Guidelines
Prevention and Management of Non-Infectious Co-Morbidities in HIV
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Available online at
www.europeanaidsclinicalsociety.org/Guidelines/G2.htm

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- Classification, doses, safety and side effects of antidepressants
- Interactions between antidepressants and antiretroviral agents
- List of selected dermal/soft tissue fillers used for restorative treatment
PREVENTION AND MANAGEMENT OF NON-INFECTIOUS CO-MORBIDITIES IN HIV

Panel Members

Jens D. Lundgren,
Copenhagen, Denmark
Chair

Manuel Battegay,
Basel, Switzerland

Georg Behrens,
Hannover, Germany

Simon Collins,
London, United Kingdom

Juliet Compston,
Cambridge, United Kingdom

Gilbert Deray,
Paris, France

Stephane De Wit,
Brussels, Belgium

Christoph A. Fux,
Bern, Switzerland

Giovanni Guaraldi,
Modena, Italy

and the EACS Executive Committee

Patrick Mallon,
Dublin, Ireland

Esteban Martinez,
Barcelona, Spain

Socrates Papapoulos,
Leiden, The Netherlands

Neil Poulter,
London, United Kingdom

Peter Reiss,
Amsterdam, The Netherlands

Jussi Sutinen,
Helsinki, Finland

Alessandra Vigano,
Milan, Italy

Ian Williams,
London, United Kingdom

Prevention and Management of Non-Infectious Co-Morbidities in HIV

Abbreviations used throughout this document

- ABC=abacavir;
- ACE=angiotensin converting enzyme;
- ALP=alkaline phosphatase;
- ALT=alanine aminotransferase;
- aMDRD=abbreviated Modification of Diet in Renal Disease formula;
- ART=antiretroviral therapy;
- AST=aspartate aminotransferase;
- ATV=atazanavir;
- BMD=bone mineral density;
- CKD=chronic kidney disease;
- CNS=central nervous system;
- COPD=chronic obstructive pulmonary disease;
- CSF=cerebrospinal fluid;
- CVD=cardiovascular disease;
- d4T=stavudine;
- dDXA=dual energy X-ray absorptiometry;
- ddl=didanosine;
- DRV=darunavir;
- EFV=efavirenz;
- eGFR=estimated glomerular filtration rate;
- ENF=enfuvirtide;
- ETV=oseltavirine;
- FPV=fos-amprenavir;
- FRAX=Fracture Risk Assessment Tool;
- FTC=emtricitabine;
- HBV=hepatitis B virus;
- HCV=hepatitis C virus;
- HDL-c=HDL-cholesterol;
- HIVAN=HIV associated nephropathy;
- IDV=indinavir;
- IHD=ischaemic heart disease;
- LDL-c=LDL-cholesterol;
- LPV=lopinavir;
- MVC=maraviroc;
- NFV=nefelnavir;
- NNRTI=non-nucleoside reverse transcriptase inhibitors;
- NRTI=nucleos(t)ide reverse transcriptase inhibitors;
- NVP=nevirapine;
- PI=protease inhibitors;
- PI/r=protease inhibitors pharmacologically boosted with ritonavir;
- PSA=prostate specific antigen;
- PTH=parathyroid hormone;
- RAL=raltegravir;
- RTV=ritonavir (used as booster= /r);
- SQV=saquinavir;
- 3TC=lamivudine;
- TC=total cholesterol;
- TG=triglycerides;
- TDF=tenofovir;
- TIP=rilpivirine;
- UA/C: urine albumin/creatinine ratio;
- UP/C: urine protein/creatinine ratio;
- ZDV=zidovudine

Acknowledgements: The guidelines panel has received helpful comments and suggestions from the following persons:
HIV specific issues to be considered in managing “non-infectious” co-morbidities

Non-infectious co-morbidities include cardiovascular, renal, hepatic, metabolic, neoplastic, bone pathologies and depression. Although HIV and other infections may be involved in their pathogenesis, these guidelines focus on preventive and/or management principles other than use of antivirals and other anti-infectious agents in adults and adolescent HIV-infected persons.

These co-morbidities are becoming increasingly important for HIV-infected persons as a consequence of increased life expectancy resulting from effective ART. Additionally, several demonstrated and proposed HIV-associated risk factors may contribute to their development including immune activation, inflammation and coagulation associated with (uncontrolled) replication of HIV, co-infections (e.g. HCV), ART itself and persistent immunodeficiency.

Health care professionals involved with the care of HIV-infected persons who are not familiar with the use of ART should consult HIV specialists before introducing or modifying any type of treatment that HIV-infected patients receive.

Conversely, many HIV physicians are not specialists in non-infectious co-morbidities, and should seek expert advice where appropriate in the prevention and management of such conditions. Situations where consultation is generally recommended are indicated in these guidelines.

Preventing or managing these diseases in HIV often involves polypharmacy, which increases the risk of suboptimal adherence and hence may compromise the continued benefit of ART. Additionally, the possibility of drug-drug interactions with ART should be carefully considered prior to introducing any treatment. Several websites exist for this purpose: www.HIV-druginteractions.org, www.HIVpharmacology.com, www.AIDSinfo.nih.gov.

These guidelines are intended to provide the best guide to clinical management, and it is recognised that the level of evidence to support the advice varies. Indeed, there is limited evidence from randomised controlled trials on best management of non-infectious co-morbidities in HIV. As a result current management is mainly derived from general medical guidelines. These guidelines therefore represent the collective consensus opinion of a panel of experts in the field of HIV and the respective range of co-morbidities, and no attempt to rate the underlying evidence and strength of the panel’s recommendations was undertaken.

Dependent on future clinical research findings, these guidelines will be regularly updated as required. The online version of guidelines, at www.europeanaidsclinicalsociety.org, contains more detailed information, links to other relevant websites and will be regularly updated.

The current guidelines highlight non-infectious co-morbidities that are seen frequently in the routine care of HIV-infected persons and those for which specific issues should be considered. Other related conditions in the management of HIV disease that are not extensively discussed, but may be included in future versions are:

- Sexual dysfunction. This is frequently encountered and often requires a multidisciplinary approach for its management that may include both expert psychological counselling and medical interventions.
- Hypogonadism,
- Other women’s health issues, and
- Neuropathy which may be caused by infections (e.g. HIV), some ARV (see p. 39), other neuropathic drugs, and by metabolic diseases (eg. diabetes).
Screening for non-infectious co-morbidities

<table>
<thead>
<tr>
<th>Assessment</th>
<th>At HIV diagnosis</th>
<th>Prior to starting cART</th>
<th>Follow up with cART</th>
<th>frequency</th>
<th>Comment</th>
</tr>
</thead>
</table>
| History    | +               | +                      | every visit         | 6-12 m    | On transfer of care repeat assessment Premature CVD: Cardiovascular events in a first degree relative: male <55, female <65 years
Adverse lifestyle habits should be addressed more frequently |
| Body composition | Body-mass index | +                      | annual              | annual    |         |
| Cardiovascular disease | Risk assessment (Framingham score) | +                       | annual              | annual    | Should be performed in every older patient without CVD (Men > 40 years; Women > 50 years) |
| Hypertension | Blood pressure | +                      | annual              | annual    |         |
| Dyslipidaemia | TC, HDL-c, LDL-c, TG | +                       | annual              | annual    |         |
| Diabetes mellitus | Serum glucose | +                      | 6-12 m              |           | Consider oral glucose tolerance test if repeated fasting glucose levels of 6.1-6.9 mmol/L (110-125 mg/dL) |
| Liver disease | Risk assessment | +                      | annual              | 3-6 m     | More frequent monitoring prior to starting and on treatment with hepatotoxic drugs |
| Renal disease | Risk assessment | +                      | annual              | 3-6 m     | More frequent monitoring if CKD risk factors present and/or prior to starting and on treatment with nephrotoxic drugs Every 6 months if eGFR <60 ml/min; If proteinuria ≥1+ and/or eGFR<60 ml/min perform UP/C or UA/C |
| Bone disease | Risk assessment | +                      | 2 yrs               | 2 yrs     | If not using FRAX®, consider DXA of spine and hip in specific patients Repeat according to risk factors |
| Neurocognitive impairment | Questionnaire | +                      | 1-2 yrs              | 1-2 yrs   | Screen risk patients |
| Depression | Questionnaire | +                      | 1-2 yrs              | 1-2 yrs   | Screen risk patients |
| Cancer | Mammography | +                      | 1-3 yrs              | 1-3 yrs   | Women 50-70 years Sexually active women, frequency depending on CD4 Controversial |

See page

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### Screening for non-infectious co-morbidities

**Cancer - screening methods**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Patients</th>
<th>Procedure</th>
<th>Evidence of benefit</th>
<th>Screening interval</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>Women 50-70 yrs</td>
<td>Mammography</td>
<td>↓ breast cancer mortality</td>
<td>1-3 years</td>
<td></td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>Sexually active women</td>
<td>Papaniculau test</td>
<td>↓ cervical cancer mortality</td>
<td>1-3 years</td>
<td>Target age group should include at least the age range 30 to 59 years. Longer screening interval if prior screening tests repeatedly negative</td>
</tr>
<tr>
<td>Anal cancer</td>
<td>Homosexual men</td>
<td>Digital rectal exam ± Papaniculau test</td>
<td>Unknown - advocated by some experts</td>
<td>1-3 years</td>
<td>If Pap test abnormal, anoscopy</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>Persons 50-75 yrs</td>
<td>Fecal Occult Blood test</td>
<td>↓ colorectal cancer mortality</td>
<td>1-3 years</td>
<td>Benefit is marginal</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Men &gt;50 yrs</td>
<td>Digital rectal exam ± Prostate specific antigen (PSA)</td>
<td>Controversial</td>
<td>1-3 years</td>
<td>Pros: ↑ early diagnosis Cons: Overtreatment, no ↓ cancer-related mortality</td>
</tr>
</tbody>
</table>

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1. Screening recommendations derived from the general population. These screenings should preferably be done as part of national general population-screening programs. Although non-Hodgkin lymphoma has a higher incidence in HIV-infected patients than in the general population, it is currently unknown whether it can be screened.

Careful examination of skin should be performed regularly to detect cancers such as Kaposi’s sarcoma, basal cell carcinoma and malignant melanoma.
Antiretroviral drugs & drug classes: frequent/severe side effects

<table>
<thead>
<tr>
<th>NRTI</th>
<th>Skin</th>
<th>Digestive</th>
<th>Liver</th>
<th>CV</th>
<th>Musculo-skeletal</th>
<th>Genitourinary</th>
<th>Nervous</th>
<th>Body fat</th>
<th>Metabolic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV</td>
<td>Nail pigmentation</td>
<td>Nausea</td>
<td>Steatosis</td>
<td>Myopathy</td>
<td>Lipoatrophy</td>
<td>Dyslipidaemia, Hyperlactataemia</td>
<td>Anemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d4T</td>
<td>Pancreatitis</td>
<td>Steatosis</td>
<td>Peripheral neuropathy</td>
<td>Lipoatrophy</td>
<td>Dyslipidaemia</td>
<td>Hyperlactataemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ddI</td>
<td>Pancreatitis</td>
<td>Steatosis, Liver fibrosis</td>
<td>IHD</td>
<td>Peripheral neuropathy</td>
<td>Hyperlactataemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td></td>
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<tr>
<td>FTC</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>Rash*</td>
<td></td>
<td>IHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTC</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ BMD, Osteomalacia, ↓ GFR, Fanconi syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NNRTI</th>
<th>Skin</th>
<th>Digestive</th>
<th>Liver</th>
<th>CV</th>
<th>Musculo-skeletal</th>
<th>Genitourinary</th>
<th>Nervous</th>
<th>Body fat</th>
<th>Metabolic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFV</td>
<td>Rash</td>
<td></td>
<td>Hepatitis</td>
<td></td>
<td>Depression, Suicidal ideation,</td>
<td>Dyslipidaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dizziness, Sleep disturbances</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>Rash</td>
<td></td>
<td>Hepatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Systemic Hypersensitivity (CD4- and gender-dependent)</td>
</tr>
<tr>
<td>ETV</td>
<td>Rash</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: Systemic Hypersensitivity (HLA B*5701 dependent)
### Antiretroviral drugs & drug classes:

#### frequent/severe side effects^1^ - 2/2

<table>
<thead>
<tr>
<th>Antiretroviral drugs &amp; drug classes</th>
<th>PI</th>
<th>Fusion inhibitors</th>
<th>Integrase inhibitors</th>
<th>CCR5 inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Digestive</td>
<td>Liver</td>
<td>CV</td>
<td>Musculo-skeletal</td>
</tr>
<tr>
<td>▪ IDV Dry skin</td>
<td>Jaundice</td>
<td>IHD</td>
<td>Nephrolithiasis</td>
<td>↑abdominal fat</td>
</tr>
<tr>
<td>▪ IDV Nail dystrophy</td>
<td>Nausea and diarrhoea</td>
<td>Jaundice</td>
<td>IHD</td>
<td>Nephrolithiasis</td>
</tr>
<tr>
<td>▪ SQV</td>
<td>Nausea</td>
<td>IHD</td>
<td>Dyslipidaemia</td>
<td></td>
</tr>
<tr>
<td>▪ LPV</td>
<td>Nausea</td>
<td>IHD</td>
<td>Dyslipidaemia</td>
<td></td>
</tr>
<tr>
<td>▪ FPV</td>
<td>Nausea</td>
<td>IHD</td>
<td>Dyslipidaemia</td>
<td></td>
</tr>
<tr>
<td>▪ ATV</td>
<td>Nausea</td>
<td>Jaundice</td>
<td>Nephrolithiasis</td>
<td>Dyslipidaemia</td>
</tr>
<tr>
<td>▪ DRV</td>
<td>Nausea</td>
<td>Jaundice</td>
<td>Nephrolithiasis</td>
<td>Dyslipidaemia</td>
</tr>
<tr>
<td>▪ TPV</td>
<td>Nausea</td>
<td>Jaundice</td>
<td>Nephrolithiasis</td>
<td>Dyslipidaemia</td>
</tr>
</tbody>
</table>

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^1^ “Severe events” (events that can put patient’s life at risk and represent a medical emergency) are marked in bold letters. “Frequent events” (events expected in at least 10% of treated patients) are marked in red. Background knowledge on tolerability of ENF, DRV, ETV, RAL, and MVC is limited because of its recent introduction into the clinical armamentarium.

^2^ Frequency and severity differs between individual agents.
### Lifestyle interventions

<table>
<thead>
<tr>
<th>INTERVENTION</th>
<th>PRINCIPLES</th>
</tr>
</thead>
</table>
| **Smoking cessation** | - Brief unambiguous statement about need to stop smoking  
- If patient is not contemplating, try to motivate and emphasize positive short-term aspects (more money for better things, better taste for food, less dyspnoea), and long-term benefits (prevention of COPD, IHD, stroke, lung cancer)  
- If patient is contemplating, try to fix stop date, establish reward system  
- Use nicotine substitution (patch, chewing gum, spray), varenicline, or bupropion (note: both drugs may cause central nervous system side effects including suicide; bupropion may interact with PI and NNRTI) during weaning phase if necessary  
- Consider referring patient to specialized stop smoking clinics  
- Anticipate relapses, explain and consider them as part of the weaning process to final nicotine abstinence |
| **Dietary counselling** | - Dietary intervention should not interfere with the dietary requirements required for appropriate absorption of ART drugs  
- Keep caloric intake balanced with energy expenditure  
- Limit intake of saturated fat, cholesterol and refined carbohydrates  
- Reduce total fat intake to < 30% and dietary cholesterol to <300mg/day  
- Emphasize intake of vegetables, fruits, grain products with fibre  
- Emphasize consumption of fish, poultry (without skin) and lean meat  
- Consider referral to dietician, one week food and drink diary to discover ‘hidden’ calories  
- Avoid binge eating (‘yo-yo dieting’)  
- In patients with HIV-related wasting and dyslipidaemia address wasting first and consider referral to dietician  
- Patients who are obviously overweight should be motivated to lose weight. Starvation diets are not recommended (immune defence mechanisms potentially decreased). Malnutrition has to be addressed where observed. Normal BMI range: 18.5-24.9; Overweight: 25.0-29.9, Obesity: > 30.0 kg/m\(^2\)  
- Intake of alcohol should be restricted to <20-40g/d |
| **Exercise promotion** | - Promote active lifestyle to prevent and treat obesity, hypertension and diabetes  
- Encourage self-directed moderate level physical activity (take the stairs, cycle or walk to work, cycling, swimming, hiking etc.)  
- Emphasize regular moderate-intensity exercise rather than vigorous exercise  
- Achieve cardiovascular fitness (e.g. 30 minutes brisk walking >5 days a week)  
- Maintain muscular strength and joint flexibility |

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i Based on recommendations by the US Preventive Services Task Force.
Prevention of CVD

Principles: The intensity of efforts to prevent CVD depends on the underlying risk of CVD, which can be estimated. 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 patients with a history of CVD.

Assess CVD risk in next 10 years

Advise on diet and lifestyle in all patients
Consider ART modification if 10 year CVD risk ≥20%

Identify key modifiable risk factors

Smoking (see p. 42)

Drug treatment if:
- SBP ≥ 140 or DBP ≥ 90 mmHg
  (especially if 10 year CVD risk ≥ 20%)

Drug treatment if:
- Established CVD or age ≥ 50 and 10 year CVD risk ≥ 20%

Confirm DM and treat with drugs

Drug treatment if:
- Established CVD or type 2 diabetes or 10 year CVD risk ≥ 20%

Target - N/A
Consider to treating with acetylsalicylic acid 75-150mg

Target HbA1C < 6.5-7.0%

Target
- Optimal
- Standard

TC
- ≤ 4 (155)
- ≤ 5 (190)

LDL
- ≤ 2 (80)
- ≤ 3 (115)

Treatment see p. 49

Treatment see p. 51

i Use the Framingham equation; a risk equation developed from HIV populations is under development (see: www.cphiv.dk/tools.aspx). This assessment and the associated considerations outlined in this figure should be repeated annually in all patients under care (see p. 34) to ensure that the various interventions are initiated in a timely way.

ii Options for ART modification include: (1) replace PI/r with NNRTI or by another PI/r known to cause less metabolic disturbances (see p. 38); (2) consider replacing d4T, ZDV or ABC with TDF.

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 greatest reductions in risk of IHD 50% - and this is additive to other interventions. This benefit only becomes apparent up to 5 years from when intervention was first applied.


v 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 p. 51).

vi Evidence for benefit when used in persons without a history of CVD (including diabetics) is less compelling.
### Hypertension: diagnosis and management - 1/2

#### Blood Pressure (mmHg) - Levels

<table>
<thead>
<tr>
<th>Other risk factors and disease history</th>
<th>Normal: SBP 120-129 or DBP 80-84</th>
<th>High normal: SBP 130-139 or DBP 85-89</th>
<th>Grade 1: SBP140-159 or DBP 90-99</th>
<th>Grade 2: SBP 160-179 or DBP100-109</th>
<th>Grade 3: SBP &gt; 180 or DBP &gt; 110</th>
</tr>
</thead>
<tbody>
<tr>
<td>No other factors</td>
<td>Average risk</td>
<td>Average risk</td>
<td>Low added risk</td>
<td>Moderate added risk</td>
<td>High added risk</td>
</tr>
<tr>
<td>No BP intervention</td>
<td>No BP intervention</td>
<td>Lifestyle changes for several months, then possible drug therapy</td>
<td>Lifestyle changes for several months, then drug therapy</td>
<td>Immediate drug therapy and lifestyle changes</td>
<td></td>
</tr>
<tr>
<td>1-2 risk factors</td>
<td>Low added risk</td>
<td>Low added risk</td>
<td>Moderate added risk</td>
<td>Moderate added risk</td>
<td>Very high added risk</td>
</tr>
<tr>
<td>Lifestyle changes</td>
<td>Lifestyle changes</td>
<td>Lifestyle changes for several months, then drug therapy</td>
<td>Lifestyle changes for several months, then drug therapy</td>
<td>Immediate drug therapy and lifestyle changes</td>
<td></td>
</tr>
<tr>
<td>3 or more risk factors or target organ disease or diabetes</td>
<td>Moderate added risk</td>
<td>High added risk</td>
<td>High added risk</td>
<td>High added risk</td>
<td>Very high added risk</td>
</tr>
<tr>
<td>Drug therapy and lifestyle changes</td>
<td>Drug therapy and lifestyle changes</td>
<td>Drug therapy and lifestyle changes</td>
<td>Drug therapy and lifestyle changes</td>
<td>Immediate drug therapy and lifestyle changes</td>
<td></td>
</tr>
<tr>
<td>Associated clinical conditions</td>
<td>High added risk</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
<td>Very high added risk</td>
</tr>
</tbody>
</table>

---

i  SBP = systolic blood pressure; DBP = diastolic blood pressure. Repeated blood pressure measurements should be used for stratification.

ii Recommended lifestyle interventions - see p. 42. Table adapted from J. Hypertension 2003; 21:1779-86.

iii See next page

iv Risk factors include age (>45 years for men; > 55 years for women), smoking, family history of premature CVD.

v Target organ disease: left ventricular hypertrophy, ultrasound evidence of arterial wall thickening, microalbuminuria.

vi Associated clinical conditions: CVD, IHD, renal disease, peripheral vascular disease, advanced retinopathy.

Warning: Caution regarding drug-drug interactions with antihypertensive drugs and ART.
Hypertension: diagnosis and management - 2/2

Choosing drugs for patients newly diagnosed with hypertension

<table>
<thead>
<tr>
<th>&lt; 55 years</th>
<th>55 years or black patients of any age</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(^{iii})</td>
<td>C or D(^{iii})</td>
</tr>
</tbody>
</table>

\[ A + C^{iii} \text{ or } A + D^{iii} \]

\[ A + C + D^{iii} \]

ADD\(^{iv}\) further diuretic therapy (e.g. spironolactone)
OR alpha-blocker (e.g. doxazosin)
OR beta-blocker (e.g. atenolol)

REFER TO SPECIALIST

Diagnostic criteria\(^{i}\)

<table>
<thead>
<tr>
<th></th>
<th>Fasting plasma glucose mmol/L (mg/dl)(^{ii})</th>
<th>Oral glucose tolerance test (OGTT) 2-h value mmol/L (mg/dl)(^{iii})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>( \geq 7.0 ) (126) \text{ OR } \rightarrow )</td>
<td>( \geq 11.1 ) (200) \text{ OR } \rightarrow )</td>
</tr>
<tr>
<td>Impaired glucose tolerance (IGT)</td>
<td>( &lt; 7.0 ) (126) \text{ AND } \rightarrow )</td>
<td>7.8 – 11.0 (140 – 199) \text{ OR } \rightarrow )</td>
</tr>
<tr>
<td>Impaired fasting glucose (IFG)</td>
<td>6.1 – 6.9 (110 – 125) \text{ AND } \rightarrow )</td>
<td>( &lt; 7.8 ) (140) \text{ OR } \rightarrow )</td>
</tr>
</tbody>
</table>

\(^{i}\) As defined by WHO and International Diabetes Federation (2005)

\(^{ii}\) An abnormal finding should be repeated before confirming the diagnosis.

\(^{iii}\) Is recommended in patients with fasting blood glucose 6.1 – 6.9 mmol/L (110 – 125 mg/dL) as it may identify patients with overt diabetes.

Both IGT and IFG increase CV morbidity and mortality, and increase the risk of developing diabetes by 4-6 fold. These patients should be targeted for life style intervention, and their CV risk factors must be evaluated and treated.

Abbreviations + details:

A = ACE inhibitor (e.g. perindopril, lisinopril, ramipril)
(consider angiotensin-II receptor antagonist (e.g. losartan, candesartan) if ACE intolerant)

C = Dihydropyridine calcium-channel blocker (e.g. amlodipine). If not tolerated, verapamil (note: dose with caution with PIs which may increase plasma concentrations leading to toxic reactions), or diltiazem may be used.

D = thiazide-type diuretic

\(^{iv}\) Requirement of 4-5 drugs to manage hypertension requires specialist training

---

Type 2 diabetes: diagnosis and management

Several anti-hypertensive drugs interact with the pharmacokinetics of ART – check always for drug-drug interactions

Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients

Await 2-6 weeks to assess whether target (p. 44) is achieved – if not go to next step.
Dyslipidaemia: management

Principles: Higher LDL-c levels increase risk of CVD and reduction thereof reduces this risk; the reverse is true for HDL-c. Conversely, the CVD risk implications from higher than normal TG levels are less clear, as is the clinical benefit of treating moderate hypertriglyceridaemia; very high TG (>10 mmol/L or >900 mg/dL) may increase risk of pancreatitis although direct evidence is lacking. Diet, exercise, maintaining normal body weight and stopping smoking tend to improve dyslipidaemia; if not effective, consider change of ART and then consider lipid-lowering medication in high-risk patients (see p. 44).

Management of patients with diabetes

Treatment goals: glucose control (HbA1c < 6.5-7.0%), without hypoglycaemia, fasting plasma glucose 4-6 mmol/L (73-110 mg/dL); normal blood lipids and blood pressure <130/80 mmHg (see p. 51 and p. 46). Acetaminophen and (75-150mg) considered in diabetics with elevated underlying CVD.

Consultation with a specialist in diabetology is recommended.

Interventions for treatment of diabetes

Metformin: Always to be considered as the first line agent (500-750 mg/d); increase to max tolerated dose of 2 g/day in 4-6 weeks. Use with PI/r, start with low dose (max: 40 mg). (May worsen lipatrophy)

Ezetimibe: May be considered for non-overweight, if glucose is very high and if lifestyle measures are insufficient. No clinical trial data in HIV+. If used with DRV/r, start with lower dose of pravastatin.

Drugs used to lower LDL-c

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug</th>
<th>Dose</th>
<th>Side effects</th>
<th>ADVISE ON USE OF STATIN TOGETHER WITH ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statin</td>
<td>Atorvastatin</td>
<td>10-80 mg QD</td>
<td>Gastrointestinal symptoms, headache, insomnia, rhabdomyolysis (rare) and toxic hepatitis</td>
<td>Start with low dose (max: 40 mg)</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin</td>
<td>20-80 mg QD</td>
<td></td>
<td>Consider higher dose</td>
</tr>
<tr>
<td></td>
<td>Pravastatin</td>
<td>20-80 mg QD</td>
<td></td>
<td>Consider higher dose</td>
</tr>
<tr>
<td></td>
<td>Rosuvastatin</td>
<td>5-40 mg QD</td>
<td></td>
<td>Consider higher dose</td>
</tr>
<tr>
<td></td>
<td>Simvastatin</td>
<td>10-80 mg QD</td>
<td></td>
<td>Consider higher dose</td>
</tr>
<tr>
<td>Cholesterol uptake</td>
<td>Ezetimibe</td>
<td>10 mg QD</td>
<td>Gastrointestinal symptoms</td>
<td>No known drug-drug interactions with ART</td>
</tr>
</tbody>
</table>

Notes:

- A statin is preferred first-line therapy; different statins have variable intrinsic LDL-c lowering ability. Target levels for LDL-c: see p. 44. In persons where LDL-c targets are difficult to achieve, consult refer to specialist.
- Expected range of reductions of LDL-c: 1.5-2.5 mmol/L (60-100 mmol/L); 0.8-1.5 mmol/L (35-60 mg/dL); 0.2-0.5 mmol/L (10-20 mg/dL).
- The ART drug may inhibit (statin toxicity, ↓dose) or induce (=less effect of statin, ↑dose gradually to achieve expected benefit) the excretion of the statin.
- Exception: If used with DRV/r, start with lower dose of pravastatin.
### Bone disease: diagnosis, prevention and management

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>CHARACTERISTICS</th>
<th>RISK FACTORS</th>
<th>DIAGNOSTIC TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osteopenia</strong></td>
<td>• Reduced bone mass</td>
<td>Consider classic risk factors(i)</td>
<td>• DXA scan</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of fractures</td>
<td>Assess risk score or need for DXA of spine and hip using FRAX® <a href="http://www.shef.ac.uk/FRAX">www.shef.ac.uk/FRAX</a></td>
<td>• Rule out secondary causes if BMD abnormal(v)</td>
</tr>
<tr>
<td></td>
<td>• Asymptomatic until fractures occur</td>
<td>- Only use if (&gt;40) years</td>
<td>• Lateral spine Xrays if low BMD (lumbar and thoracic)</td>
</tr>
<tr>
<td></td>
<td>Common in HIV</td>
<td>- May underestimate risk in HIV patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Up to 60% prevalence of osteopenia</td>
<td>- Consider using HIV as secondary cause of osteoporosis(i)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Up to 10-15% prevalence of osteoporosis</td>
<td>- Assess risk biannually</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Aetiology multifactorial</td>
<td>If not using FRAX® consider DXA in any patient with (\geq 1) of:(ii)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Postmenopausal women</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Men (\geq 50) years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. History of low impact fracture or high risk for falls(iv)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Hypogonadism</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Oral glucocorticoid use (minimum 5mg prednisone equivalent for &gt;3 months)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Measure 25-OH vitamin D in all patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deficiency (\text{ng/ml nmol/L})</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insufficiency (&lt;10 ,&lt;25)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insufficiency (&lt;20 ,&lt;50)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyperparathyroidism, hyperthyroidism, malabsorption, hypogonadism / amenorrhoea, autoimmune disease, diabetes mellitus, chronic liver disease</td>
<td></td>
</tr>
<tr>
<td><strong>Osteoporosis</strong></td>
<td>• Reduced bone mass</td>
<td>• Dietary deficiency</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Increased risk of fractures</td>
<td>• Lack of sunlight exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Asymptomatic until fractures occur</td>
<td>• Dark skin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Common in HIV</td>
<td>• Malabsorption</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Up to 60% prevalence of osteopenia</td>
<td>• Renal phosphate wasting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Up to 10-15% prevalence of osteoporosis</td>
<td>• Risk factors:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Aetiology multifactorial</td>
<td>- Advanced HIV disease (low CD4+ T-cell counts)</td>
<td>• MRI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Glucocorticoid exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Intravenous drug use</td>
<td></td>
</tr>
<tr>
<td><strong>Osteomalacia</strong></td>
<td>• Defective bone mineralisation</td>
<td>• Dietary deficiency</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Increased risk of fractures and bone pain</td>
<td>• Lack of sunlight exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Vitamin D deficiency may cause proximal muscle weakness</td>
<td>• Dark skin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• High prevalence (&gt;80%) of vitamin D insufficiency in some HIV cohorts</td>
<td>• Malabsorption</td>
<td></td>
</tr>
<tr>
<td><strong>Osteonecrosis</strong></td>
<td>• Infarct of epiphyseal plate of long bones resulting in acute bone pain</td>
<td>• Renal phosphate wasting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Rare but increased prevalence in HIV</td>
<td>• Risk factors:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Advanced HIV disease (low CD4+ T-cell counts)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Intravenous drug use</td>
<td></td>
</tr>
</tbody>
</table>

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\(i\) Classic risk factors: older age, female gender, hypogonadism, family history of hip fracture, low BMI (\(\leq 19\) kg/m\(^2\)), vitamin D deficiency, smoking, physical inactivity, history of low impact fracture, alcohol excess (>3 units/day), steroid exposure (minimum prednisone 5mg or equivalent for >3 months)

\(ii\) Although use of HIV as a secondary risk factor in FRAX® has not been validated, including HIV as a secondary cause in a risk assessment will help identify those patients NOT requiring further assessment / DXA

\(iii\) If T-score normal, repeat after 3-5 years in groups 1 and 2, no need for re-screening with DXA in groups 3 & 4 unless risk factors change and only rescreen group 5 if steroid use ongoing


\(v\) Hyperparathyroidism, hyperthyroidism, malabsorption, hypogonadism / amenorrhoea, autoimmune disease, diabetes mellitus, chronic liver disease
### Management of osteoporosis and vitamin D deficiency

#### Vitamin D replacement
- Suggested regimens for vitamin D replacement:
  - 800-2,000 IU daily
  - Can be provided according to national recommendations / availability of preparations (oral and parenteral formulations)
  - Aim to increase serum 25-OH vitamin D >50nmol/L and maintain serum PTH levels within normal range
  - Combine with calcium where there is insufficient dietary calcium intake

#### Reducing risk of fractures
- Decrease falls by addressing falls risks
- Ensure sufficient dietary calcium (1-1.2g daily) and vitamin D (800-2,000 IU daily) intake
- Refer to national / regional guidelines on treatment of osteoporosis
  - if no guidelines available consider bisphosphonate treatment in all osteoporotic postmenopausal women and men > 50 years old and those with a history of fragility fracture
  - use bisphosphonate with calcium and vitamin D replacement
  - no significant interactions between bisphosphonates and antiretrovirals
- If on TDF consider renal bone disease ([p. 60](#))
- In complicated osteoporotic cases (e.g. young men, premenopausal women, recurrent fracture despite bone protective therapy) refer to endocrinologist
- If osteoporotic and on bisphosphonate treatment, repeat DXA after 2 years

---

i Bisphosphonate treatment with either of: Alendronate 70 mg once weekly po; Risedronate 35 mg once weekly po; Ibandronate 150mg oral monthly or 3mg i.v. every 3 months; Zoledronate 5 mg i.v. once yearly
Depression: diagnosis and management

Significance
- Higher prevalence of depression in HIV-infected patients (20-40% versus 7% in general population) due to stigma, sexual dysfunction, side effects of cART, co-morbidities
- Significant disability associated with depression

Screening and diagnosis

<table>
<thead>
<tr>
<th>Who?</th>
<th>How to screen?</th>
<th>How to diagnose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk population</td>
<td>Screen every 1-2 years</td>
<td>Symptoms – evaluate regularly with screening questions</td>
</tr>
<tr>
<td>Positive history of depression in family</td>
<td>Two main questions: 1. Did you feel frequently depressed, sad and without hope in the last months? 2. Were you uninterested in undertaking something in the last month?</td>
<td><strong>A.</strong> At least 2 weeks of depressed mood OR <strong>B.</strong> loss of interest OR <strong>C.</strong> diminished sense of pleasure</td>
</tr>
<tr>
<td>Depressive episode in personal history</td>
<td>Special symptoms in men: - Stressed, burn out, angry outbursts, coping through work or alcohol - Rule out organic cause (hypothyroidism, Addison’s disease, non-HIV drugs, Vit B12 deficiency)</td>
<td>PLUS 4 of 7 of the following: 1. Weight change of ≥ 5% in one month or a persistent change of appetite, 2. insomnia or hypersomnia in most days, 3. changes in psychomotor state, 4. fatigue, 5. feelings of guilt and worthlessness, 6. diminished concentration and decisiveness, 7. suicidal ideation or a suicide attempt</td>
</tr>
</tbody>
</table>

Management

<table>
<thead>
<tr>
<th>Degree of depression</th>
<th>Number of symptoms (see diagnosis: A-C + 1-7)</th>
<th>Treatment</th>
<th>Refer to expert</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>&lt; 4</td>
<td>problem focused consultation, consider antidepressive treatment, recommend physical activity</td>
<td>• Severe depression • Depression not responding to treatment • Suicidal ideation • Complex situations such as drug addiction, anxiety disorders, personality disorders, dementia, acute severe life event</td>
</tr>
<tr>
<td>Mild</td>
<td>4</td>
<td>start antidepressive treatment, consider referral</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>5-6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Degree of depression: Maximum effectiveness reached after 10 weeks, one episode usually 6 months treatment; optimize treatment, i.e. increase dosage or change drug if side effects; partial or no response after 4-6 weeks of antidepressant treatment at adequate dosage: reassess diagnosis; depression in persons ≥ 65 years generally requires relatively low doses of antidepressants; preferred antidepressants for HIV-infected patients: sertralin, paroxetine, venlafaxine, citalopram, mirtazapin, but also other antidepressants may be given. Citalopram may be preferred because of low interactions. For classification, doses, safety and side effects of antidepressants, see [www.europeanaidsclinicalsociety.org/Guidelines/index.htm](http://www.europeanaidsclinicalsociety.org/Guidelines/index.htm). For interactions with antidepressants see [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org) and [www.europeanaidsclinicalsociety.org/Guidelines/index.htm](http://www.europeanaidsclinicalsociety.org/Guidelines/index.htm)
Hyperlactataemia: diagnosis, prevention and management

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Prevention / Diagnosis</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Use of ddl&gt; d4T &gt; ZDV</td>
<td>Avoid d4T + ddl combination</td>
<td>• Hyperlactataemia: unexplained nausea, abdominal pain, hepatomegaly, elevated ALT and/or AST, weight loss</td>
</tr>
<tr>
<td>• HCV/HBV co-infection</td>
<td>Routine monitoring of serum lactate levels not recommended - does not predict risk of lactic acidosis.</td>
<td></td>
</tr>
<tr>
<td>• Use of ribavirin</td>
<td>Measurement of serum lactate, bicarbonate &amp; arterial blood gases+pH indicated in case of symptoms suggestive of hyperlactataemia</td>
<td></td>
</tr>
<tr>
<td>• Liver disease</td>
<td>Close monitoring for symptoms if &gt; 1 risk factor</td>
<td></td>
</tr>
</tbody>
</table>

Management of hyperlactataemia

<table>
<thead>
<tr>
<th>Serum Lactate (mmol/L)</th>
<th>Symptoms</th>
<th>Action</th>
</tr>
</thead>
</table>
| >5                    | Yes/No   | Repeat test under standardized conditions to confirm & obtain arterial pH and bicarbonate
|                        |          | if confirmed, exclude other causes - Arterial pH ↓ and/or bicarbonate ↓: Stop NRTIs - Arterial pH and/or bicarbonate normal: Consider switch from high to low risk NRTI & monitor carefully OR Stop NRTIs |

| 2-5                   | Yes      | Exclude other causes; if none found: watchfully follow up OR consider switch from high to low risk NRTI OR Stop NRTI |
|                       |          | |
| 2-5                   | No       | Repeat test - if confirmed: watchfully follow up |
| <2                    | None     | |

Kidney disease: diagnosis, prevention and management

Management of lactic acidosis (irrespective of serum-lactate level):
Admit patient. Stop NRTIs. Provide intravenous fluids. Vitamin supplementation can be used (vitamin B complex forte 4 ml bid, riboflavin 20 mg bid, thiamine 100 mg bid; L-carnitine 1000 mg bid), although benefit is unproven
**Lipodystrophy: prevention and management**

**Lipoatrophy**
- **Prevention**
  - Avoid d4T and ZDV or pre-emptively switch away from them

**Lipohypertrophy**
- **Prevention**
  - No proven strategy
  - Weight gain expected with effective ART reflecting “healthy” response
  - Weight reduction or avoidance of weight gain may decrease visceral adiposity
  - Avoid inhaled fluticasone with some PI

**Management**
- **Diet and exercise** may reduce visceral adiposity; limited data, but possibly reduction of visceral adipose tissue and improvement in insulin sensitivity and blood lipids, especially in obesity associated with lipohyperthrophy
- **Pharmacological interventions to treat lipoatrophy** have not been proven to provide long-term effects and may introduce new complications
  - Growth hormone: decreases visceral adipose tissue, may worsen subcutaneous lipoatrophy, may worsen insulin resistance
  - Metformin: decreases visceral adipose tissue in insulin resistant persons, may worsen subcutaneous lipoatrophy
  - Surgical therapy can be considered for localized lipomas/buffalo humps

---

### Screening for tenofovir renal toxicity

<table>
<thead>
<tr>
<th>Screening</th>
<th>Frequency</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) eGFR (aMDRD)</td>
<td></td>
<td>Consider stopping tenofovir if:</td>
</tr>
</tbody>
</table>
| b) serum phosphate | | • Confirmed significant hypophosphatemia of renal origin and no other cause
| c) urine dipstick analysis | | • Progressive decline in eGFR and no other cause
| | | • Confirmed proximal renal tubulopathy / Renal Fanconi syndrome |

Prior to starting tenofovir, after 2-4 and 12 weeks; then every 3-6 months

---

**Screening for tenofovir renal toxicity**

<table>
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<tr>
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<td>serum phosphate</td>
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<tr>
<td>urine dipstick analysis</td>
<td></td>
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</tr>
</tbody>
</table>

---

- **Screening**
  - a) eGFR (aMDRD)
  - b) serum phosphate
  - c) urine dipstick analysis

- **Measure UP/C if**
  - • decline in eGFR (deterioration >10 ml/min compared to pre-tenofovir level & eGFR<90 ml/min)
  - • confirmed hypophosphatemia
  - • if urine dipstick proteinuria ≥ 1+

- **Frequency**
  - Prior to starting tenofovir, after 2-4 and 12 weeks; then every 3-6 months

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**PREVENTION AND MANAGEMENT OF NON-INFECTIOUS CO-MORBIDITIES IN HIV**

**Screening for tenofovir renal toxicity**

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Prior to starting tenofovir, after 2-4 and 12 weeks; then every 3-6 months

---

**Screening for tenofovir renal toxicity**

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<td>• Confirmed proximal renal tubulopathy / Renal Fanconi syndrome</td>
</tr>
</tbody>
</table>

Prior to starting tenofovir, after 2-4 and 12 weeks; then every 3-6 months
Does the patient take any potentially hepatotoxic medication/herbal product/illicit drug?

- **YES**
  - Stop the drug or replace if feasible; if ARV potentially involved, do not impair efficacy of the regimen
  - Disappearance of liver abnormalities
  - Adapt treatment regimen accordingly

- **NO**

Can you identify recent/chronic alcohol intake?

- **YES**
  - Recommend stopping alcohol intake and follow ALT/AST (4-8 weeks may be needed for improvement)

- **NO**

**STEP 1**

**STEP 2**

**Exclude viral hepatitis**

- Test for:
  - Hepatitis A (HAV IgM), if status unknown or patient non-immune
    - **POS**: Manage accordingly
  - Acute/chronic HBV (HbsAg) or HCV (HCV-Ab), if status unknown or patient non-immune/negative
    - **POS**: refer to Guidelines on hepatitis

**STEP 3**

**Identify other causes of increased ALT/AST**

- Steatosis
- NASH (metabolic syndrome diabetes)
- HCV associated steatosis

- Nodular regenerative hyperplasia (more frequent in HIV patients)
- Other viral diseases (CMV, EBV)

- Non-hepatic causes of increased ALT/AST
  - coeliac disease
  - myopathy
  - portal hypertension
  - heart failure

- Rare disorders
  - autoimmune hepatitis
  - Hemochromatosis
  - Wilson’s disease
  - Alpha-1 anti-trypsin deficiency

**IN ALL CASES PERFORM:**

- liver ultrasonography
- liver biopsy

**Cirrhotic patients**

- Use clinical (Child Pugh) and pathological (METAVIR) scores to monitor the degree of liver insufficiency (MELD to be used if the patient is listed for liver transplant)
- Perform alpha foetoprotein (α FP) and ultrasound every 6 months
  - Consider liver MRI if:
    - nODULES AT ULTRASOUND
    - α FP > 200ng/ml
    - If α FP abnormal exclude seminoma (by ultrasound of testes)

- Perform oesophago-gastroscopy every 2 years.
  - If varices present, start beta blockers – ligation of varices only in case of hemorrhage or intolerance to beta-blockers.

- For management of liver decompensation refer to guidelines for general population and to hepatologist

**PREVENTION AND MANAGEMENT OF NON-INFECTIOUS CO-MORBIDITIES IN HIV**
Neurocognitive impairment: diagnosis and management

Any HIV-infected person complaining of disturbances in his/her memory (comprehension, clarity or speed) should be evaluated extensively, including neurological examination, neuropsychological assessment, cerebrospinal examination and imaging of the brain.

- **Patients without such symptoms that should be targeted for screening**
  - Uncontrolled HIV infection (detectable plasma HIV RNA)
  - Use of antiretroviral agents with limited CNS penetration
  - Low CD4 nadir (<200 cells/mm3)
  - Ongoing depression

- **Screening tool**
  - International HIV Dementia Scale (IHDS)i

- **Interventions if neurocognitive impairment detected:**
  - If patient is not on ART:
    - Consider initiation of ART in which at least 2 drugs penetrate CNSii
    - Consider risk for antiretroviral resistance if prior virological failure
  - If patient is already on ART:
    - Consider changing antiretroviral treatment to active drugs with better CNS penetration
    - Consider genotyping of plasma and CSF HIV RNA whenever feasible prior to changing ART

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i See [www.europeanaidsclinicalsociety.org/Guidelines/index.htm](http://www.europeanaidsclinicalsociety.org/Guidelines/index.htm) for components of the IHDS scale

ii See [www.europeanaidsclinicalsociety.org/Guidelines/index.htm](http://www.europeanaidsclinicalsociety.org/Guidelines/index.htm) for list of drugs with favourable and poor CNS penetration