HIV in Primary Care? Implications of the ACA on HIV care delivery—
And some HIV basics for PCPs.

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Associate Professor
General Internal Medicine
Disclosures

• No financial disclosures
• I agree with the basic tenets of the Affordable Care Act (ACA)
• I’m pretending that I know what’s going to happen with the ACA
Outline

• Case presentation
• Why HIV may become a Primary Care condition
• Antiretroviral basics
  – HIV basic science and epidemiology
  – Treatment Naïve patients
Case Presentation

• 41 y/o male who has had HIV for about 8 – 9 years and has never been on therapy.
• Meds: Acyclovir 400 bid
• PE: 36.6, 121/83, 67. Exam is unremarkable
• Labs:
  – CD4 700 (28%)
  – VL 47,100
  – Liver and kidney function are normal
Why HIV may become a primary care condition

- HIV treatment is very effective and much less complicated than in the past.

- Decreased funding of the Ryan White Care Act.
Why HIV may remain a subspecialist condition

- Adequate numbers of HIV specialists in urban areas.

- Little enthusiasm among HIV specialists for turning over care to PCPs.
Why HIV may become predominantly a primary care condition

Affordable Care Act and the AIDS Education and Training Center Program (AETC) Support for Comprehensive HIV Care

**Affordable Care Act (ACA) Attributes**
- Integration of HIV care into primary care
- Promotion of Patient-Centered Medical/Health Homes
- Accountable Care Organization promotion of quality care
- Increased insured rate among persons living with HIV (PLWH)
- Decrease in new HIV infections as more PLWH are engaged in care ("prevention with positives")

**Vulnerable Populations**
- Individuals/Families Living in Poverty
- Gay, Bisexual, & Other Men-Who-Have-Sex-With-Men
- Transgender
- Women
- Immigrants
- Medically Underserved
- Homeless/Unstably Housed
- Mentally Ill/Substance using
- Adolescents/Young Adults
- Low Health/Numerical/Reading Literacy

**Workforce Concerns**
- National Healthcare provider shortage
- Aging HIV expert provider workforce
- PLWH are living longer, but the chronic healthcare needs of PLWH have expanded
- Increased need for more HIV counseling and testing, and care services for identified PLWH and those at high-risk of new infection
- Healthcare Inequities & Disparities

The Ryan White Care Act
The Ryan White Care Act

• “…for individuals living with HIV/AIDS who have no health insurance, have insufficient health care coverage, or lack financial resources to get the care they need…”


Federal Funding for the Ryan White Program, FY 1991-2012

http://kff.org/hivaids/fact-sheet/the-ryan-white-program/
HIV Care Going Forward

• The Ryan White Care Act is maintained
  – HIV care remains a subspecialty condition.

• The Ryan White Care Act is reduced.
  – HIV care remains mostly a subspecialty condition, *but* without the additional support non-HIV specialists.

• The Ryan White Care Act is eliminated.
  – HIV care becomes mostly a primary care condition.
Why can’t HIV specialist still see their patients without the extra funds?

• HIV in the U.S. 2009
  – 24.8% Private insurance
  – 53.4% Public (Medicare/Medicaid)
  – 18.9% no insurance
  – 43.8% at or below the federal poverty line
  – 49.4% no education beyond high school

MMWR 2014;63(5):1-28
Questions thus far...
Antiretroviral basics for PCPs

- HIV basic science and epidemiology
- Treatment naïve individuals
  - No drug resistance
  - Normal renal and liver functions
HIV Basic Science

1. Fusion of HIV to the host cell surface
2. HIV RNA, reverse transcriptase, integrase, and other viral proteins enter the host cell.
3. Viral DNA is formed by reverse transcription
4. Viral DNA is transcribed across host nucleus and integrates into the host DNA.
5. New viral RNA is used as genomic RNA and to make viral proteins.
6. New viral RNA and proteins move to the cell surface and a new, immature HIV forms.
7. The virus matures by protease releasing individual HIV proteins.

http://ryanshivforum.files.wordpress.com/2013/04/hivreplicationcycle.gif
HIV Basic Science

- $\approx 10,000,000,000$ new virions per day
- $\approx 3,000,000,000$ nucleotide mutation per day
- $\approx 10,000$ drug resistant virions per day

Science 1996;271(5255):1582-1586
J Virology 1995;69(8):5087-5094
HIV Basic Science

Nature 1995;373(12):117-122
HIV Epidemiology

Trends in Annual Age-Adjusted* Rate of Death Due to HIV Infection, United States, 1987–2010

Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
*Standard: age distribution of 2000 US population

Case Presentation

• 41 y/o male with HIV for 8 – 9 years who has never been on therapy.
  – CD4 700 (28%)
  – VL 47,100
  – No HIV drug resistance mutations on genotype
  – Liver and kidney function are normal
Question 1:

Antiretroviral therapy should be started...

a. When the CD4 count drops below 500.
b. When the CD4 count drops below 350.
c. As soon as the patient is ready, regardless of CD4 count.
Question 1:

Antiretroviral therapy (ART) is recommended *for all HIV infected individuals* to reduce the risk of disease progression (AI to BIII) and *to prevent transmission of HIV (AI to Alll).*

http://aidsinfo.nih.gov/guidelines
AIDS 2009;23:1397-1404
Lancet 2010;375(9731):2092-2098
NEJM 2011;365(6):493-505
Baseline testing

• HIV viral load
• HIV genotype
• CD4 count

• CBC with diff
• CMP
• Lipid panel

• Urinalysis

• HAVAb, HBsAg, HBsAb, HCVAb
• TPPA (Syphilis), GC/Chlamydia

• Pregnancy test (women of childbearing age)

http://aidsinfo.nih.gov/guidelines
Baseline testing—Our patient

HIV GENOTYPING PLUS

Reverse Transcriptase Mutations: SEE BELOW

NRTI Resistance Mutations: None
Nucleoside and Nucleotide RT Inhibitors:
Abacavir (ABC) No evidence of resistance
Didanosine (DDI) No evidence of resistance
Lamivudine (3TC)/FTC No evidence of resistance
Stavudine (D4T) No evidence of resistance
Zidovudine (AZT) No evidence of resistance
AZT+3TC (CBV) No evidence of resistance
Tenofovir (TDF) No evidence of resistance
NNRTI Resistance Mutations: A98S
Non-Nucleoside RT Inhibitors:
Delavirdine (DLV) No evidence of resistance
Efavirenz (EFV) No evidence of resistance
Nevirapine (NVP) No evidence of resistance
Etravirine (ETR) No evidence of resistance
Rilpivirine (RPV) No evidence of resistance
Protease Mutations: L63H
Protease Inhibitors:
Fosamprenavir (FPV/APV) No evidence of resistance
Indinavir (IDV) No evidence of resistance
Lopinavir/RTV (LPV) No evidence of resistance
Nelfinavir (NFV) No evidence of resistance
Saquinavir (SQV) No evidence of resistance
Atazanavir (ATV) No evidence of resistance
Tipranavir (TPV) No evidence of resistance
Darunavir (DRV/TMC114) No evidence of resistance
HLA B5701-Associated Mutations: V245T

Please call CLINICAL LAB - MOLECULAR DIAGNOSTICS
LAB @ 720–848–6892 for test interpretation if needed.
Non-Baseline testing—High Level Resistance

NUCLEOSIDE and NUCLEOTIDE RT INHIBITORS [NRTI]:
- Abacavir [ABC] HIGH LEVEL RESISTANCE
- Didanosine [Ddi] HIGH LEVEL RESISTANCE
- Lamivudine [3TC] LOW LEVEL RESISTANCE
- Stavudine [D4T] HIGH LEVEL RESISTANCE
- Zalcitbine [DDC] INTERMEDIATE LEVEL RESISTANCE
- Zidovudine [AZT] HIGH LEVEL RESISTANCE
- AZT+3TC [CBV] HIGH LEVEL RESISTANCE
- Tenofovir [TNV] HIGH LEVEL RESISTANCE

Nonnucleoside Reverse Transcriptase Mutations: K101E, Y181C, G190A
NONNUCLEOSIDE RT INHIBITORS [NNRTI]:
- Delavirdine [DLV] HIGH LEVEL RESISTANCE
- Efavirenz [EFV] HIGH LEVEL RESISTANCE
- Nevirapine [NVP] HIGH LEVEL RESISTANCE

- Amprenavir [APV] HIGH LEVEL RESISTANCE
- Indinavir [IDV] HIGH LEVEL RESISTANCE
- Lopinavir [RTV] [LPV] HIGH LEVEL RESISTANCE
- Nelfinavir [NFV] HIGH LEVEL RESISTANCE
- Ritonavir [RTV] HIGH LEVEL RESISTANCE
- Saquinavir [SQV] HIGH LEVEL RESISTANCE
Baseline testing—Our patient

**HIV GENOTYPING PLUS**

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</table>
Question 2:

The most appropriate antiretroviral (ART) regimen would be:

a. Tenofovir/Emtricitabine (TNF/FTC) + Dolutegravir (DTG)
b. TNF/FTC + Efavirenz (EFV)
c. TNF/FTC + Atazanavir/Ritonavir (ATZ/r)
d. TNF/FTC + Darunavir/Ritonavir (DRV/r)
e. TNF/FTC + Elvitegravir/Cobicistat (EVG/cobi)
f. TNF/FTC + Raltegravir (RAL)
g. TNF/FTC + Rilpivirine (RPV)
h. Abacavir/Lamivudine (ABC/3TC) + DTG
i. ABC/3TC + EFV
j. ABC/3TC + ATZ/r
k. Any of the above would be appropriate

http://aidsinfo.nih.gov/guidelines
Patterns in the word soup...

- All regimens have one of two fixed dose nucleoside backbone combinations

<table>
<thead>
<tr>
<th>Name</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tenofovir/Emtricitabine (Truvada)</strong></td>
<td>One pill a day, no food requirement</td>
<td>Potential renal toxicity</td>
</tr>
<tr>
<td></td>
<td>Superior virologic compared with Epzicom</td>
<td>Potential decrease BMD</td>
</tr>
<tr>
<td></td>
<td>Active against Hepatitis B</td>
<td></td>
</tr>
<tr>
<td><strong>Abacavir/Lamivudine (Epzicom)</strong></td>
<td>One pill a day, no food requirement</td>
<td>Hypersensativity reaction →</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ HLA-B57 before starting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potential increased risk of CV disease</td>
</tr>
</tbody>
</table>

http://aidsinfo.nih.gov/guidelines
Patterns in the word soup...

• Pick your third agent (unless there’s also a fourth...)
  
c. TNF/FTC + Atazanavir/*/Ritonavir* (ATZ/r)
d. TNF/FTC + Darunavir/*/Ritonavir* (DRV/r)
e. TNF/FTC + Elvitegravir/*/Cobicistat* (EVG/cobi)
k. ABC/3TC + Atazanavir/*/Ritonavir* (ATZ/r)

http://www.thebody.com/content/art42268.html
# Preferred Regimens—Integrase Inhibitors

http://aidsinfo.nih.gov/guidelines

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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</table>
| Truvada 1 qd* + Dolutegravir (Tivicay) 50 mg qd | • No food requirements  
• Minimal side effects  
• Minimal drug interactions  
• High barrier to resistance | • Two pills instead of one  
• Al, Ca, Mg antacids can ↓ absorption  
• Annual cost = $35,405  
• New, so not a long track record |
| Truvada 1 qd + Raltegravir (Isentress) 400 mg po bid | • No food requirements  
• Minimal side effects  
• Minimal drug interactions | • Raltegravir is twice a day  
• Al, Mg antacids can ↓ absorption.  
*CaCO3 is OK.*  
• Annual cost = $34,703 |
| [Truvada + Elvitegravir + Colbicistat (Stribild)] 1 po qd | • One pill a day | • Food requirement  
• Al, Mg antacids can ↓ absorption.  
• Cr Cl > 70  
• CYP3A4 Inhibitor--↑ drug interactions  
• Annual cost $ 35,384 |

Note: Resistance testing for integrase inhibitors not part of standard genotype.

*Abacavir/Lamivudine/Dolutegravir (Triumeq) FDA approved 08/23/14
# Preferred Regimens—Protease Inhibitors

http://aidsinfo.nih.gov/guidelines

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| **Truvada 1 qd** + **Darunavir (Prezista)** 800 mg qd + **Ritonavir (Norvir)** 100 mg po qd | • Once daily dosing  
  • Very high barrier to resistance       | • Three pills  
  • Should be taken with food  
  • GI side effects  
  • CYP3A4 Inhibitor: ↑ drug interactions  
  • Annual cost $ 38,973 |
| **Truvada 1 qd** + **Atazanavir (Reyataz)** 300 mg po qd + **Ritonavir (Norvir)** 100 mg po qd | • Once daily dosing | • Three pills  
  • Should be taken with food  
  • GI side effects  
  • CYP3A4 Inhibitor: ↑ drug interactions  
  • Needs low pH for best absorption  
  • Elevation of indirect bilirubin  
  • Annual cost $ 39,095 |
# Preferred Regimens—NNRTI

http://aidsinfo.nih.gov/guidelines

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Truvada + Rilpivirine]</td>
<td>• One pill a day</td>
<td>• Not recommended with VL &gt; 100,000 or CD4 &lt; 200</td>
</tr>
<tr>
<td>(Complera) 1 po qd</td>
<td>• Annual cost $ 29,567</td>
<td>• Should be taken with food</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Integrase Inhibitor &lt; Drug interaction &lt; Protease Inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Needs low pH for best absorption</td>
</tr>
<tr>
<td>[Truvada + Efavirenz]</td>
<td>• One pill a day</td>
<td>• Should be taken without food</td>
</tr>
<tr>
<td>(Atripla) 1 po qd</td>
<td>• Effective regardless of baseline VL and CD4 count</td>
<td>• Neuropsychiatric side effects</td>
</tr>
<tr>
<td></td>
<td>• Effective with long term experience</td>
<td>• Increased risk of suicide recently reported on analysis of RCTs (1)</td>
</tr>
<tr>
<td></td>
<td>• Annual cost = $ 28,824</td>
<td>• Integrase Inhibitor &lt; Drug interaction &lt; Protease Inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pregnancy category C</td>
</tr>
</tbody>
</table>

Case Presentation

- 41 y/o male with HIV for 8 – 9 years who has never been on therapy.
  - CD4 700 (28%)
  - VL 47,100
  - Started Truvada 1 po daily & Raltegravir 1 po bid.
  - One month later VL < 20 copies
  - VL remains either < 20 or TND (target not detected).
  - One episode of gonorrhea in the interim
Conclusions

• HIV is now a treatable chronic disease.
• The complexity of HIV management has decreased significantly in the last decade.
• Changes to Ryan White Funding under the ACA could make the current model subspecialty based HIV care difficult to maintain.
• Primary care physicians with an interest in HIV may be needed to meet the HIV care demands of the future.
Thanks and Questions ...

• Thanks to Lisa Lawrence and the AIDS Education and Training Center (AETC).

• Questions...