Aging with HIV

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Aging with HIV

- Increased life expectancy on ARVs. However, life expectancies still shorter than for general population
  - Especially for low CD4 and/or salvage regimens

- What is the impact of increased life expectancy on comorbidity prevalence?

- The impact of increased comorbidity on
  - Timing of ARV initiation
  - Appropriateness of primary care practice guidelines (e.g., colorectal cancer screening). No systematic method to predict whether guidelines developed on general population should apply to individuals with HIV

Braithwaite RS Arch Intern Med 2007;167:2361-5
Aging and HIV

- ART may produce chronic adverse effects
  - CHD risk increased
  - Metabolic abnormalities more common
- ART may not protect from CANCER with AGE
  - Esophageal / Lung / Rectal (HPV) / Renal / Liver
- Conditions seen at earlier age
  - Osteoporosis/ hypogonadism
Age Disproportionately Affects Care Resources

- 80% have at least one chronic disease
- Most common conditions
  - Arthritis, hypertension, hearing impairment, heart disease, vision impairment, orthopedic disabilities, diabetes
- The elderly make up 13% of the population but
  - utilize 30% of the prescription drugs
  - 40% of the OTC medications
- On average the elderly take 3 times more drugs than younger counterparts
- The elderly suffer 2-3 times the rate of adverse drug reactions
  - Most explainable to changes in renal and hepatic function and changes in body composition
Payoff Time

- Payoff Time = Minimum time until incremental benefits > incremental harms
  - Applies to any guideline where harms are short-term and benefits are long-term
    - Colorectal cancer screening (CRC)
      - Will vary by guideline and by patient population
- Payoff time can be compared to life expectancy
  - If death likely before payoff time, guideline not advised
  - If death unlikely before payoff time, guideline advised

Braithwaite RS Arch Intern Med 2007;167:2361-5; Braithwaite RS Med Care 2009 Jun;47(6):610-7
Compare payoff time to life expectancy

Case 1: 60 year-old HIV+ male on salvage ARV, CD4 count 46 severe COPD and HCV

- Payoff time for Case 1 is 7.3 years
- Life Expectancy for Case 1 is 5.1 years
- Because life expectancy is less than payoff time (minimum time until benefits exceed harms), Case 1 is unlikely to benefit from colorectal cancer screening

Braithwaite RS Arch Intern Med 2007;167:2361-5; Braithwaite RS Med Care 2009 Jun;47(6):610-7
Compare payoff time to life expectancy

Case 2: 60 year-old HIV+ female on 1st line ARV, CD4 count 392, DM

- Payoff time for Case 2 is 5.7 years
- Life Expectancy for Case 2 is 15.1 years
- Because life expectancy is more than payoff time (minimum time until benefits exceed harms), Case 2 is likely to benefit from colorectal cancer screening
Braithwaite Conclusion

- Payoff time is quantitative objective framework for predicting who will benefit
- CRC screening may not always be appropriate for HIV+ individuals
  - Low CD4
  - Salvage ARV
- May simultaneously improve quality of care and reduce resource expenditures
- May impact quality measures
Figure 1 Prevalence of neoplastic lesions in the HIV-infected subjects and control subjects. Note: These categories are not mutually exclusive since advanced neoplasia includes all patients with adenomas $\geq 10$ mm, those with adenomas of any size with villous histology or high-grade dysplasia, and individuals with adenocarcinoma.

Prostate Cancer: Risk?

- Association between HIV status and positive prostate biopsy in a study of US veterans (Atlanta)
  - Over a 5.5 year period, patients referred to the urology clinic (elevated PSA or abnormal DRE): markedly higher rate of prostate cancer in HIV patients when compared to HIV-negative or HIV-unknown population


- In men receiving HAART, their age, PSA levels, clinical presentation, management, and outcome from treated prostate carcinoma does not appear to be significantly altered by HIV status.

  Pantanowitz L, BJU Int. 2008 June
Geriatric Periodic Health Exam

• An assessment that is aimed at preventing, detecting and controlling specific conditions or risk factors

• The GPHE specifically addresses those over age 65 and allows detection of the common health issues that require further assessment and/or early intervention

• Targets conditions like frailty, sensory loss, cognitive impairment, depression, polypharmacy among others

• Opportunity for screening for “risky” behaviors (smoking, obesity, nutrition, medications)

• Self administered. Initial screen takes less than 30 minutes
GPHE Summary of Benefits from Chronic Disease Management

• Chronic diseases, if left untreated and undiagnosed, such as DM and depression are causally related to other diseases

• 90% DM and 80% CHD can be avoided with good nutrition, regular exercise, smoking cessation and stress management

• 20% reduction in cancer rates with daily diets high in vegetables and fruit

• Mammography screening for 70% of women aged 50-69 would prevent 1/3 of breast cancers over a 10 yr period

• 90% of cervical cancer is preventable with regular screening

• FOBT in those aged 50-75 could reduce colorectal cancer mortality by 15-33%
Develop an HIV GPHE?

• Interprofessional screening form, patient tracking form, health questionnaire and patient information on all specific conditions
• Web tools for fracture risk and cardiac risk
• Early identification of chronic disease (case finding)
  – Diabetes
  – Thyroid Disease
  – Cancer
  – Asthma/COPD
  – Obesity
  – Coronary Heart Disease
  – Stroke
  – Arthritis
  – Osteoporosis
D:A:D Study: Is the Framingham Risk Estimation Valid in HIV-Infected Patients?

Observed and predicted MI rates according to ART exposure
(D:A:D Study; n=23,468)

Incidence of MIs is low: 345 over 94,469 patient-years’ follow-up (3.7/1,000 patient-years)

- **Observed rates**
- **Best estimate of predicted rates**

Using the Framingham Risk Score

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Units</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male or Female</td>
<td>M</td>
</tr>
<tr>
<td>Age</td>
<td>Years</td>
<td>46</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>mg/dL</td>
<td>200</td>
</tr>
<tr>
<td>HDL</td>
<td>mg/dL</td>
<td>24</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>mmHg</td>
<td>118</td>
</tr>
<tr>
<td>Treatment for hypertension (only if SBP &gt;120)</td>
<td>Yes or No</td>
<td>N</td>
</tr>
<tr>
<td>Current smoker</td>
<td>Yes or No</td>
<td>Y</td>
</tr>
</tbody>
</table>

Risk Factor Units

 Treatment for hypertension

Current smoker

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>0% - 15%</td>
</tr>
<tr>
<td>Moderate Risk</td>
<td>15% - 25%</td>
</tr>
<tr>
<td>High Risk</td>
<td>25% - 30%</td>
</tr>
</tbody>
</table>

IDSA Guidelines for Managing Lipid Disorders and CVD Risk in Patients Receiving HAART

- Obtain fasting lipid profile prior to starting antiretrovirals and within 3-6 months of starting new regimen
- Count number of CHD risk factors and determine level of risk. If ≥2 risk factors, perform a 10-year risk calculation
- Intervene for modifiable nonlipid risk factors, including diet and smoking
- If above the lipid threshold based on risk group despite vigorous lifestyle interventions:
  - Consider lipid-lowering drugs
    - Serum LDL-C ≥100mg/dL or TGs 200-500 mg/dL with elevated non-HDL-C: STATIN
  - Consider altering antiretroviral therapy
    - Serum TGs >500 mg/dL: FIBRATE

Epidemiology: MIs and Strokes Among Californians With and Without HIV

- Kaiser Permanente
- >35,000 HIV+ patients, >6 million HIV-individuals
- Incidence of MIs and strokes between 1996 and 2008

Hurley L, et al. 16th CROI, Montreal 2009, #710
Why the Decrease in CV Event Incidence?

Better drugs  More attention to lipids

Figure 3. Changes in prescribing patterns over time that may lead to improved lipid profiles

Figure 4. Percent of KPNC HIV patients taking lipid lowering therapy by ARV status: 1996 - 2008

Hurley L, et al. 16th CROI, Montreal 2009, #710
Meta-analysis: Prevalence of Osteoporosis in HIV-Infected Patients vs Uninfected Controls

Overall prevalence of osteoporosis in HIV-infected patients = 15%

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiel (2004)</td>
<td>5.03 (1.47,17.27)</td>
</tr>
<tr>
<td>Brown (2004)</td>
<td>4.26 (0.22,82.64)</td>
</tr>
<tr>
<td>Bruera (2003)</td>
<td>4.51 (0.26,79.27)</td>
</tr>
<tr>
<td>Dolan (2004)</td>
<td>2.11 (0.54,8.28)</td>
</tr>
<tr>
<td>Huang (2002)</td>
<td>3.52 (0.15,81.92)</td>
</tr>
<tr>
<td>Knobel (2001)</td>
<td>5.13 (1.80,14.60)</td>
</tr>
<tr>
<td>Loiseau-Peres (2002)</td>
<td>4.28 (0.46,39.81)</td>
</tr>
<tr>
<td>Madeddu (2004)</td>
<td>29.84 (1.80,494.92)</td>
</tr>
<tr>
<td>Tebas (2000)</td>
<td>3.40 (0.19,61.67)</td>
</tr>
<tr>
<td>Teichman (2003)</td>
<td>17.41 (0.97,313.73)</td>
</tr>
<tr>
<td>Yin (2005)</td>
<td>2.37 (1.09,5.16)</td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>3.68 (2.31,5.84)</td>
</tr>
</tbody>
</table>

US data suggest it's cost-effective to treat if 10-year probability of hip fx is ≥3% or major osteoporotic fx is ≥20%  


*1 unit = 8 g alcohol ~ 1/2 pt. beer ~ glass wine
Evaluation for Secondary Causes of Osteoporosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-OH vitamin D</td>
<td>Vitamin D deficiency</td>
</tr>
<tr>
<td>Free/total testosterone; menstrual hx</td>
<td>Hypogonadism</td>
</tr>
<tr>
<td>Serum calcium, phosphate (iPTH)</td>
<td>Hyperparathyroidism, phosphate wasting</td>
</tr>
<tr>
<td>24 hr urine calcium</td>
<td>Idiopathic hypercalciuria</td>
</tr>
<tr>
<td>TSH</td>
<td>Subclinical hyperthyroidism</td>
</tr>
</tbody>
</table>
### 25-OH Vitamin D Levels

<table>
<thead>
<tr>
<th>Levels</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 ng/ml</td>
<td>Deficiency</td>
</tr>
<tr>
<td>20-29 ng/ml</td>
<td>Insufficiency</td>
</tr>
<tr>
<td>30-60 ng/ml</td>
<td>Preferred</td>
</tr>
</tbody>
</table>

n = 57 HIV+ pts at MGH:
- 37% moderate deficiency (10-20 ng/ml)
- 10% severe deficiency (<10 ng/ml)

Osteoporosis Recommendations

- Low bone mass and osteoporosis are prevalent in HIV-infected patients
- No consensus/guidelines for screening or treatment of HIV-infected patients
  - May be reasonable to screen postmenopausal women and men > age 50; possibly those 40-50 years with risk factors
  - Calcium/vitamin D, smoking cessation, weight-bearing exercise, bisphosphonates, fall prevention

Glesby M. The NY Course 2009
Summary

- ARV has dramatically increased survival
  - Is HIV just another chronic disease, like diabetes?
- Increased survival has increased prevalence of non-HIV-related comorbidities
- Comorbidities may occur at Younger Age in HIV
- Increasing evidence favors starting HAART earlier
  - Benefit may be lower with age or comorbidity
- Primary care screening guidelines are often applicable to HIV patients
  - *Payoff time* may help to determine when particular guidelines are applicable
  - Caution we do not under screen because of wrong assumptions
  - Need to implement general medical screening and treat conditions identified