pou *et al. Clin Infect Dis* 2014 Aug 15;59(4):578-88



Bar plot represents the prevalence of PRMs for PI/NRTI/NNRTI in 149 patients with PBMCs and previous plasma. Panel A: Prevalence of PRMs to PIs; Panel B: Prevalence of PRMs to NRTIs; Panel C: prevalence of PRMs to NNRTIs.

Zaccarelli M *et al. J Clin Virol.* 2016; 82(5):94-100

Viro-immunological monitoring

- **Viral load (strong recommendation, moderate quality evidence)**
  - Every 3–4 months (untreated patients and patients on stable ART)
  - Every 6 months (adherent patients whose viral load has been suppressed for more than 2–3 years and whose clinical and immunologic status is stable)
  - Within 2–4 weeks and not more than 8 weeks (after initiation or modification of HAART) with repeat testing every 4–8 weeks (until viral load becomes undetectable)
- **CD4 cell counts (strong recommendation, moderate quality evidence)**
  - Every 3–4 months
  - Every 6-12 months (patients on suppressive ART regimens whose CD4 counts have increased well above the threshold for OI risk)
- **CD8 cell count and the ratio of CD4 cells to CD8 cells is unnecessary** as the results are not used in clinical decision making
(strong recommendation, high quality evidence)

Table 1

Projected costs with different strategies of CD4 monitoring in routine care for the estimated 270,000 HIV-infected patients on suppressive ART in the US

Frequency (months)	Annual costs[a]		Lifetime costs[a] projected for LE 22 years		Lifetime costs[a] projected for LE 34 years	
	CD4 Test Cost		CD4 Test Cost		CD4 Test Cost	
	$38	$67	$38	$67	$38	$67
Every 3	41.0	72.4	902.9	1591.9	1395.4	2460.2
Every 6[b]	20.5	36.2	451.4	796.0	697.7	1230.1
Every 12	10.3	18.1	225.7	398.0	348.8	615.1

Abbreviations: HIV, Human Immunodeficiency Virus; ART, antiretroviral therapy;US, United States; LE, life expectancy.

[a] All costs in US$ (millions).

[b] Assumed current standard of care.

Emily P. Hyle *et al. JAMA Intern Med*. 2013 October 14; 173(18): 1746–1748

Immunological assessment

- **Monitoring of CD4+ count is less cost-effective than viral load**

- **CD4+ should be monitored**
  - 3 months after start of therapy [AIII]
  - Every 1-3 months after switching ART for viral failure [AIII]
  - Every 4-6 months after 2 years of ART (undetectable HIV-RNA, CD4+ 300-500/µL) [BII]
  - Every 6-12 months after 2 years of ART (undetectable HIV-RNA, CD4+ >500/µL) [BII]

- **CD4+/CD8+ ratio should be measured together with CD4+ [AII]**

Distribution of PCP cases in the MACS

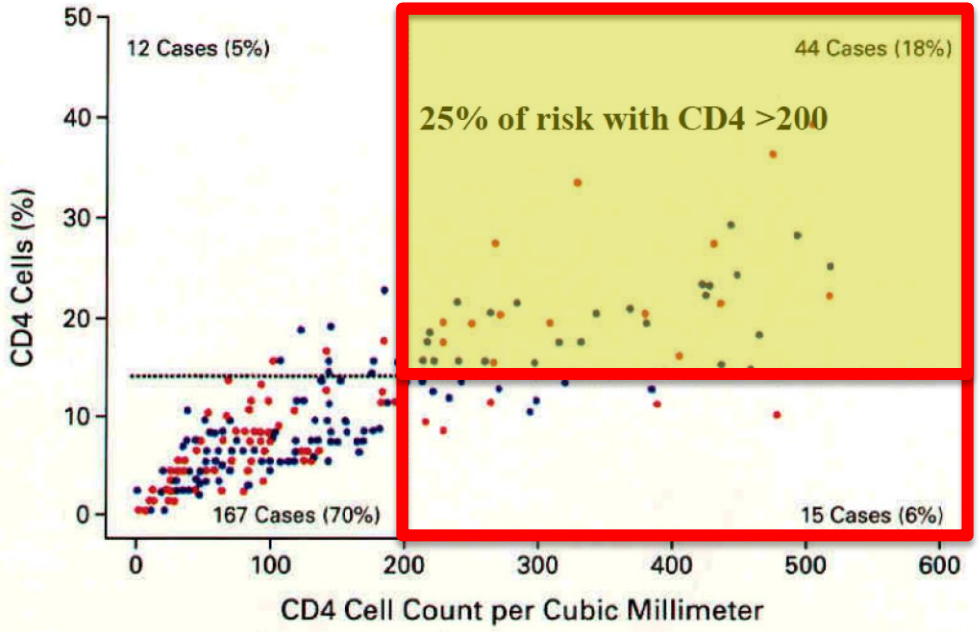


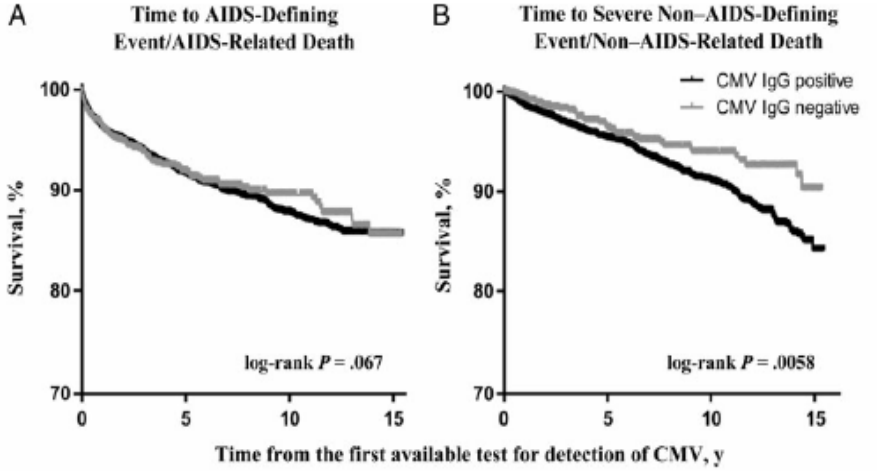
Table 5. Conditional logistic regression analysis: Predicted morbidity and mortality by the CD4+ and CD8+ T cell counts and the CD4/CD8 ratio in the Madrid cohort and SOCA cohort mortality nested studies.

	Beta	Std. error	P value
Madrid cohort (N = 66) (all subjects CD4≥500 cells/mm^3)			
CD4+ T cells			
Unadjusted	−1.86	2.85	0.514
Adjusted by ART duration	−0.66	3.76	0.859
CD8+ T cells			
Unadjusted	2.80	1.12	0.013
Adjusted by ART duration	2.29	1.16	0.048
CD4/CD8 ratio			
Unadjusted	−6.23	2.48	0.012
Adjusted by ART duration	−5.08	2.53	0.045
SOCA cohort (N = 192)			
CD4+ T cells			
All subjects	−1.52	0.58	0.009
Subjects with CD4≥500 cells/mm^3*	−4.09	6.43	0.525
CD8+ T cells			
All subjects*	0.28	0.33	0.392
Subjects with CD4≥500 cells/mm^3*	2.37	2.05	0.246
CD4/CD8 ratio			
All subjects*	−1.38	0.55	0.012
Subjects with CD4≥500 cells/mm^3*	−5.04	3.88	0.194

*N = 47.
Because of colinearity, we fitted one model to calculate the coefficients of CD4+ and CD8+ T cells, and a different model for the CD4/CD8 ratio.
Variables CD4+ and CD8+ T cells, and the CD4/CD8 ratio were log transformed.
Coefficients are adjusted by age, gender, nadir CD4+ T cell count and duration of viral suppression.
To interpret the logarithmically transformed coefficients, we applied the following formula: *Beta*log(1.10)*, resulting in the % of change in the odds of the outcome predicted by each 10% increase in the independent variable.
doi:10.1371/journal.ppat.1004078.t005

Serrano-Villar S *et al. PLoS Pathog*. 2014 May 15;10(5):e1004078

	Assessment	At HIV diagnosis	Prior to starting ART	Follow-up frequency	Comment
CO-INFECTIONS					
STIs	Syphilis serology	+		Annual/ as indicated	Consider more frequent screening if at risk
	STI screen	+		Annual/ as indicated	Screen if at risk
Viral Hepatitis	HAV serology	+		Annual/ as indicated	Screen at risk; vaccinate if non-immune
	HCV screen	+			Annual screen if ongoing risk Measure HCV-RNA if HCV Ab pos or if acute infection suspected
	HBV screen	+	+		Annual screen in susceptible persons; vaccinate if non-immune
Tuberculosis	CXR	+		Re-screen if exposure	Consider routine CXR in persons from high TB prevalence populations. Use of PPD/IGRA depending on availability and local standard of care. IGRA should, however, be tested before PPD if both are to be used, given the potential for a false positive IGRA after PPD See Diagnosis and Treatment of TB in HIV-positive Persons
	PPD if CD4 count > 400 cells/µL	+			
	IGRA in selected high-risk populations (if available)	+			
Others	Varicella zoster virus serology	+			Offer vaccination where indicated
	Measles/Rubella serology	+			Offer vaccination where indicated
	Toxoplasmosis serology	+			
	CMV serology	+			
	Cryptococcus antigen	+/-			Consider screening for cryptococcus antigen in serum in persons with CD4 count < 100 cells/µL
	Leishmania serology	+/-			Screen according to travel history/origin
	Tropical screen (e.g. Schistosoma serology)	+/-			Screen according to travel history/origin
	Influenza virus	+		Annual	In all HIV-positive persons, see Vaccination
	Streptococcus pneumonia	+			No recommendations available regarding the need for a booster dose, see Vaccination

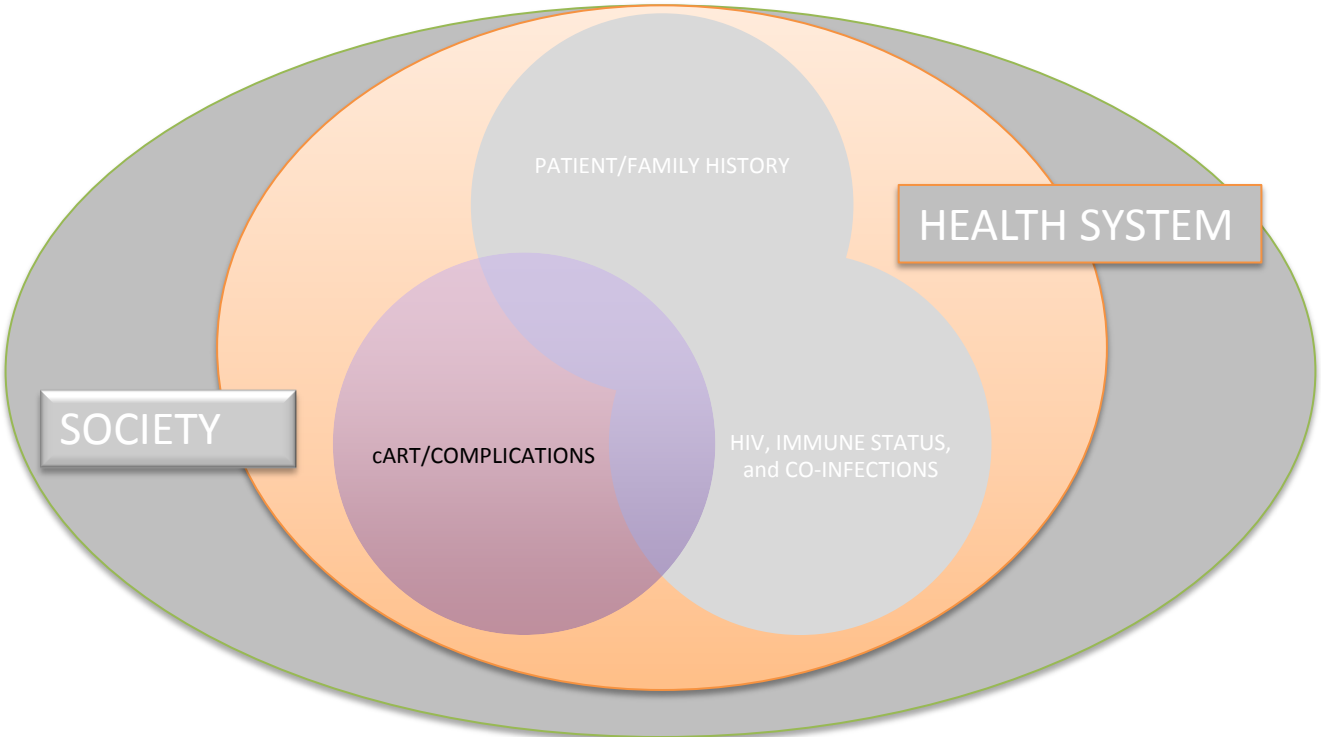


CMV-negative patients, no.	992	501	248	17	992	506	250	18
CMV-positive patients, no.	5119	2413	1116	76	5119	2438	1135	80

Figure 1. Kaplan–Meier survival curve for AIDS-defining event/AIDS-related death and severe non–AIDS-defining event/non–AIDS-related death, by cytomegalovirus (CMV) serostatus. *A*, CMV-infected patients did not show an increased risk of developing AIDS-defining events/AIDS-related death. *B*, CMV-infected patients had an increased risk of developing severe non–AIDS-defining events/non–AIDS-related death. Abbreviation: IgG, immunoglobulin G.

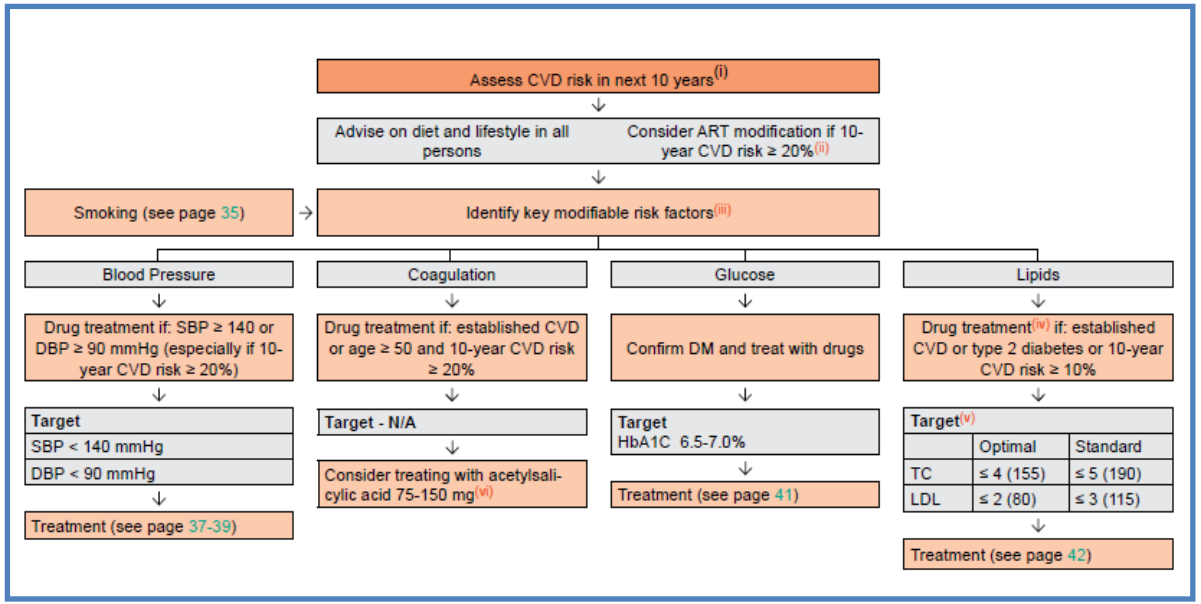
Lichtner M *et al. J Infect Dis.* 2015 Jan 15;211(2):178-86

cART/complications



	Assessment	At HIV diagnosis	Prior to starting ART	Follow-up frequency	Comment
CO-MORBIDITIES					
Haematology	FBC	+	+	3-12 months	
	Haemoglobinopathies	+			Screen at risk persons
	G6PD	+			Screen at risk persons
Body Composition	Body-mass index	+	+	Annual	
Cardiovascular Disease	Risk assessment (Framingham score[iii])	+	+	2 years	Should be performed in all men > 40 years and women > 50 years without CVD
	ECG	+	+/-	As indicated	Consider baseline ECG prior to starting ARVs associated with potential conduction problems
Hypertension	Blood pressure	+	+	Annual	
Lipids	TC, HDL-c, LDL-c, TG[iv]	+	+	Annual	Repeat in fasting state if used for medical intervention (i.e. ≥ 8h without caloric intake)
Glucose	Serum glucose	+	+	Annual	Consider oral glucose tolerance test / HbA1c if fasting glucose levels of 5.7-6.9 mmol/L (100-125 mg/dL)
Pulmonary Disease	CXR	+/-		As indicated	Consider CXR if prior history of pulmonary disease
	Spirometry			As indicated	Screen for COPD in at risk persons[xii]
Liver Disease	Risk assessment[v]	+	+	Annual	
	ALT/AST, ALP, Bilirubin	+	+	3-12 months	More frequent monitoring prior to starting and on treatment with hepatotoxic drugs
	Staging of liver fibrosis			12 months	In HCV and/or HBV co-infected persons (e.g. FibroScan, serum fibrosis markers)
	Hepatic ultrasound			6 months	Persons with liver cirrhosis and persons with HBV co-infection at high risk of HCC[xiii]
Renal Disease	Risk assessment[vi]	+	+	Annual	More frequent monitoring if eGFR < 90mL/min, CKD risk factors present[vi] and/or prior to starting and on treatment with nephrotoxic drugs[ix]
	eGFR (CKD-EPI)[vii]	+	+	3-12 months	
	Urine dipstick analysis[viii]	+	+	Annual	Every 6 months if eGFR < 60 mL/min, if proteinuria ≥ 1+ and/or eGFR < 60 mL/min perform UP/C or UA/C[viii]
Bone Disease	Bone profile: calcium, PO_4, ALP	+	+	6-12 months	
	Risk assessment[x] (FRAX®[xi] in persons > 40 years)	+	+	2 years	Consider DXA in specific persons (see page 43 for details)
Vitamin D	25(OH) vitamin D	+		As indicated	Screen at risk persons
Neurocognitive Impairment	Screening questionnaire	+	+	As indicated	Screen all persons without highly confounding conditions. If abnormal or symptomatic, see algorithm page 68 for further assessment.
Depression	Questionnaire	+	+	As indicated	Screen at risk persons
Cancer	Mammography			1-3 years	Women 50-70 years
	Cervical PAP			1-3 years	Sexually active women
	Rectal exam and anoscopy (MSM)			1-3 years	Evidence of benefit not known
	Ultrasound and alpha-foetoprotein			6 months	Controversial; persons with cirrhosis and persons with HBV co-infection at high risk of HCC[xiii]
	Others				Controversial

Cardiovascular prevention



Use the Framingham equation or whatever system local National Guidance recommends

Cardiovascular prevention

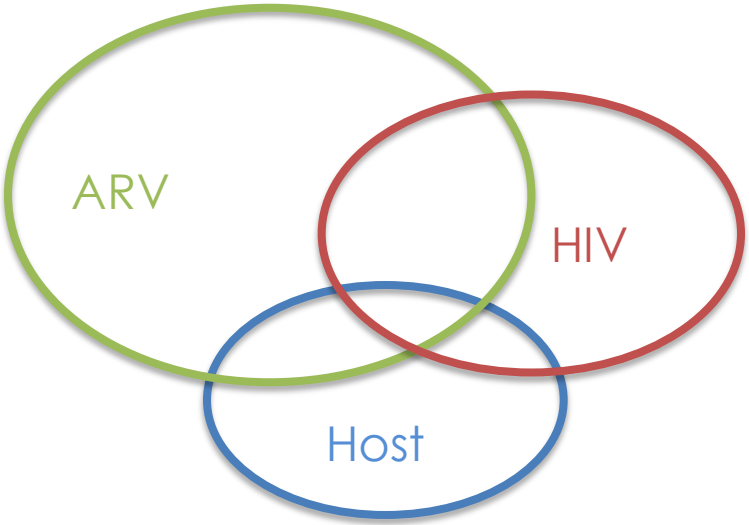
- **The same cardiovascular risk factor of general population should be evaluated**
  - Age > 50 years
  - Gender
  - Positive family history for MACE (< 55 years for males, < 65 years for females)
  - Cholesterol (total, HDL, LDL) positive family history for dyslipidemia
  - Blood pressure
  - Smoke
  - Diabetes
- **Update cardiovascular risk factors yearly and discuss treatment and prevention measure with patients**
- **American Heart Association CVD-Risk score is more reliable than other scores [All]**

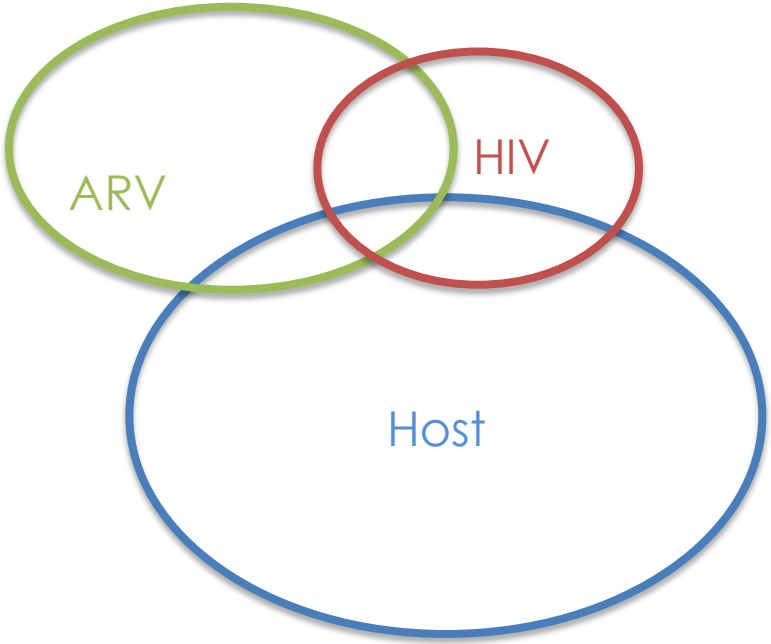
Risk score comparisons in CNICS

	Framingham		ATP3		DAD		ASCVD	
	HC	CI	HC	CI	HC	CI	HC	CI
Type 1	0.73*	0.69,0.77	0.74*	0.70,0.78	0.73*	0.68,0.78	0.77	0.73,0.81
Type 2	0.63*	0.57,0.69	0.63*	0.56,0.69	0.62*	0.55,0.68	0.72	0.67,0.78
All MI	0.68*	0.65,0.72	0.69*	0.65,0.72	0.68*	0.64,0.71	0.74	0.71,0.77

* Harrell's C significantly different from ASCVD HC

Crane HM *et al. Oral #42, CROI* 2016



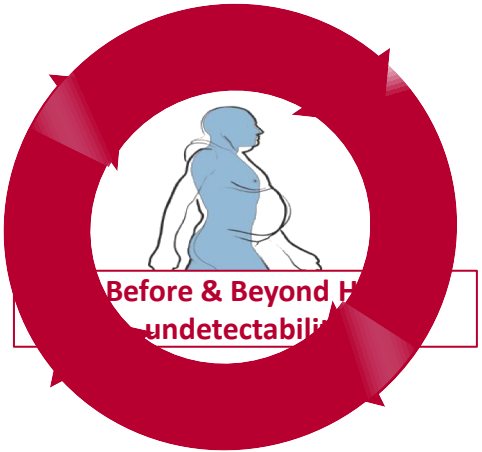


Ageing alter the interplay between Host, HIV and ARV toxicities in the development of HIV associated non AIDS (HANA) conditions

Clinical management of comorbidities

How to screen for comorbidities

1. Collect modifiable and not modifiable **risk factors**
2. Estimate **risk probability** with algorithms
3. Evaluate **vulnerability** with markers of subclinical disease



How to treat comorbidities

1. Get HIV **un-detectability**
2. Reactive or pre-emptive **ARV switch**
3. **Treat risk factors** or existing comorbidities
4. **Empower the patients for life style changes**

Pharmacologic interactions management in patients with polypharmacy

Actions	Strength of evidence
Register all patient therapy and not only the ART in the medical records	[BII]
Instruct the patient about the potential risk of drug-drug interactions and who they should contact in case of prescription changes	[AII]
Consider the increased risk in 10% of adverse reaction, in each new prescription introduced in a complex therapeutic regiment. Ponder the use of alcohol, smoke and abuse substances	[AII]
Ponder individual paths of supervision and management of all therapy, because neurocognitive deficits and / or dementia are frequently present	[BII]
Consider the inclusion of the pharmacist, as an important element in the multidisciplinary approach of the patient	[BII]
Periodically evaluate the prescription adequacy, pondering the indication and cost-benefit of each therapy	[BII]

Cancer screening

Problem	Persons	Procedure	Evidence of benefit	Screening interval	Additional comments
Anal cancer	MSM	Digital rectal exam ± anal cytology	Unknown; advocated by some experts	1-3 years	If anal cytology abnormal, anoscopy
Breast cancer	Women 50-70 years	Mammography	↓ Breast cancer mortality	1-3 years	
Cervical cancer	Sexually active women	Liquid based cervical cytology test	↓ Cervical cancer mortality	1-3 years	Target age group should include the 25 to 64 years at least. HPV testing may aid screening
Colorectal cancer	Persons 50-75 years	Faecal occult blood test	↓ Colorectal cancer mortality	1-3 years	Flexible sigmoidscopy at 55-years is an alternative
Hepatocellular carcinoma	Persons with cirrhosis & persons with HBV co-infection at high risk of HCC[ii]	Ultrasound and alpha-foetoprotein	Earlier diagnosis allowing for improved ability for surgical eradication	Every 6 months	See pages 52 and 69
Prostate cancer	Men > 50 years	Digital rectal exam ± PSA	Use of PSA is controversial	1-3 years	Pros: ↑ early diagnosis. Cons: overtreatment; ambiguity about size of ↓ cancer-related mortality

Cancer screening

Cancer	Population	Screening methods	Screening schedule	Recommendation
Cervical	Women > 18 years	PAP test Colposcopy	Every year in case of 2 negative exams Colposcopy If altered PAP test	AI
Anal	MSM, people with anal condylomas, women with genital diseases	PAP test Anoscopy in case of MSM	Yearly in case of 2 negative exams	AIII
Liver	Cirrhotic HCV+ or HCV/HBV+	Abdomen ultrasound and alphafetoprotein	Every 6-12 months	AI
Lung	**Smokers (>30 packages/years), ex smokers (within 15 years from cessation), age >40 years**	**TC**	**Yearly**	**AI**
Skin	**Caucasian (non-hispanic)**	**Clinical exam**	**Yearly**	**AIII**

Vaccinations

Infection	Vaccination rationale in HIV-positive persons	Comment
Influenza Virus	Higher rate of pneumonia. Explicitly recommended in all HIV-positive persons	Yearly
Human Papilloma Virus (HPV)	Shared risk with HIV of contracting infection. Higher rate of cervical and anal cancer	If HPV infection is established, efficacy of vaccine is questionable
Hepatitis B Virus (HBV)	Shared risk with HIV of contracting infection. HIV accelerates liver disease progression	Vaccinate if seronegative. Consider double dose (40 µg) in non-responders, in particular with low CD4 count and high HIV-VL. Repeat doses until HBs antibodies ≥ 10 IU/L / ≥ 100 IU/L according to national guidelines. See page 69
Hepatitis A Virus (HAV)	According to risk profile (travel, MSM, IVDU, active hepatitis B or C infection)	Vaccinate if seronegative. Check antibody titres in individuals with risk profile See page 69
Neisseria meningitidis	As general population	Use conjugated[(1)] vaccine (2 doses 1-2 months apart) if available. Booster every five years if exposure continues. Polysaccharide vaccine not recommended anymore.
Streptococcus pneumoniae	Higher rate and severity of invasive disease. Vaccine explicitly recommended for all HIV-positive persons	Use conjugated[(1)] 13-valent vaccine instead of PPV-23 polysaccharide vaccine if available. No recommendations yet about the need for a booster dose.
Varicella Zoster Virus (VZV)	Higher rate and severity of both chickenpox and zoster	Perform serology if exposure history negative. Vaccinate if seronegative. For contra-indications, see*
Yellow Fever Virus	Mandatory for travel to selected countries (provide exemption letter if no true risk of exposure)	Contra-indicated if past or current haematological neoplasia or thymus affection (thymoma, resection/radiation) For other contra-indications, see*

- Vaccinate according to national guidelines for healthy population
- Consider repeating vaccination performed at CD4 count < 200 cells/µl following adequate immune-reconstitution
- Attenuated live vaccine are contra-indicated if CD4+ count <200 cell/µl

Vaccinations

The same of European Guidelines without varicella-zoster, but adding typhoid fever

MenACWY is recommended for these groups:

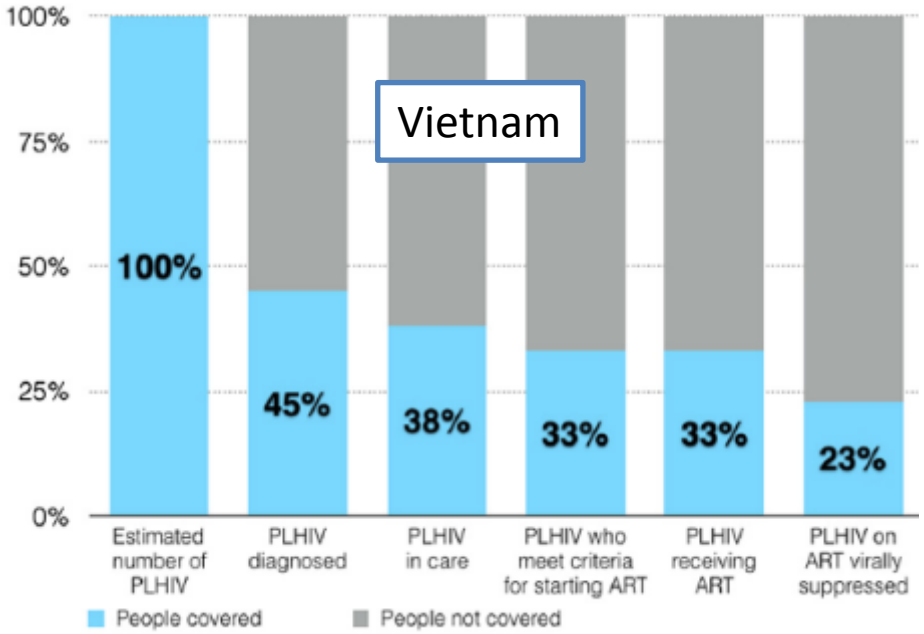
- All children and teens, ages 11 through 18 years
- People age 2 months and older with functional or anatomic asplenia (MenHibrix may be used for children age 6 weeks through 18 months in this group)
- People age 2 months and older who have persistent complement component deficiency (an immune system disorder, including people taking eculizumab [Soliris]) (MenHibrix may be used for children age 6 weeks through 18 months in this group)
- People age 2 months and older with HIV infection
- People younger than 22 years of age if they are or will be a first-year college student living in a residential hall
- People age 2 months and older who are at risk during an outbreak caused by a vaccine serogroup (MenHibrix may be used for children age 6 weeks through 18 months in this group)
- People age 2 months and older who reside in or travel to certain countries in sub-Saharan Africa as well as to other countries for which meningococcal vaccine is recommended (e.g., travel to Mecca, Saudi Arabia, for the annual Hajj)
- Microbiologists who work with meningococcus bacteria in a laboratory

CDC

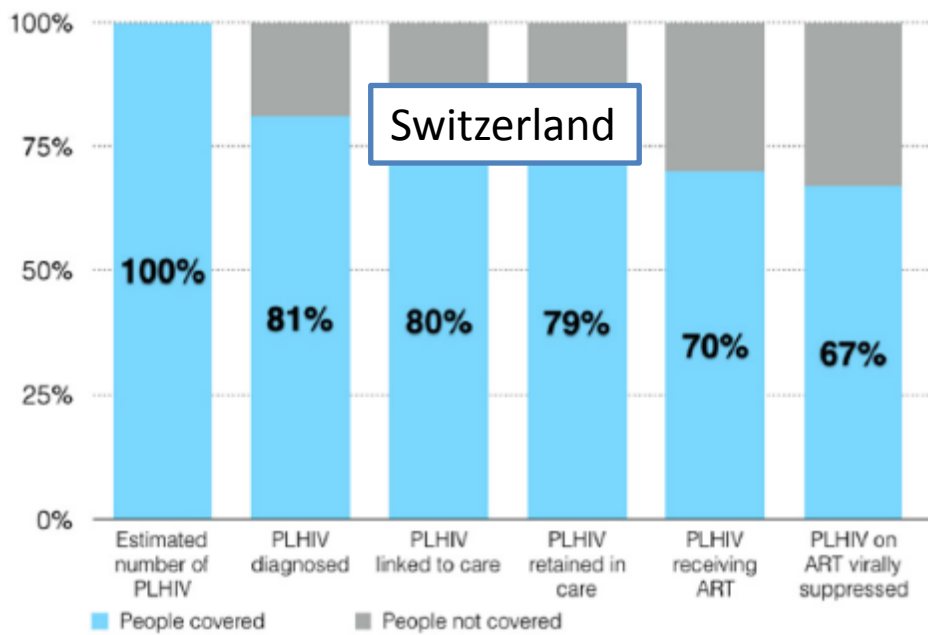
Agenda

- PART 1: General overview on mandatory screening
- **PART 2: Standard of care / Cascade of care**
- PART 3: How to measure patient's satisfaction of care?

90-90-90 • Where are we now?



*Adapted from UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. 2014. Available at http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf. Accessed on 25 April 2016



*Adapted from Philipp Kohler, Axel J. Schmidt, Matthias Cavassini, Hansjakob Furrer, Alexandra Calmy, Manuel Battegay, *et al.* The HIV care cascade in Switzerland: reaching the UNAIDS/WHO targets for patients diagnosed with HIV. *AIDS* 2015; 18: 2509-2515

Table 7. Multivariate logistic regression model: association of demographical and clinical features with loss to follow-up according to observation period

		Total period			1985-1991			1992-1997			1998-2003			2004-2009			2010-2012		
Variable	**Category**	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Gender	Male vs Female	0.98	0.91-1.06	0.662	1.09	0.93-1.29	0.289	1.00	0.86-1.15	0.989	1.03	0.88-1.20	0.672	0.79	0.66-0.96	0.018	0.85	0.55-1.30	0.460
Age at enrollment years	<25	1.60	1.28-2.00	<0.001	3.29	0.68-15.7	0.135	2.42	1.54-3.80	<0.001	1.38	0.90-2.13	0.135	2.17	1.37-3.44	0.001	1.29	0.48-3.51	0.610
	25-34	1.63	1.32-2.01	<0.001	4.33	0.91-20.67	0.065	1.81	1.18-2.76	0.006	1.20	0.84-1.71	0.306	2.18	1.47-3.24	<0.001	1.40	0.62-3.18	0.418
	35-44	1.42	1.15-1.75	0.001	3.95	0.82-19.04	0.086	1.55	1.01-2.37	0.047	1.02	0.71-1.44	0.932	1.74	1.18-2.56	0.005	1.33	0.60-2.97	0.476
	45-54	1.06	0.84-1.33	0.646	2.89	0.55-15.08	0.207	1.19	0.73-1.94	0.483	0.77	0.52-1.15	0.198	1.16	0.76-1.75	0.492	1.00	0.44-2.29	0.996
	≥55	Ref			Ref			Ref			Ref			Ref			Ref		
Country of Origin	Others vs Italy	2.57	2.28-2.89	<0.001	5.56	2.46-12.57	<0.001	2.75	1.92-3.94	<0.001	3.18	2.62-3.86	<0.001	2.17	1.79-2.62	<0.001	1.91	1.23-2.95	0.004
HIV exposure category	Heterosexuals	Ref			Ref			Ref			Ref			Ref			Ref		
	MSM	0.98	0.88-1.10	0.735	0.93	0.62-1.40	0.730	0.78	0.61-0.98	0.033	1.14	0.94-1.39	0.189	1.28	1.03-1.57	0.021	0.56	0.30-1.03	0.061
	IDUs	2.36	2.16-2.57	<0.001	1.91	1.49-2.44	<0.001	1.95	1.66-2.28	<0.001	2.66	2.27-3.12	<0.001	3.48	2.83-4.28	<0.001	3.95	2.31-6.74	<0.001
	MSM-IDUs	2.58	1.76-3.78	<0.001	2.81	1.38-5.69	0.004	2.45	1.33-4.55	0.004	1.48	0.57-3.84	0.417	2.55	0.72-8.95	0.143	-	-	-
	Heterosexuals-IDUs	1.13	0.94-1.35	0.190	0.57	0.34-0.92	0.023	0.69	0.51-0.93	0.014	2.2	1.55-3.14	<0.001	3.28	2.08-5.16	<0.001	3.07	1.11-8.56	0.031
	Haemophilia /Perinatal transmission	2.54	1.47-4.38	0.001	3.73	1.47-9.50	0.006	2.25	0.71-7.16	0.170	2.68	0.69-10.40	0.154	1.01	0.11-9.31	0.990	0.94	0.11-7.97	0.956
	Unknown	4.69	2.83-7.79	<0.001	-	-	-	16.88	3.79-75.23	<0.001	4.24	0.59-30.27	0.150	2.04	0.76-5.50	0.156	2.58	0.94-7.11	0.066
	Others	3.83	3.19-4.59	<0.001	5.86	3.03-11.32	<0.001	4.38	3.05-6.29	<0.001	4.93	3.43-7.09	<0.001	2.73	1.92-3.88	<0.001	2.80	1.56-5.06	0.001
Late presentation with advanced disease	Yes vs No	0.60	0.56-0.64	<0.001	0.33	0.28-0.38	<0.001	0.55	0.49-0.62	<0.001	0.78	0.69-0.89	<0.001	0.89	0.76-1.04	0.140	0.93	0.63-1.36	0.707
Period of enrollment	1985-1991	Ref																	
	1992-1997	1.22	1.11-1.33	<0.001															
	1998-2003	1.25	1.13-1.38	<0.001															
	2004-2009	0.98	0.88-1.10	0.784															
	2010-2012	0.24	0.19-0.29	<0.001															

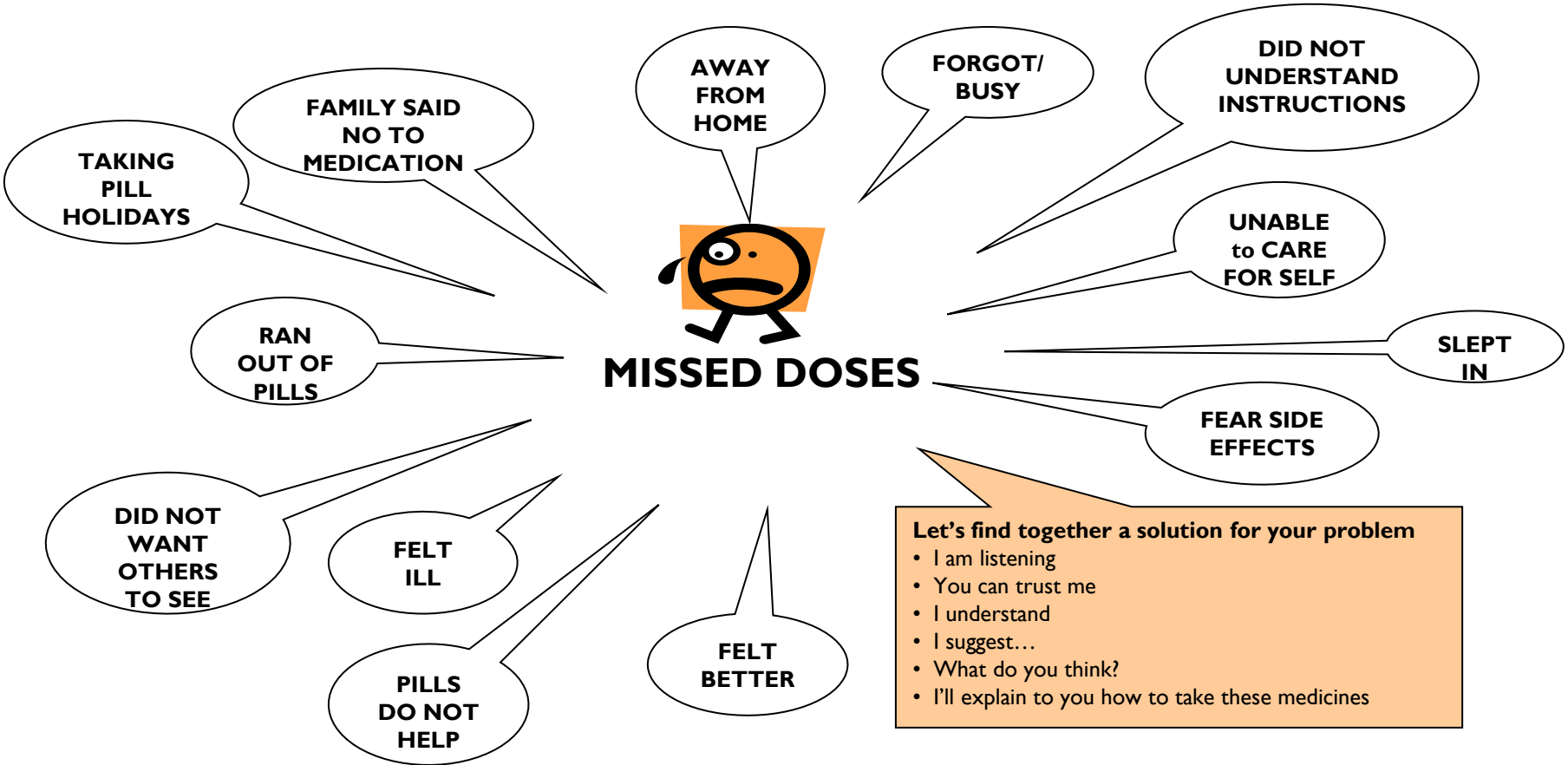
The associations of demographical and clinical features with loss to follow-up were investigated using a logistic regression model, providing estimates of the odds ratios (ORs) as measures of association. The fitted models included all the variables associated with each infection at the univariate analysis at the first step, and then excluding the variables not associated with each infection using a backward approach. Separate analyses have been performed in different time periods. **95% CI** : 95% confidence interval; **OR**: odds ratio.

Torti C et al. *Int J Epidemiol. 2015 Oct 7.* pii: dyv192

Barriers against adherence

- Communication difficulties
- Literacy levels
- Inadequate knowledge of HIV disease
- Inadequate understanding of effectiveness of medications
- Lack of social support
- Discomfort with disclosure of HIV status
- Difficult life conditions
- Alcohol and drug use
- Depression and other psychiatric problems
- System barriers

Why do patients miss doses?



Continuum of care

Several barriers are known to influence ART decision making and adherence to ART	
Screen for and talk about problems and facilitators	
Consider systematic assessment of: • Depression[vii], see page 64-65 • Cognitive problems[viii], see page 68 • Harmful alcohol[ix] or recreational drug use, see page 33, 35	Consider talking about: • Social support and disclosure • Health insurance and continuity of drug supply • Therapy-related factors
Recognise, discuss and reduce problems wherever possible in a multidisciplinary team approach.	

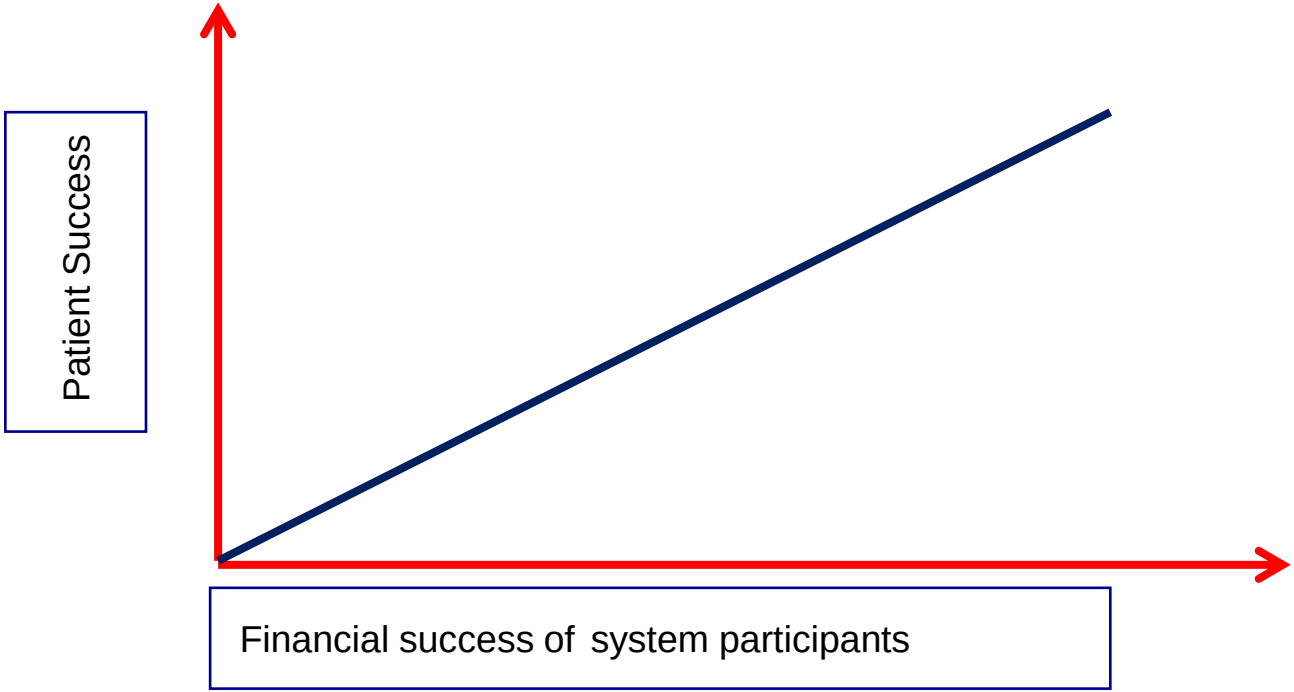
Continuum of care

- Use new technologies (apps for smartphones, web sites) [AII]
- Participate with patient's associations [AII]
- Involve social assistance groups [AII]

Agenda

- PART 1: General overview on mandatory screening
- PART 2: Standard care / Cascade of care
- **PART 3: How to measure patient's satisfaction of care?**

Resolve the disconnect between value and cost: reimbursement should be aligned with value



Quality of life as a health check (no data)

*Adapted from: UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. 2014. Available at http://unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf. Accessed on 25 April 2016

Fig. 1 The 'fourth 90': proposed revision to the UNAIDS 90-90-90 targets*

Lazarus JV *et al. BMC Med.* 2016.14:94

What are PROMs?

- Needs and perceptions of patients are not the needs of public health system
- Many scores of tools to measure outcomes that are important for the patient have been developed in the recent past
- **Measures of subjective well-being (like satisfaction or happiness) experienced by the patient**

Outcomes of commonly used PRO measurement in clinical trials

Study reference	Treatment/dosing regimen	Domain	Baseline score mean (SD)	Follow-up score (time, mean)	Effect size	Summary of PRO results
Instrument: *Centre for Epidemiologic Studies – Depression Scale (CES-D)*						
Lake (2012) [9]	Immediate switch of PI or NNRTI to RAL (continuing prior NRTI backbone)	Depression	NR	24 weeks, NR	N/A	• The CES-D was administered at 0, 4, 8, 12, 16, and 24 weeks, but patient-reported depression scores were not reported in this study.
	Delayed switch (at 24 weeks) of PI or NNRTI to RAL (continuing prior NRTI backbone)	Depression	NR	24 weeks, NR	N/A	
Clifford (2009) [22]	ZDV/3TC/EFV	Depression	12.2 (10.5)	184 weeks[†], 10.1[*]	0.20	• In participants who continued EFV-based regimens, neuropsychological performance improvement from baseline was maintained over 5 years.
	ZDV/3TC/ABC	Depression	11.8 (10.5)	184 weeks[†], 10.4	0.13	• There was statistically significant decrease in depression symptoms over the course of the study with the median score decline of 1.0 ($P = 0.03$).
	Various regimens (± EFV)	Depression	13.3 (11.1)	184 weeks[†], 16.8	0.30	• In the long term EFV treated group, the percent with CES-D scores >16 declined from 34.1% to 22.3% over the duration of the study.
	ZDV/3TC/ABC initially, then EFV added (± ABC)	Depression	13.8 (12.5)	184 weeks[†], 8.6	0.42	
Journot (2006) [29]	PI-based therapy	Depression[‡]	23%	48 weeks, 25%	N/A	• Proportion of patients with depression was approximately 24% at BL and remained stable during the 48 week follow up with no difference between treatment arms, $P = 0.065$).
	EFV based therapy	Depression[‡]	25%	48 weeks, 24% 96 months, 24%	N/A N/A	
						• Patients with a history of depression experienced depressive symptoms more frequently than those without such history (36% and 22% at week 48, respectively; $P = 0.03$).
Instrument: *Functional Assessment of HIV Infection (FAHI)*						
Campo (2010) [34]	Switch to EFV/3TC/ddI	Total Score	130	48 weeks, 134[#]	N/A	• In the overall patient population, FAHI total score increased significantly from BL to week 48 ($P < 0.001$) and at every other time point; changes in total score were associated with improvements in the physical and emotional well being domains ($P < 0.001$ for both).
	Switch PI to EFV (continuing prior NRTIs)	Total Score	132	48 weeks, 138[#]	N/A	• No significant between group differences observed.
Cella (2010) [15]	ETR 200 mg twice-daily[§]	Total Score	121.7 (23.2)[¶]	24 weeks, 122.3[¶,**]	0.21	• The change in physical well-being, emotional well-being/living with HIV and total scores from BL to Week 24 were statistically different from zero for both groups, with statistically significant greater improvements observed in the ETR group.
	Placebo[§]	Total Score	120.9 (26.7)[¶]	24 weeks, 124.0[¶,**]	0.11	
Boyle (2008) [23]	Continue BL ARVs (BID dosing)	Total Score	130.4	48 weeks, NR	N/A	• A small improvement (5% or less) for the emotional well-being and a small reduction (5% or less) for functional and global well-being were observed at some time points in both arms; however, these were not considered clinically relevant, as the effect sizes were small.
	Switch to once-daily ddI/3TC/EFV	Total Score	131.4	48 weeks, NR	N/A	• No significant differences observed between arms.
Instrument: *HIV Symptom Index / Symptom Distress Module (HIV-SI / SDM)*						
Hudelist (2010) [19]	EFV/FTC/TDF	Dizziness	28%	4 weeks, 59%[dd] 48 weeks, 28%	N/A N/A	• Simplification from PI-based or NNRTI-based regimens to EFV/FTC/TDF was associated with transient worsening or emergence of dizziness and sustained improvements in several other HIV related symptoms: diarrhea or loose bowel movements; bloating, pain or gas in the stomach; changes in body appearance; and problems having sex.
	Remain on BL antiretroviral regimen	Dizziness	27%	4 weeks, 25%[ee] 48 weeks, 28%	N/A N/A	
Potard (2010) [21]	EFV- or NVP-based therapy	Symptom Count	11.9 (8.1)	12 months, 9.0[ff]	0.32	• Overall, there was a small improvement in HIV symptoms at 1 year (effect size 0.32).
		Symptom Bother Count	7.7 (5.9)	12 months, 6.0[ff]	0.29	• An initial difference between groups in mean change in other symptoms, bothersome symptoms, and other bothersome symptoms observed at 1 month was not maintained at months 6 and 12.
Reginault (2009) [18]	ZDV/3TC + MVC 300 mg twice dailyZDV/3TC + MVC 600 mg once dailyZDV/3TC + FFV 600 mg once daily	Symptom Count	Mean score ranged from −5 (European Romance group) to −10 (Bantu group)	96 weeks, NR	N/A	• The study assessed the cross-cultural validity of the HIV-SI using pre-ARV treatment cross-sectional data of the MIRIT trial.
						• Statistically significant differential item functioning between cultural groups was observed for 4 items: fatigue, fever, anxiety, and headache.
		Symptom Bother Count	Mean score ranged from 10.08 (European Romance group) to 24.00 (Bantu group)	96 weeks, NR	N/A	• The authors concluded that the absence of meaningful explanations for statistically significant differences between cultural groups supports the cross-cultural validity of the HIV-SI versions used in the MIRIT trial.
Delissus (2008) [26]	Switch from twice-daily AZT/3TC to once-daily TDF/FTC with EFV	Symptom Count	NR	24 weeks, NR	N/A	• Significant differences were observed in the percentage of patients reporting the absence of the symptom at Week 24 compared to BL for 17 of the 20 items assessed.
		Symptom Bother Count	NR	24 weeks, NR	N/A	• Compared to BL, significantly more patients reported the absence of fatigue, absence of nausea and vomiting, absence of diarrhea, and absence of headache.
Instrument: *Medical Outcomes Study HIV health survey (MOS-HIV)*						
Jayaweera (2009) [24]	ddI/3TC/EFV once-daily	Total Score	874	96 weeks, 934	N/A	• The overall MOS-HIV QoL score, which is the sum of all individual MOS-HIV scores (range: 0 to 1,100), significantly improved from BL (874) to Week 96 (934; $P < 0.05$).
Jayaweera (2009) [24]	d4T/3TC/EFV once-daily	Total Score	832	12 weeks, 880	N/A	• The overall MOS-HIV QoL score significantly improved from BL (832) to Week 12 (880; $P < 0.05$).
Lafauric (2008) [28]	PI containing regimen	PHS MHS	56.5 (50.0 61.8)[gg] 40.2 (33.8-45.3)[gg]	48 weeks, 1.04[hh] 48 weeks, 0.00[hh]	0.24 0.00	• The mean change from BL to week 48 in the PCS and MCS were 1.04 and +0.0 in the maintenance arm and −1.76 and +1.01 in the switch arm, respectively ($P = 0.57$ and 0.42).
	EFV/ddI/FTC	PHS MHS	57.4 (51.5-60.4)[gg] 38.3 (33.4-43.6)[gg]	48 weeks, −1.76[hh] 48 weeks, 1.01[hh]	0.53 −0.27	• Specific items such as physical functioning, social functioning, and emotional functioning remained unchanged in both treatment groups during follow up.

Simpson *et al. Health and Quality of Life Outcomes* 2013;11:164.

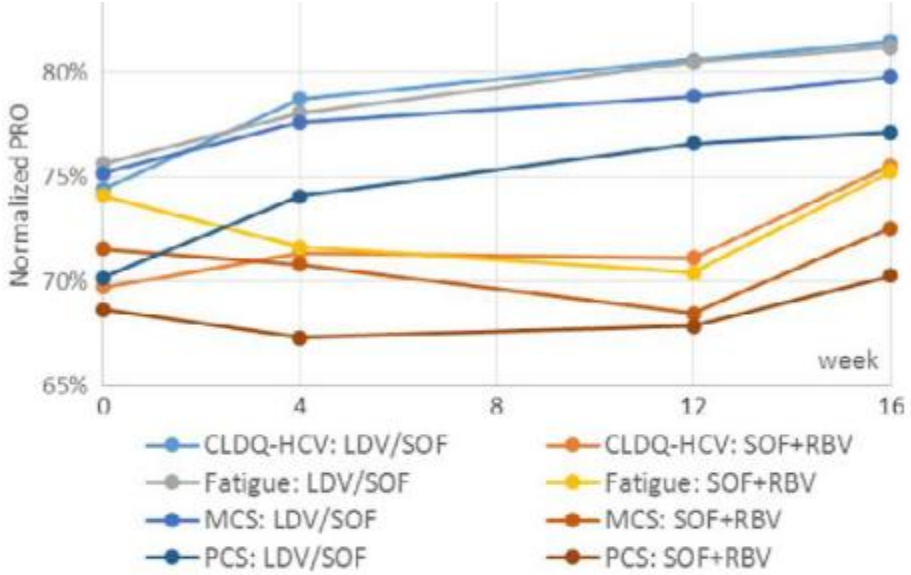
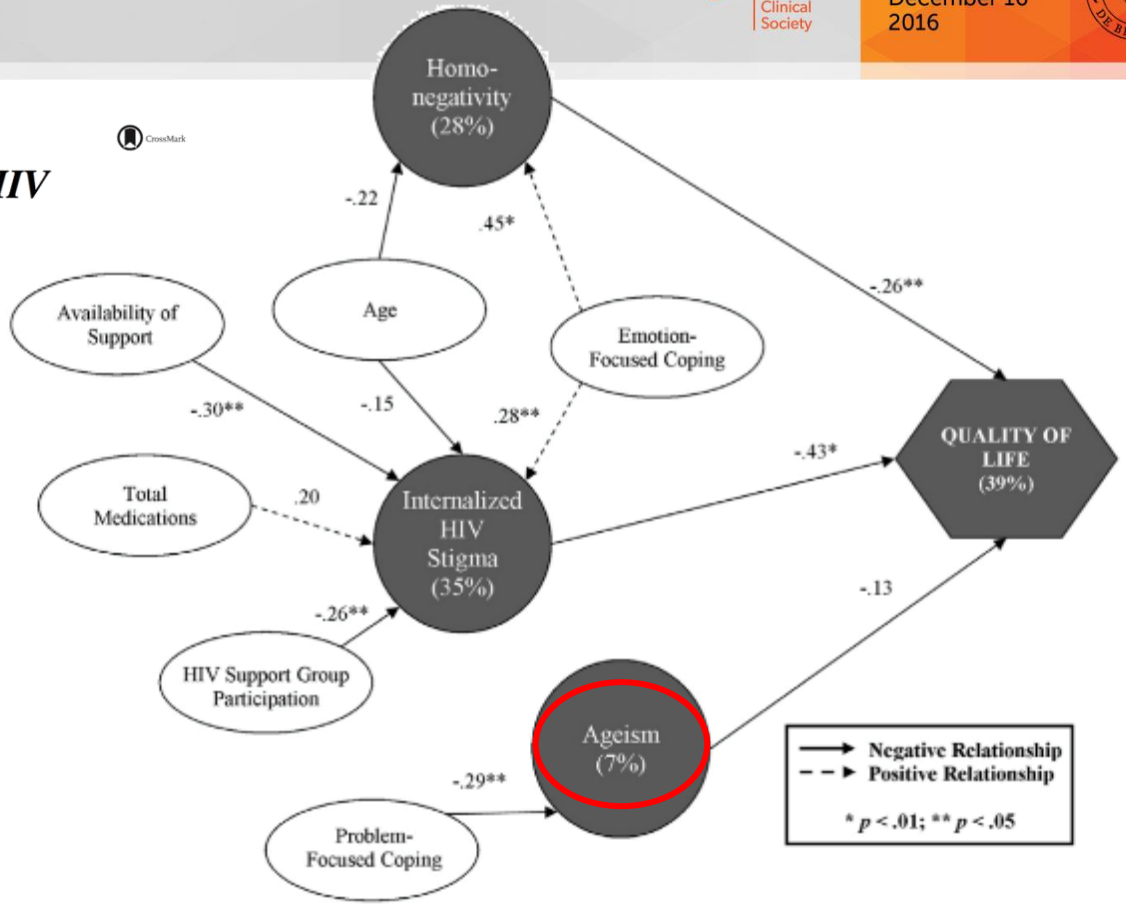


Fig. 2 Patient-reported outcomes in HIV–HCV-co-infected patients treated with 12 weeks of LDV/SOF (ION-4) *vs* 12 weeks of SOF+RBV (PHOTON-1). All $P < 0.001$ between regimens after treatment initiation (except for PCS and CLDQ-HCV at treatment week 4: both $P = 0.$

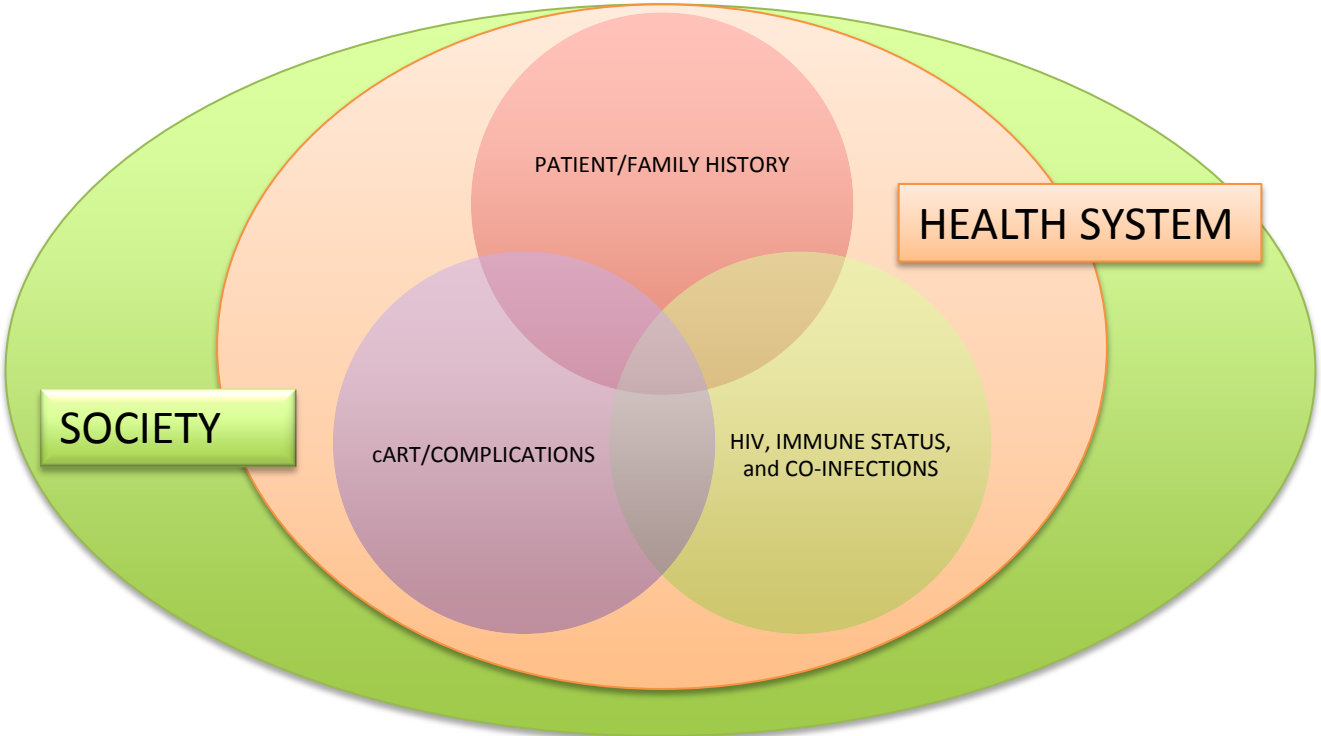
Yanoussi ZM *et al. J Viral Hep*. 2016; 23:857-865

The Multiple Stigma Experience and Quality of Life in Older Gay Men With HIV



Slater LZ *et al. J Assoc Nurses AIDS Care*. 2015 Jan-Feb;26(1):24-35

Not only medicine in the checks for health care



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- Antonella Cingolani (UCSC, Rome) – PROM's
- Giovanni Guaraldi (Modena University) – ageing & metabolic complications
- Alessio Strazzulla/Maria Mazzitelli ("Magna Graecia" University) – drafting the presentation/PROM's
- **THANK YOU FOR YOUR ATTENTION**

Screening and medical care of specific populations

Nuno Marques
Hospital Garcia de Orta, E.P.E., Portugal

Clinical case #1

- Angolan black female
- 42 years-old
- Living in Almada, PT since 02/2016
- Anorexia, weight loss, upper abdominal discomfort, chills
- PMH: malaria in childhood

Migrant Health Assessment – Problems and Priorities

- Exclude an infectious disease – TB, malaria, HIV, other…
- Exclude a non-infectious condition – anemia, woman's health, other…
- Assess mental and emotional health and wellbeing
- Consider social issues; housing, financial security, education, social supports

Clinical case #1

- Apyretic
- Fine crackles on the auscultation of lungs
- Discrete axillary lymphadenopathy

- Fever – exclude malaria
- BCG scar
- Cervical, axillary and inguinal lymphadenopathy – TB, HIV
- Cardiorespiratory exam – TB, COPD, CVD
- Hepatosplenomegaly – consider chronic malaria, chronic liver disease including HBV, schistosomiasis, TB, HIV
- Visual acuity
- ENT - middle ear disease, dental caries
- Neurologic examination
- BP, BMI, nutritional status

Testing for Infectious Diseases – All migrants

- Full blood count (eosinophilia…)
- HIV serology
- TB (latent *vs* active infection)
  - TST and/or IGRA
- HBAg, HBcAb, HBsAb
- Strongyloides serology
- Varicella serology (>14 yrs)
- Rubella serology (women of child bearing age)
- Catch-up vaccination

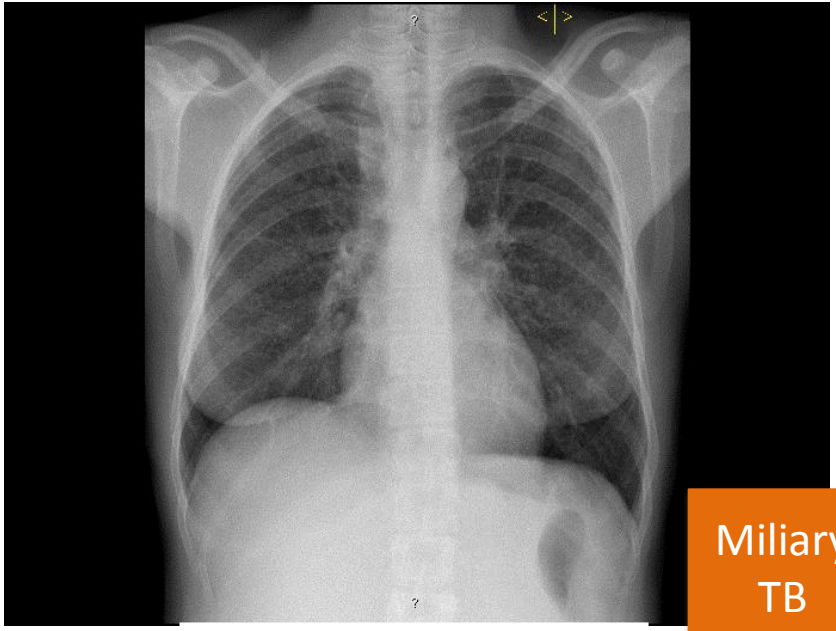
- Full blood count
  - A mild leucopenia and neutropenia are common in African and several other ethnic groups and do not require follow-up
  - If leucopenia is more severe, consider testing for visceral leishmaniasis or HIV
  - If thrombocytopenia, consider testing for malaria or visceral leishmaniasis. If LFTs are also abnormal and no other cause is found, test for *Entamoeba*

Clinical case #1

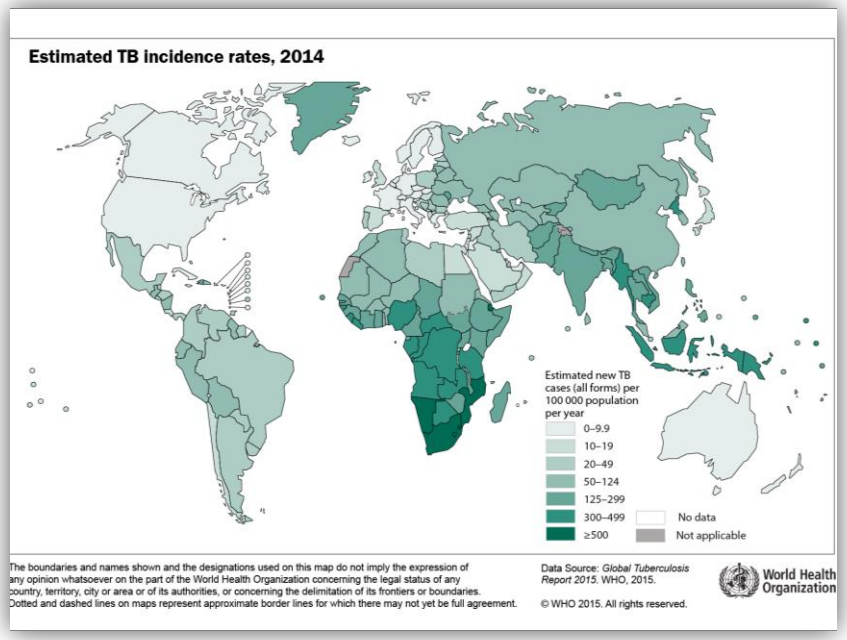
HIV negative
TST: cutaneous anergy
Non-immune to HBV
Immune for *Varicella* and *Rubella*
Negative *Strongyloides* serology

Clinical case #1

- What is your diagnostic procedure?



Miliary TB


Estimated TB incidence rates, 2014
Estimated new TB cases (all forms) per 100 000 population per year
0–9.9
10–19
20–49
50–124
125–299
300–499
≥500
No data
Not applicable
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Data Source: Global Tuberculosis Report 2015. WHO, 2015.
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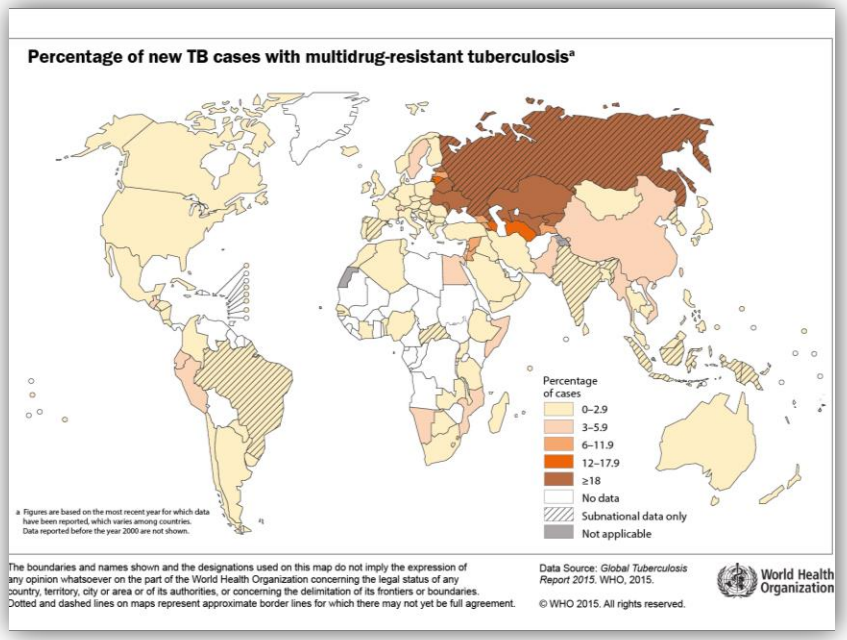
World Health Organization


Percentage of new TB cases with multidrug-resistant tuberculosis[a]
a Figures are based on the most recent year for which data have been reported, which varies among countries. Data reported before the year 2000 are not shown.
Percentage of cases
0–2.9
3–5.9
6–11.9
12–17.9
≥18
No data
Subnational data only
Not applicable
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.
Data Source: Global Tuberculosis Report 2015. WHO, 2015.
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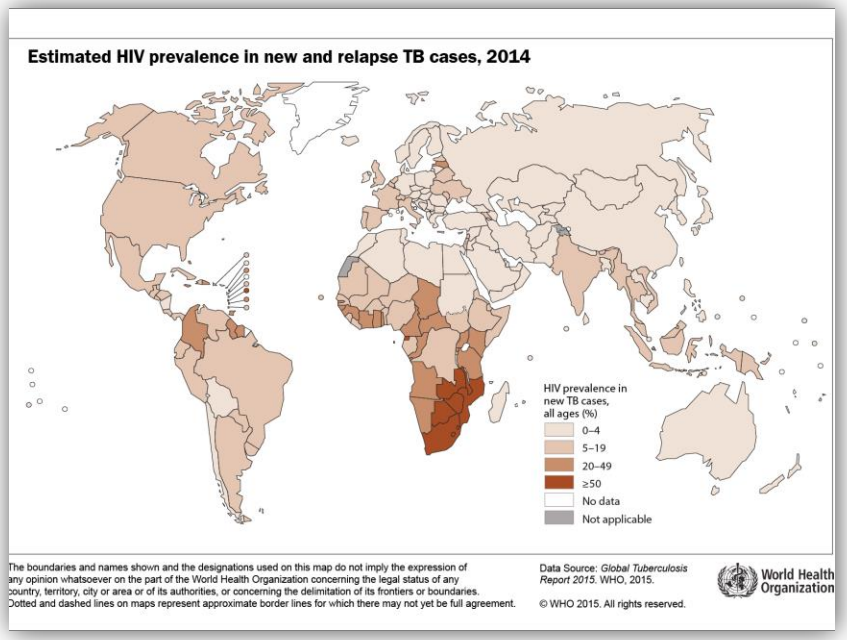
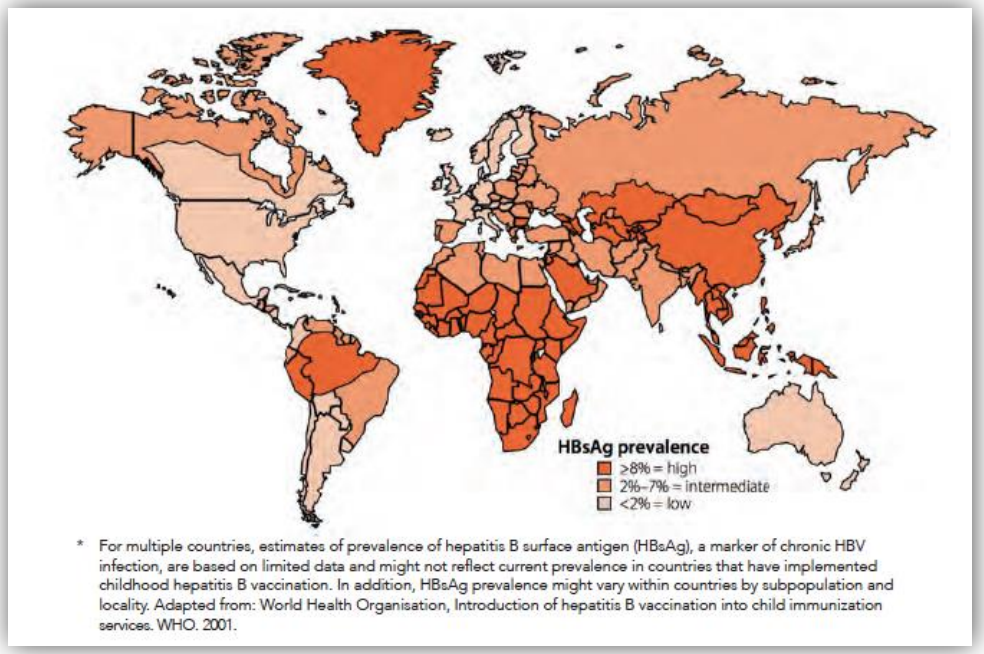
World Health Organization

Clinical case #1

- What is the most important known risk factor for progression from latent TB infection to TB disease?

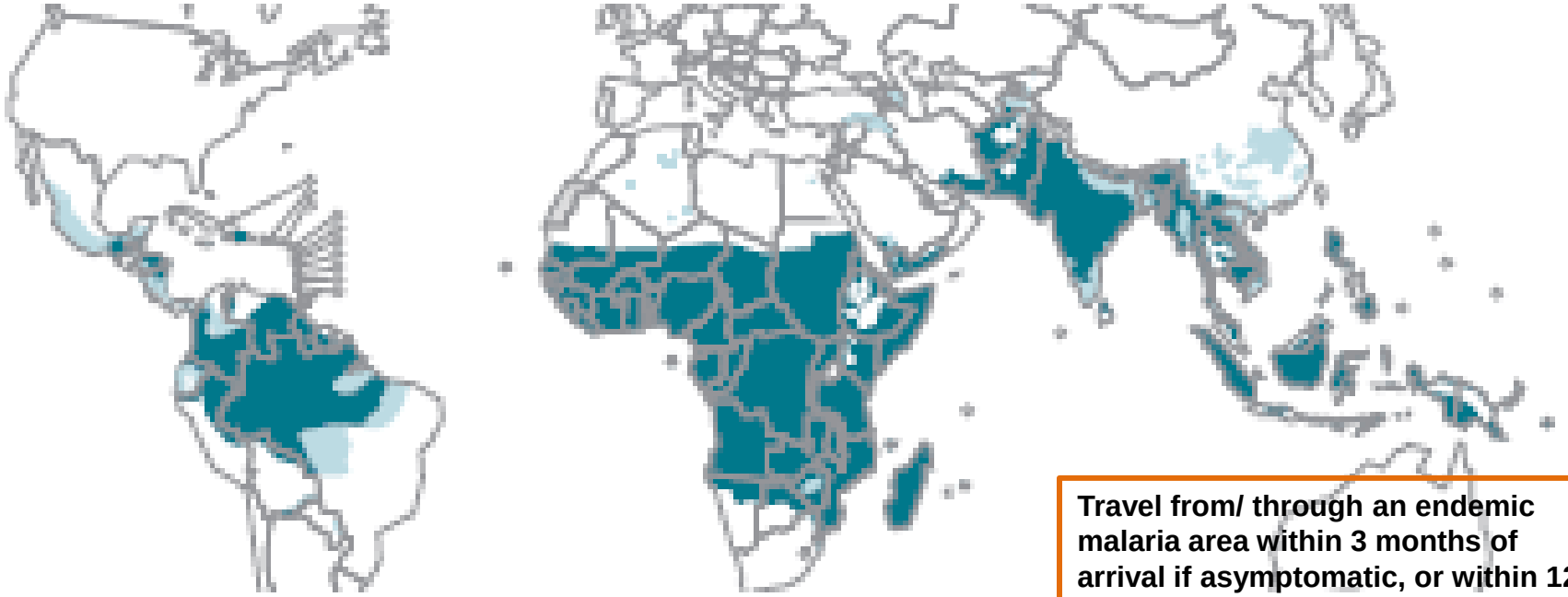


Testing for Infectious Diseases – All migrants



* For multiple countries, estimates of prevalence of hepatitis B surface antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg prevalence might vary within countries by subpopulation and locality. Adapted from: World Health Organisation, Introduction of hepatitis B vaccination into child immunization services. WHO. 2001.

Testing for Infectious Diseases – Country risk based



Travel from/ through an endemic malaria area within 3 months of arrival if asymptomatic, or within 12 months if symptoms of fever

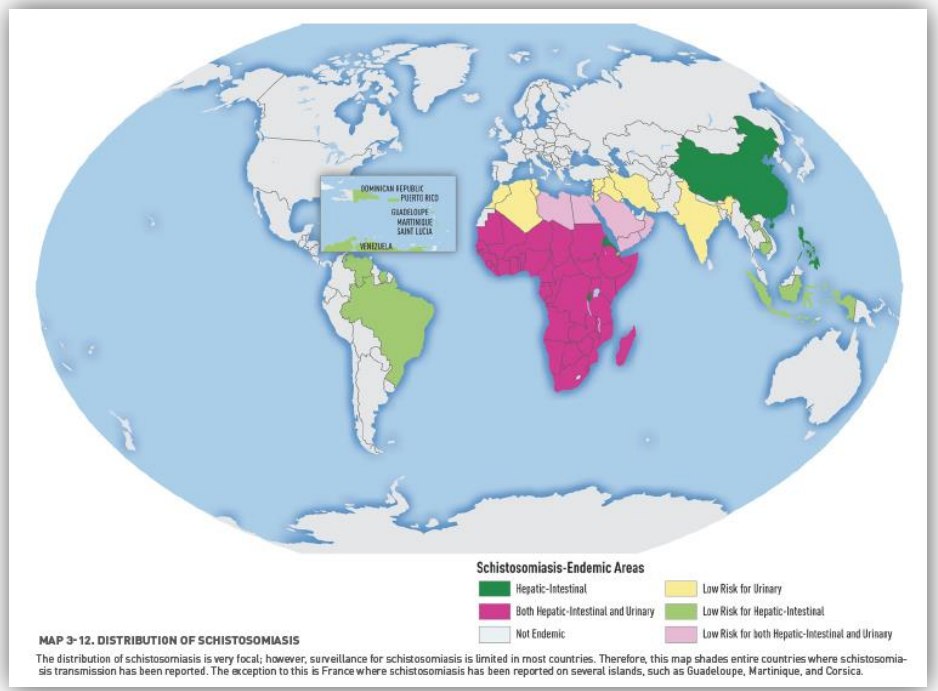
http://www.who.int/malaria/travellers/en/

Clinical case #1

- Malaria RDT
- Thick and thin blood films

Malaria RDT negative

Testing for Infectious Diseases – Country risk based



MAP 3-12. DISTRIBUTION OF SCHISTOSOMIASIS

The distribution of schistosomiasis is very focal; however, surveillance for schistosomiasis is limited in most countries. Therefore, this map shades entire countries where schistosomiasis transmission has been reported. The exception to this is France where schistosomiasis has been reported on several islands, such as Guadeloupe, Martinique, and Corsica.

http://www.cdc.gov/travel-static/yellowbook/2016/map_3-12.pdf

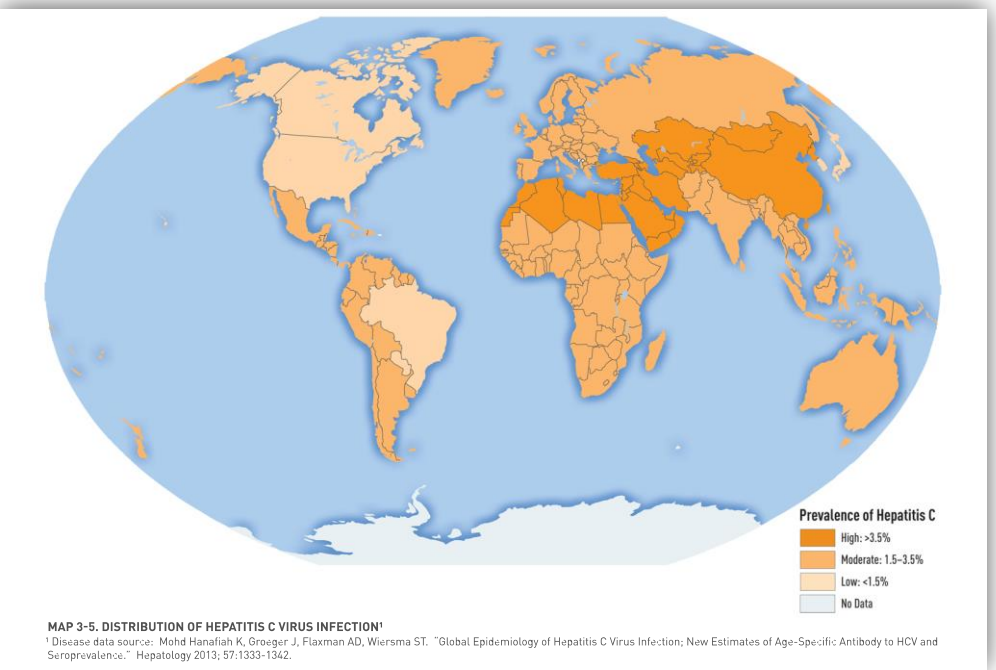
Clinical case #1

Negative Schistosomiasis serology

Schistosomiasis

- Stool microscopy for ova
- Dipstick for hematuria
- Urine microscopy for ova (ideally collected between 10am – 2pm)
- End organ disease with ultrasound and LFTs

Testing for Infectious Diseases – Country risk based



MAP 3-5. DISTRIBUTION OF HEPATITIS C VIRUS INFECTION[1]

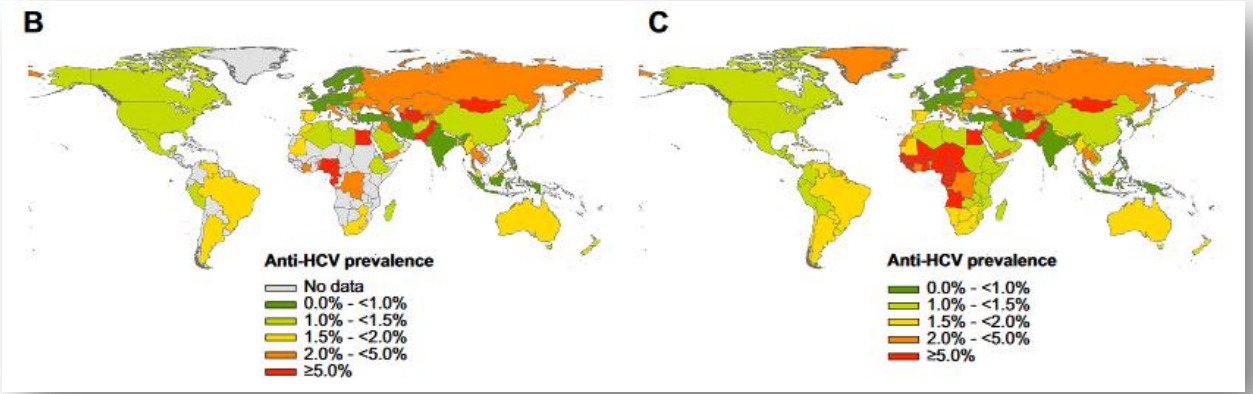
[1] Disease data source: Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. "Global Epidemiology of Hepatitis C Virus Infection; New Estimates of Age-Specific Antibody to HCV and Seroprevalence." Hepatology 2013; 57:1333-1342.

+ Risk factors

http://www.cdc.gov/travel-static/yellowbook/2016/map_3-05.pdf

Clinical case #1

Negative HCV Ab

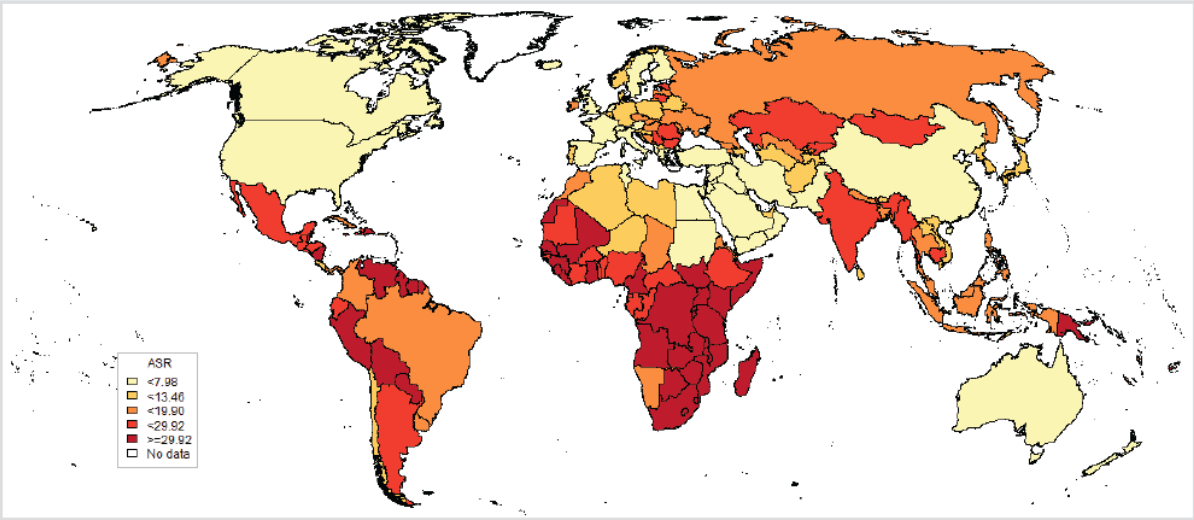


Gower E *et al. J Hepatol.* 2014 Nov;61(1 Suppl):S45-57

Testing for Infectious Diseases – Other risk based

- **STI**
  - NAAT test – self collected low vaginal sampling or first past urine and consideration of throat and rectal swabs for *Chlamydia trachomatis* and *Neisseria gonorrhoea*
  - Syphilis serology
- ***Helicobacter pylori***
  - *H. pylori* stool Ag or breath test
  - High risk groups: family history gastric cancer, and/or symptoms/ signs of dyspepsia or peptic ulcer disease
- **Intestinal parasites**
  - Empiric single dose albendazole therapy
  - If eosinophilia at baseline recheck in 8 weeks. If eosinophilia persists perform stool microscopy for OCP
  - Perform stool microscopy OCP followed by directed treatment.
    Recheck eosinophils and stool microscopy OCP at 8 weeks after directed treatment

High risk HPV: Age standardized incidence rates of cervical cancer in the World



Data accessed on 15 Nov 2015.

ASR: Age-standardized rate, Standardized rates have been estimated using the direct method and the World population as the reference;
Rates per 100,000 women per year.
For Sudan, South Sudan: Estimate for Sudan and South Sudan
Data sources: Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr.

Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, Bosch FX, de Sanjosé S. ICO Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary Report 29 November 2016. [Date Accessed]

ACIP recommendations for HPV vaccine

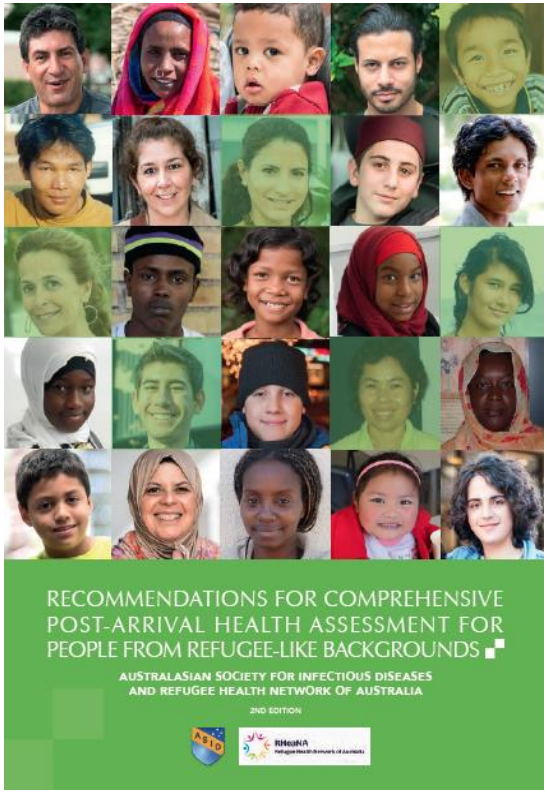
- 9vHPV, 4vHPV or 2vHPV can be used for routine vaccination of females aged 11 or 12 years and females through age 26 years who have not been vaccinated previously or who have not completed the 3-dose series.
- 9vHPV or 4vHPV can be used for routine vaccination of males aged 11 or 12 years and males through age 21 years who have not been vaccinated previously or who have not completed the 3-dose series.
- ACIP recommends either 9vHPV or 4vHPV vaccination for men who have sex with men and immunocompromised persons (including those with HIV infection) through age 26 years if not vaccinated previously.

Testing for Non-Infectious Conditions

- Anemia (all)
- Iron deficiency (women and children, men where risk factors are present)
- Low vitamin D (dark skin, lack of sun exposure/covering clothing)
- Vitamin B12 deficiency (history of food insecurity, or if vegan diet)
- Women's heath (Cervical cancer, breast cancer, contraception, antenatal/ perinatal care, sexual violence and/or sexual abuse, intimate partner violence, female genital mutilation/cutting, forced marriage)

Testing for Non-Infectious Conditions

- Hypertension, obesity, CVD, diabetes, COPD, dyslipidemia, breast/ cervical/ bowel cancer, smoking, alcohol use and substance use
- Dental caries and oral health concerns (all)
- Visual impairment (all)
  - Consider vitamin A deficiency or trachoma
- Glaucoma (African descent >40 years, all others >50 years)
- Hearing impairment (all)
- Mental health, social and emotional health (all)


RECOMMENDATIONS FOR COMPREHENSIVE POST-ARRIVAL HEALTH ASSESSMENT FOR PEOPLE FROM REFUGEE-LIKE BACKGROUNDS
AUSTRALASIAN SOCIETY FOR INFECTIOUS DISEASES AND REFUGEE HEALTH NETWORK OF AUSTRALIA
2ND EDITION

Clinical case #2

- Caucasian, male
- 45 years-old
- Co-infected with HIV/HCV
- HCV genotype 3a
- HCV viral load of 875437 IU/ml
- Undetectable HIV viral load (cART: FTC/TDF+DTG)
- CD4+ count: 538/mm^3
- Natural immunity for HBV and HAV

Regarding HCV, what is the clinical priority?

- HCV treatment
- Status of liver damage
  - Staging of fibrosis
    (e.g. FibroScan®, liver biopsy, serum fibrosis markers)
  - Hepatic synthetic function (e.g. coagulation, albumin, cholinesterase)
  - Ultrasound
- HCC surveillance

European Journal of Cancer (2012) 48, 599–641

Available at www.sciencedirect.com

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Clinical Practice Guidelines

EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma☆

European Association for the Study of the Liver*, European Organisation for Research and Treatment of Cancer

Geographical distribution of main risk factors for hepatocellular carcinoma (HCC) worldwide[a].

Geographic area	AAIR M/F	Risk factors		Alcohol	Others
		HCV (%)	HBV (%)	(%)	(%)
Europe	6.7/2.3	60–70	10–15	20	10
Southern	10.5/3.3				
Northern	4.1/1.8				
North America	6.8/2.3	50-60	20	20	10 (NASH)
Asia and Africa		20	70	10	10 (Aflatoxin)
Asia	21.6/8.2				
China	23/9.6				
Japan	20.5/7.8	70	10–20	10	10
Africa	1.6/5.3				
WORLD	16/6	31	54	15	

AAIR, age-adjusted incidence rate.

[a] Updated from Llovet *et al.*, Lancet 2003,[99] according to IARC data.[4]

European Journal of Cancer (2012) 48, 599–641

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EJC

Clinical Practice Guidelines

EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma☆

European Association for the Study of the Liver*, European Organisation for Research and Treatment of Cancer

Recommendations for hepatocellular carcinoma (HCC) surveillance: categories of adult patients in whom surveillance is recommended.

1. Cirrhotic patients, Child-Pugh stage A and B[a]
2. Cirrhotic patients, Child-Pugh stage C awaiting liver transplantation[b]
3. Non-cirrhotic HBV carriers with active hepatitis or family history of HCC[c]
4. Non-cirrhotic patients with chronic hepatitis C and advanced liver fibrosis F3[d]

[a] Evidence 3A; strength B1.
[b] Evidence 3D; strength B1.
[c] Evidence 1B; strength A1 for Asian patients; Evidence 3D; strength C1 for Western patients
[d] Evidence 3D; strength B1 for Asian patients; Evidence 3D; strength B2 for Western patients.

European Journal of Cancer (2012) 48, 599–641

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EJC

Clinical Practice Guidelines

EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma☆

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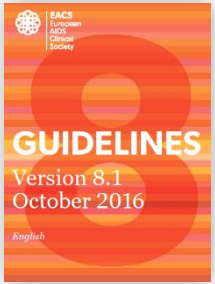
- Surveillance should be performed by experienced personnel in all at-risk populations using abdominal ultrasound every 6 months **(evidence 2D; recommendation 1B)**. Exceptions: A shorter follow-up interval (every 3–4 months) is recommended in the following cases: 1. Where a nodule of less than 1 cm has been detected (see recall policy), 2. In the follow-up strategy after resection or loco-regional therapies **(evidence 3D; recommendation 2B)**

- Accurate tumour biomarkers for early detection need to be developed. Data available with tested biomarkers (i.e. AFP, AFP-L3 and DCP) show that these tests are suboptimal for routine clinical practice **(evidence 2D; recommendation 2B)**
- Patients on the waiting list for liver transplantation should be screened for HCC in order to detect and manage tumour progression and to help define priority policies for transplantation **(evidence 3D; recommendation 1B)**



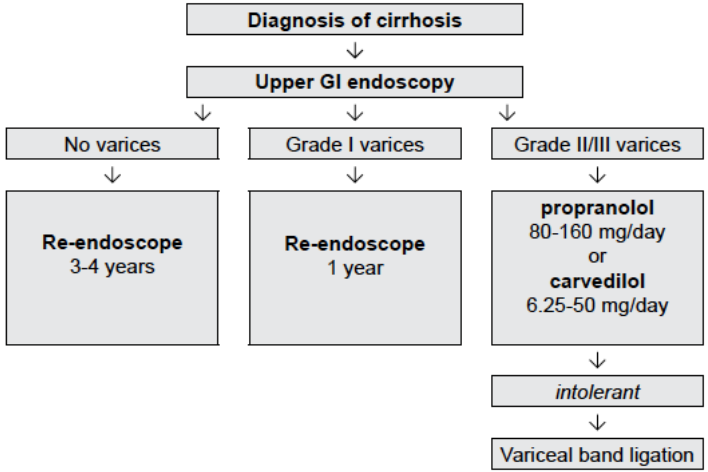
Liver Cirrhosis: Classification and Surveillance

Child-Pugh classification of the severity of cirrhosis

	Point[i]		
	1	2	3
Total bilirubin, mg/dL (µmol/L)	< 2 (< 34)	2-3 (34-50)	> 3 (> 50)
Serum albumin, g/L (µmol/L)	> 35 (> 507)	28-35 (406-507)	< 28 (< 406)
INR	< 1.7	1.7-2.20	> 2.20
Ascites	None	Mild/Moderate (diuretic responsive)	Severe (diuretic refractory)
Hepatic encephalopathy	None	Grade I-II (or suppressed with medicine)	Grade III-IV (or refractory)

i 5-6 points: Class A
7-9 points: Class B
10-15 points: Class C

Algorithm for surveillance for varices and primary prophylaxis



HCV extrahepatic manifestations affecting oral cavity

- Xerostomia
  - Increases patient vulnerability to caries and oral soft tissue disorders
- Sjögren's syndrome
- Sialadenitis
- Lichen planus

+ Oral deficient hygiene

Immunization – chronic liver disease

- Influenza
- Tdap
- Pneumococcal vaccine
- Hepatitis B
- Hepatitis A
- Zoster vaccine (>60 years)
- HPV (woman up to age 26; man up to age 21)
- MMR
- Varicella

Thanks for your attention