The Impact of Alcohol and Substance Use on the Prevention and Treatment of HIV/AIDS

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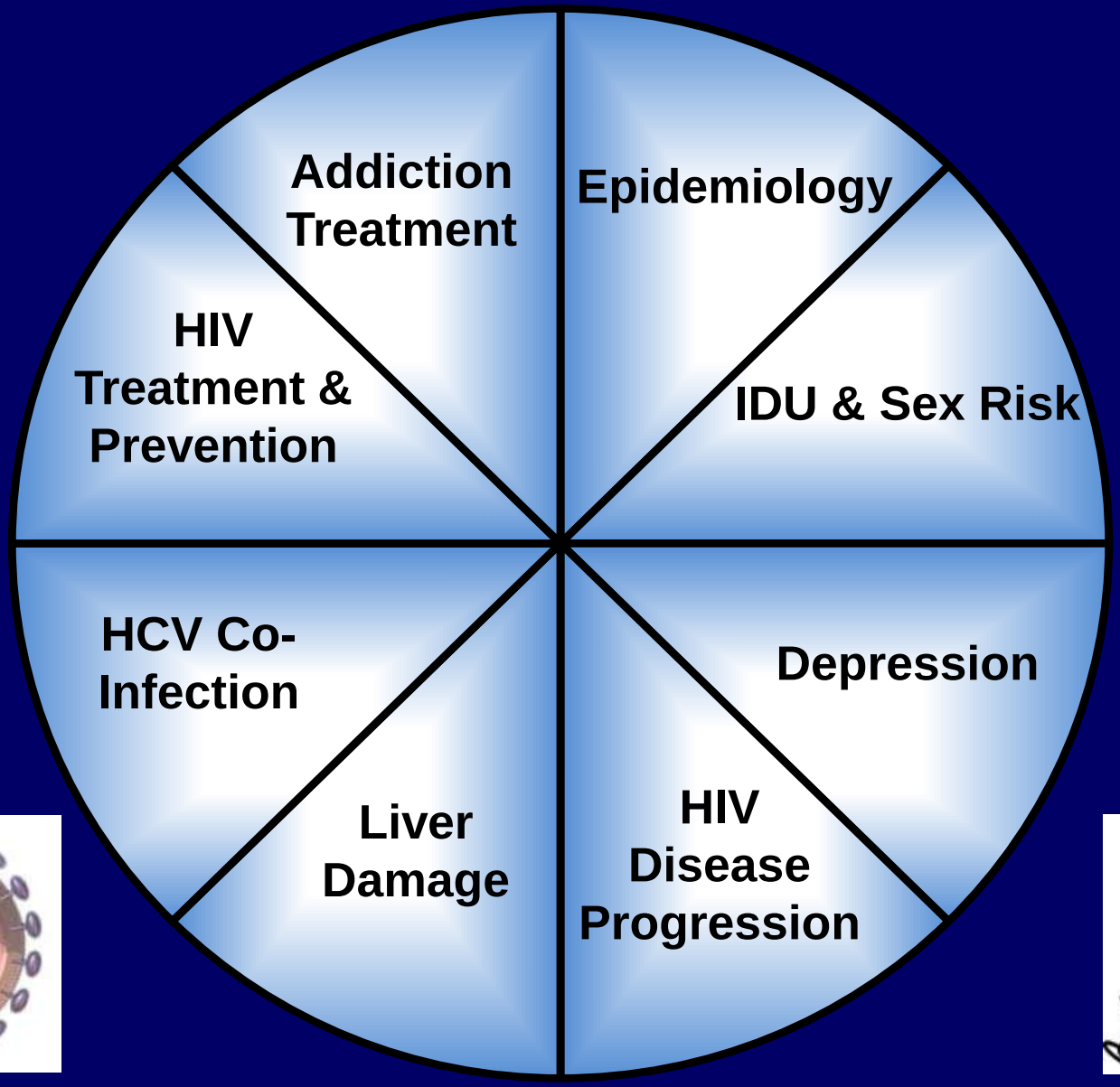
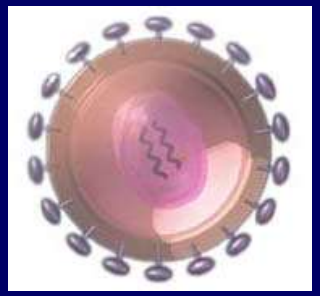
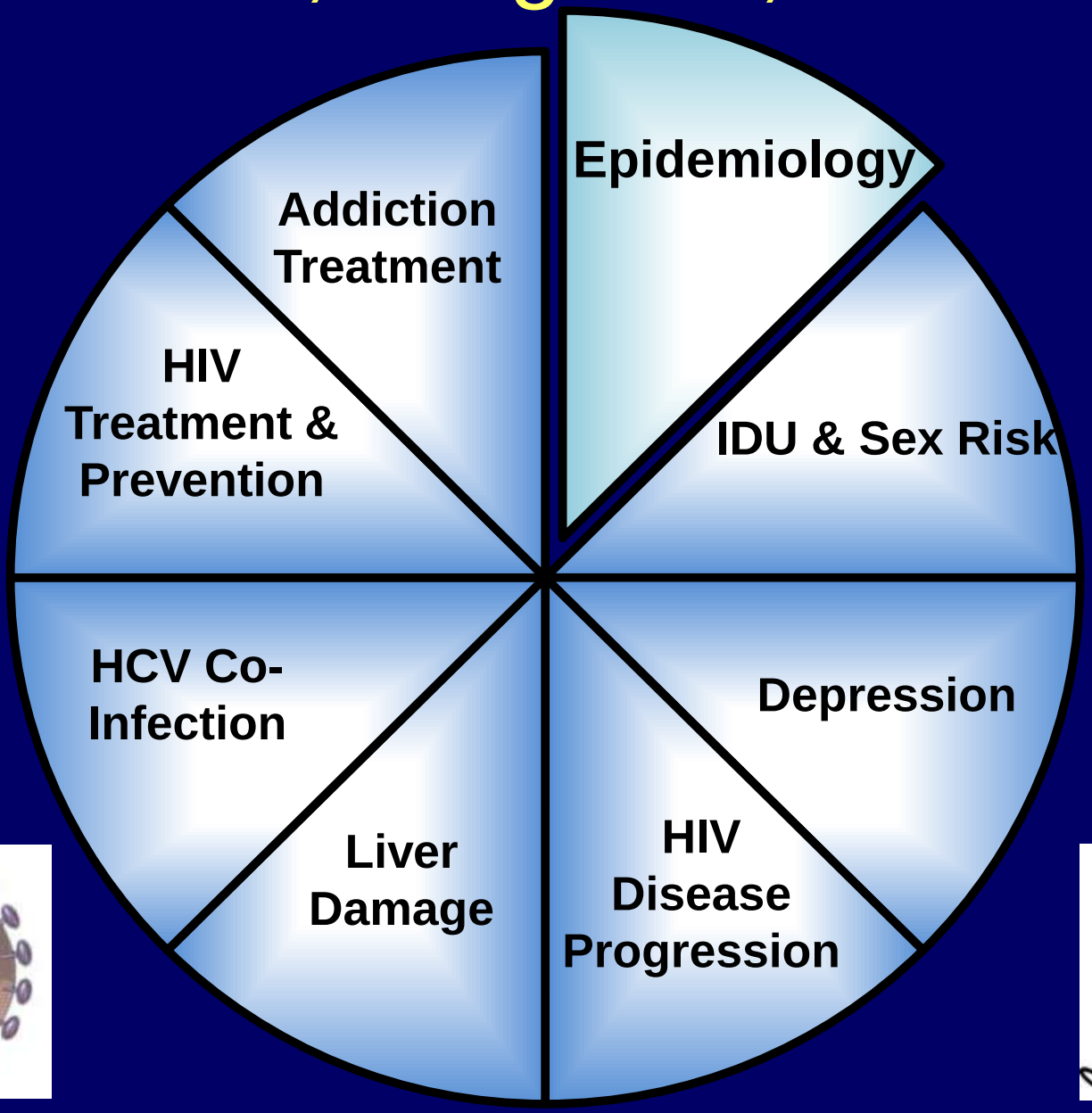
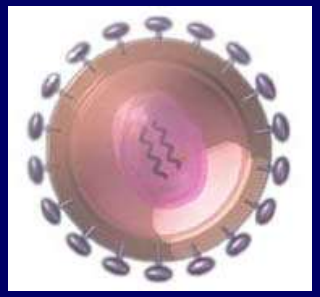
Alcohol, Drug Use, and HIV





Alcohol, Drug Use, and HIV





Alcohol Problems among HIV-Infected Persons in USA

- HIV Cost and Services Utilization Study (n=2864)*
  - 8% current hazardous drinkers
- HIV Research Network (14 sites, n=951)†
  - 11% current hazardous drinkers
- Women's Interagency HIV Study (WIHS, 6 sites, n=2,770)‡
  - 14-24% past-year hazardous drinkers (11-year period)
- Veterans Aging Cohort Study (VACS, n=881)[1]**
  - 36% past-year hazardous drinkers (AUDIT ≥ 8)

[1] >7000 HIV-infected veterans and non-infected controls, 8 sites, 98% men

* Galvan, Bing, Fleishman, et al. *J Stud Alcohol*. 2002;63:179-186.

† Chander, Josephs, Fleishman, et al. *HIV Med.* 2008;9:196-202.

‡ Cook, Zhu, Belnap, et al. *Am J Epidemiol*. 2009;169:1025-1032.

** Conigliaro, Gordon, McGinnis, Rabeneck, Justice. *J AIDS*. 2003;33:521-525.

HIV Research Cohorts

- **HIV** - **L**ongitudinal **I**nterrelationships of **V**iruses and **E**thanol (HIV-LIVE)
  - 400 HIV-infected adults in Boston with current or past alcohol problems, 50% infected with hepatitis C (HCV), 25% female
  - 2000-2005
- **V**eteran's **A**ging **C**ohort **S**tudy (VACS)
  - Approx. 3,700 HIV-infected veterans (as of 2012)
  - 1:1 matched to HIV-uninfected veterans
  - 1997-present

Alcohol Problems among HIV-Infected Persons Globally

- Cape Town, South Africa – outpatients at HIV clinic (n=465)*
  - 27% past-year hazardous drinkers (AUDIT ≥ 8)
- St. Petersburg, Russia – hospitalized patients (n=201)†
  - 47% alcohol abuse or dependence

* Myer, Smit, Roux, Parker, Stein, Seedat. *AIDS Patient Care and STDs.* 2008;22:147-158.
† Krupitsky, Horton, Williams, et al. *Drug Alcohol Depend*. 2005;79:251-256.

Blood Tests to Assess Alcohol Consumption

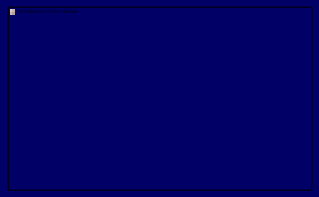
- Carbohydrate-deficient transferrin (%CDT)
  - Typically elevated after 60g ethanol/day*
  - In HIV-infected, only 36% sensitivity for “heavy” drinking†
- Phosphatidylethanol (PEth)
  - Significantly correlated with ethanol use in last 7 days‡
  - Does not produce false positives
  - Processed in specialized laboratories only

* Golka, Wiese. *J Toxicol Environ Health.* 2004;7:319-337.
† Ireland, Cheng, Samet, Bridden, Quinn, Saitz. *AIDS Care.* 2011;23:1483-1491.
‡ Wurst, Thon, Aradottir, et al. *Addict Biol*. 2010;15:88-95.

IDU and HIV in USA

- In USA, IDU accounted for*
  - 8% of new HIV infections (2010)
  - 17% of people living with HIV (2010)

- In Massachusetts, IDU accounted for†
  - 24% of adult HIV/AIDS cases (2011)



*** CDC. *HIV Surveillance – Epidemiology of HIV Infection (through 2010)*. Published March 2012. http://www.cdc.gov/hiv/topics/surveillance/resources/slides/general/index.htm?utm_source=At-a-Glance&utm_medium=e-mail&utm_campaign=Epidemiology%2Bof%2BHIV%2BInfection. Accessed 06/11/13.**

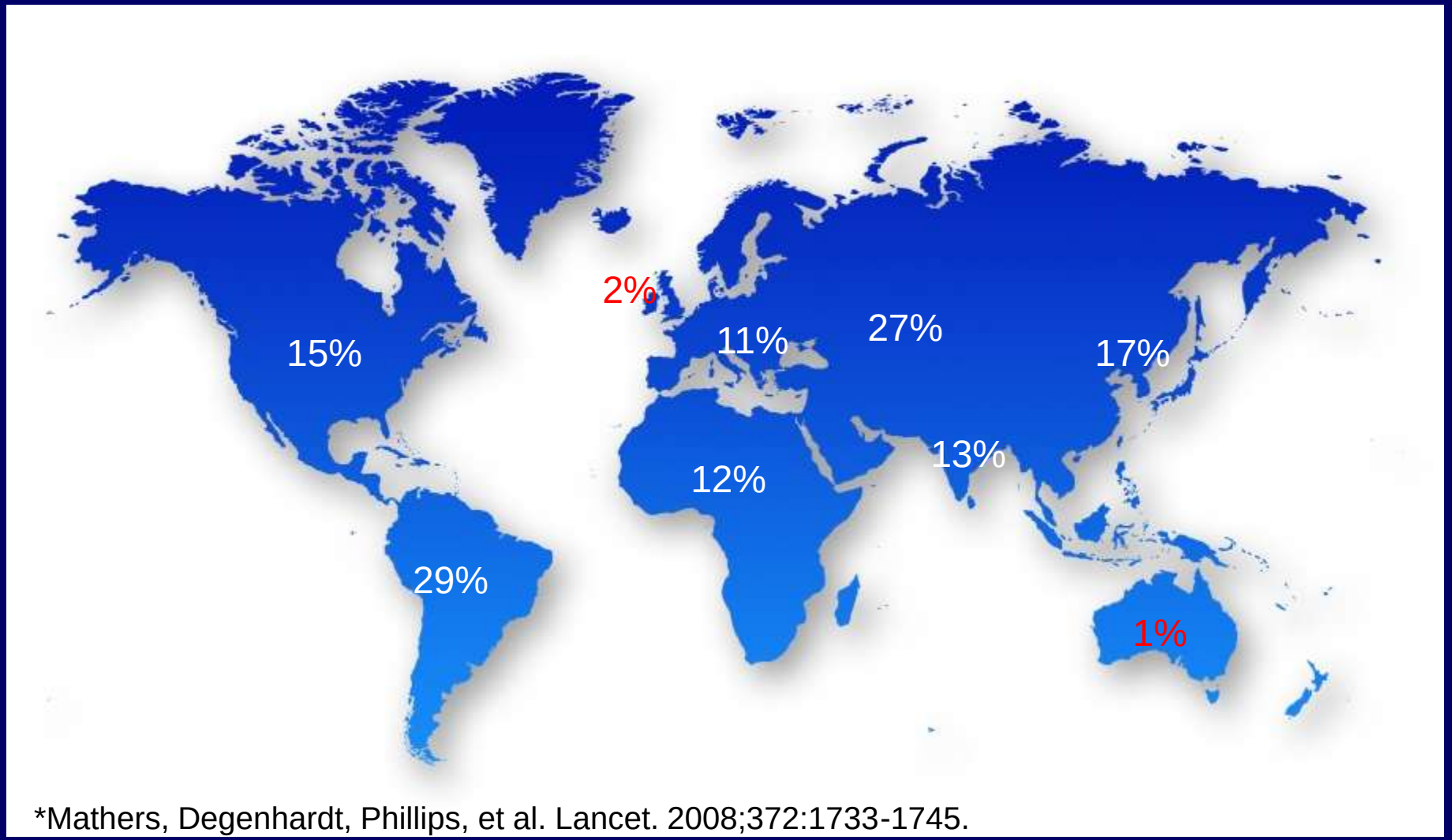
† http://www.mass.gov/eohhs/docs/dph/aids/2012-profiles/idu.pdf. Accessed 06/11/13.

Drug Use as a Risk Factor for HIV

- IDU
  - Typically heroin
    - Other drugs (e.g. cocaine, amphetamines)
  - Estimated 3 million HIV-infected via IDU worldwide*
- HIV prevalence elevated among non-injecting drug users
  - IDU (past 6-month) vs. never injecting, heroin/cocaine users†
    - 13% (CI 12-15%) vs. 12% (CI 9-16%)
      - Addiction treatment center (n=2,121)
    - 15% (CI 11-19%) vs. 17% (CI 12-21%)
      - Respondent-driven store-front sampling (n=448)

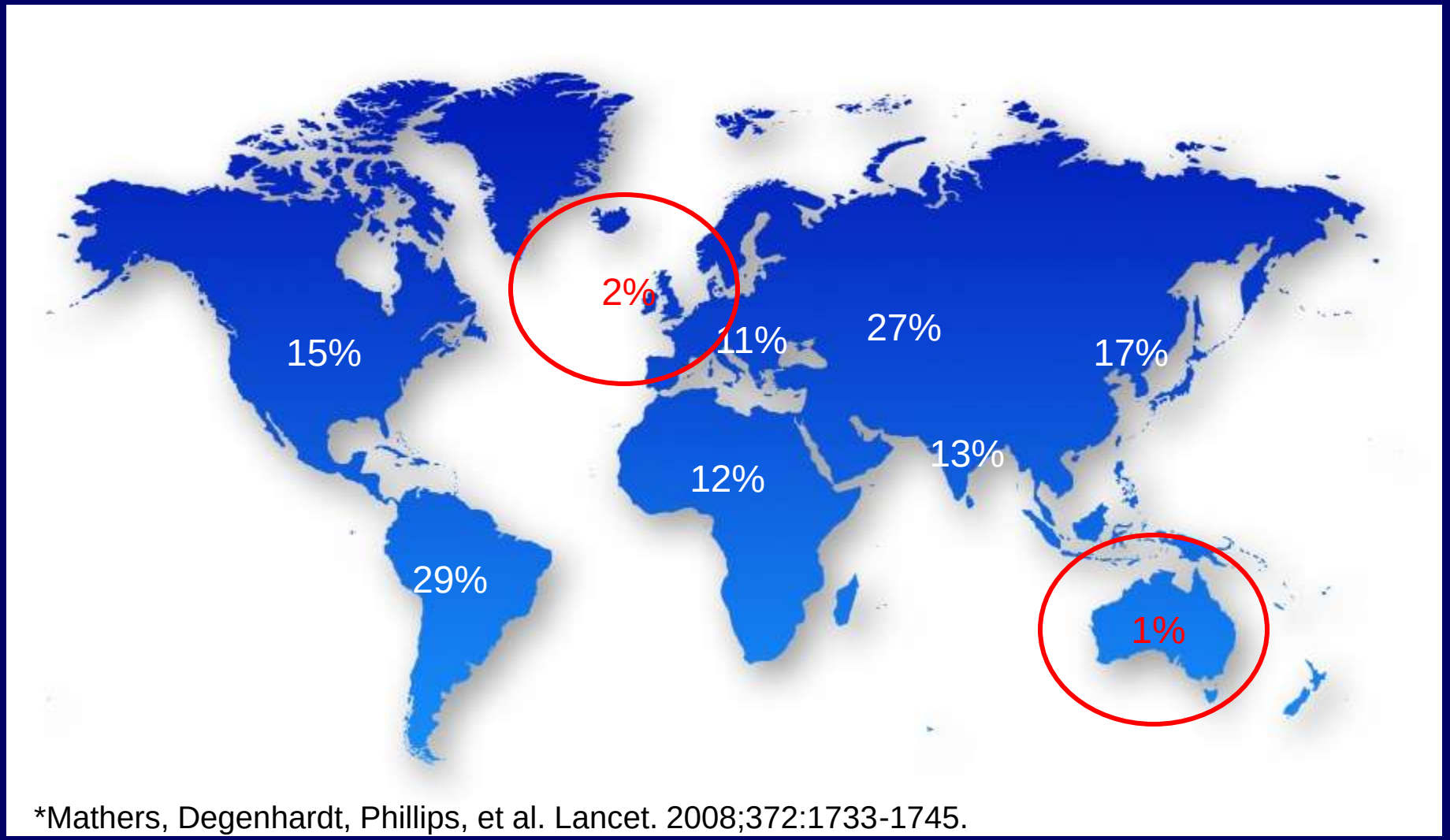
* Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.
† Des Jarlais, Arasteh, Perlis, et al. *AIDS*. 2007;21:231-235.

Global HIV Prevalence Among IDUs



*Mathers, Degenhardt, Phillips, et al. Lancet. 2008;372:1733-1745.

Global HIV Prevalence Among IDUs



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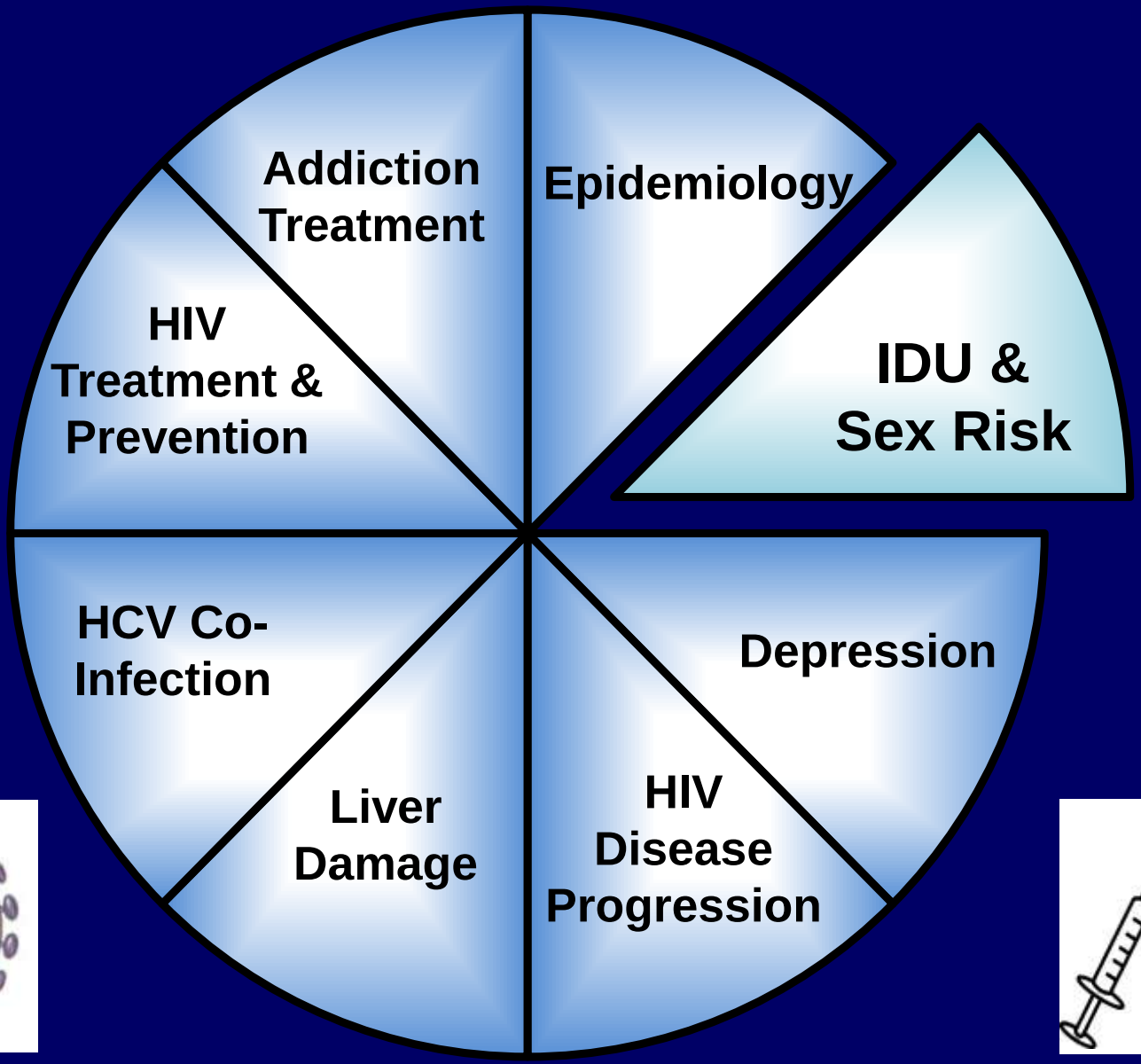

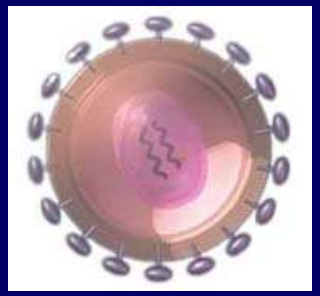

HIV Risk Behaviors in Binge Drinkers

- 2008 Behavioral Risk Factor Surveillance System Binge Drinkers
  (41,083 binge drinkers; 240,230 non-binge drinkers)
- HIV Risk Behaviors defined as past year:
  - Injection drug use
  - Exchange of sex for money/drugs
  - Unprotected anal sex
- HIV risk behaviors higher among binge drinkers: 7.0% vs. 2.9% (OR 1.8, CI 1.58-2.00)

* Wen, Balluz, Town. *J Community Health*. 2012;37:72-79.

Alcohol Use and Risky Sex

- Meta-analysis (27 studies, n=10,536) found unprotected sex among HIV-infected individuals significantly associated with:
  - Alcohol consumption (OR 1.6, CI 1.4-1.9)
  - Problematic drinking (OR 1.7, CI 1.5-2.0)
  - Alcohol use in sexual contexts (OR 2.0, CI 1.6-2.4)

* Shuper, Jonarchi, Irving, Rehm. *AIDS Behav*. 2009;13:1021-1036.

Alcohol Use and Vaginal HIV Detection

- HIV infected women (n=160)*

	Recent Drinking (past 24 hrs.)		
	≤ 1 drink	≥ 2 drinks	p-value
Vaginal Detectable Virus	27%	40%	<.05

  - When stratified by ART status, recent drinking effect only observed in those on ART (n=87)

- Longitudinal cohort study of HIV-infected women (n=481)†
  - High frequency vaginal detection associated with alcohol use (OR 2.20, CI 1.08-4.49)

* Theall, Amedee, Clark, Dumestre, Kissinger. *J Stud Alcohol Drugs.* 2008;69:454-458.
† Homans, Christensen, Stiller, et al. *J AIDS.* 2012;60:e106.

Drug Use and Sex Risk

- Crystal meth among HIV-infected MSM (n=398)*
  - Greater sex risk - unprotected anal sex with possible serodiscordant partner - past 6 months (OR 2.6, CI 1.4-4.8)

- HIV-infected crack cocaine users, binge vs. non-binge users (n=303)†
  - Greater mean # of sex partners - past 6 months (12 vs. 4)
  - More likely never use a condom - past 30 days (OR 2.5, CI 1.1-5.5)

- Past 30 day cannabis use among sexually active HIV-infected Russian risky drinkers (n=700) associated with:‡
  - Needle sharing (AOR 2.23, CI: 1.5-3.4)
  - Number of injections (IRR 1.5, CI: 1.2-1.9)
  - Multiple sex partners(AOR 1.7, CI:1.2-2.5)

* Mayer, O'Celirigh, Skeer, et al. *Sexually Transmitted Infec*. 2010;86:66-70.
† Harzke, Williams, Bowen. *AIDS Behav*. 2009;13:1106-1118.
‡ Tyurina, Krupitsky, Cheng, et al. *Drug Alcohol Depend*. 2013, Feb 11 [Epub ahead of print].

Alcohol and Drug Use and HIV Disclosure

- Primary care patients at two urban hospitals (n=203)*
  - Among 40% of subjects who did not disclosed to all sex partners, 57% used condoms less than all the time
  - No association found between history of addiction (alcohol or IDU) and disclosure
- HIV-infected Russian risky drinkers (n=605)†
  - No association between past 30 day risky alcohol use (OR 1.31, CI 0.79-2.17) or alcohol use at time of sex with recent nondisclosure (OR 0.75, CI 0.54-1.05)
- HIV-infected female sex workers (n=211) and male clients (n=205) in India‡
  - Any alcohol use in past 30 days was associated with non-disclosure among women (OR 2.8, CI 1.5–5.3)

* Stein, Freedberg, Sullivan, et al. *Arch Intern Med.* 1998;158:253-7.
† Lunze, Cheng, Quinn, et al. *AIDS Behav.* 2013;17:390-398.
‡ Saggurti, Raj, Mahapatra, et al. *AIDS Behav*. 2013;17:399-406.

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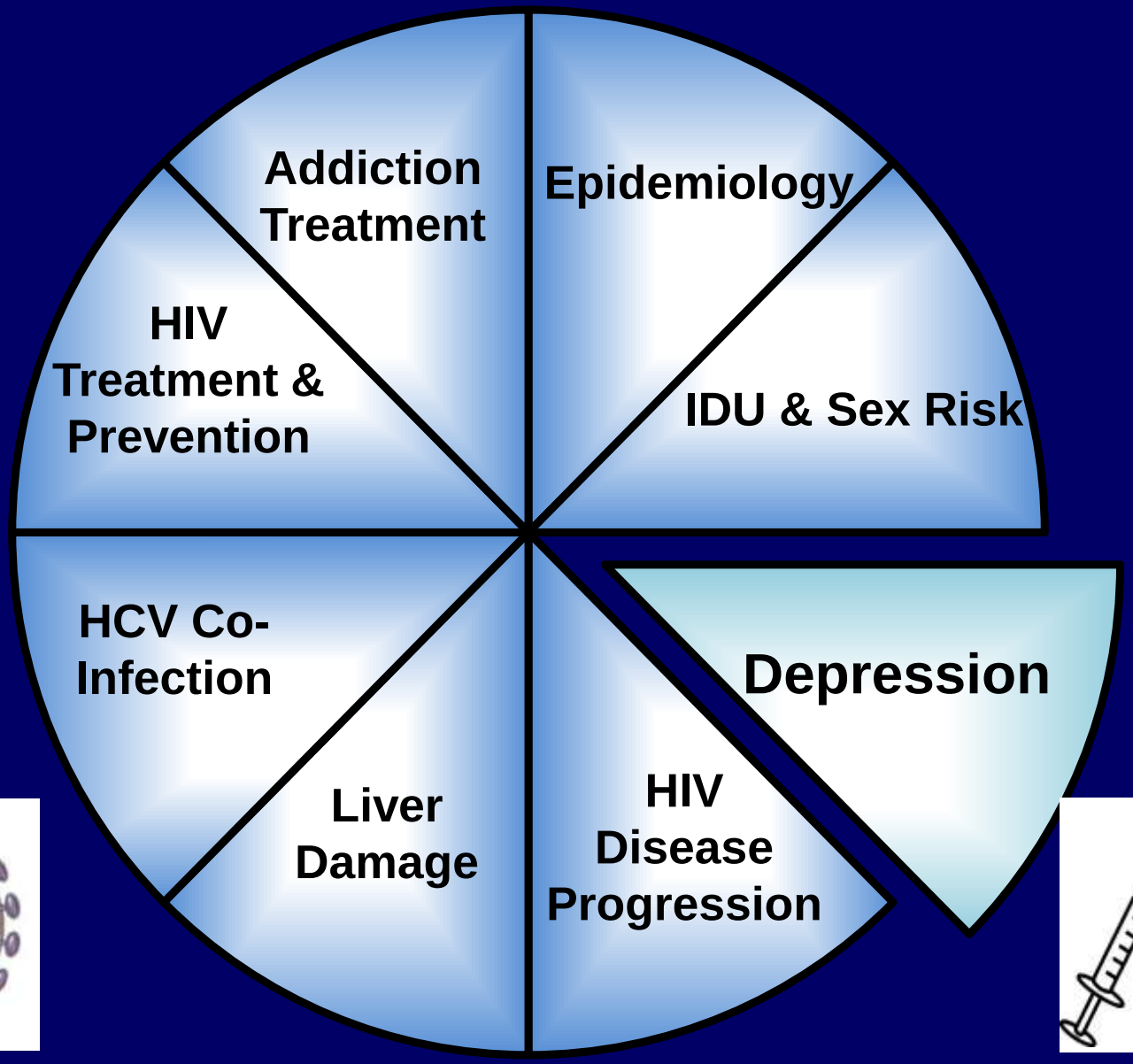

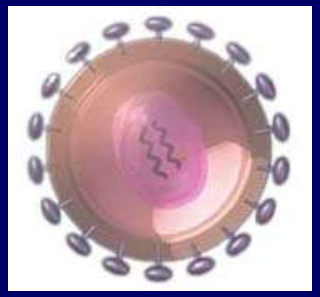

Depression

- HIV-LIVE (n=400)*
  - Alcohol dependence associated with ↑ depressive symptoms (CES-D mean difference 3.49, CI 1.76-5.22)*
- VACS (n=2446; 55% HIV-infected)†
  - Hazardous and binge drinking associated with depression (PHQ-9 ≥ 9) (OR 2.53, CI 1.34-4.81)†
  - HIV status did not modify alcohol's impact on depression (not an effect modifier)
- HERS (n=871)‡
  - Moderate drinking (OR 1.93, $p<0.01$) and heavy drinking (OR 3.94, $p<0.01$) associated with increased depressive symptoms (↑CES-D), regardless of ART status

* Sullivan, Saitz, Cheng, Libman, Nunes, Samet. *Addiction*. 2008;103,1461-1467.
† Sullivan, Goulet, Justice, Fiellin. *Drug Alcohol Depend.* 2011;117:158-163.
‡ Ghebremichael, Paintsil, Ickovics, et al. *AIDS Care*. 2009;21:834-841.

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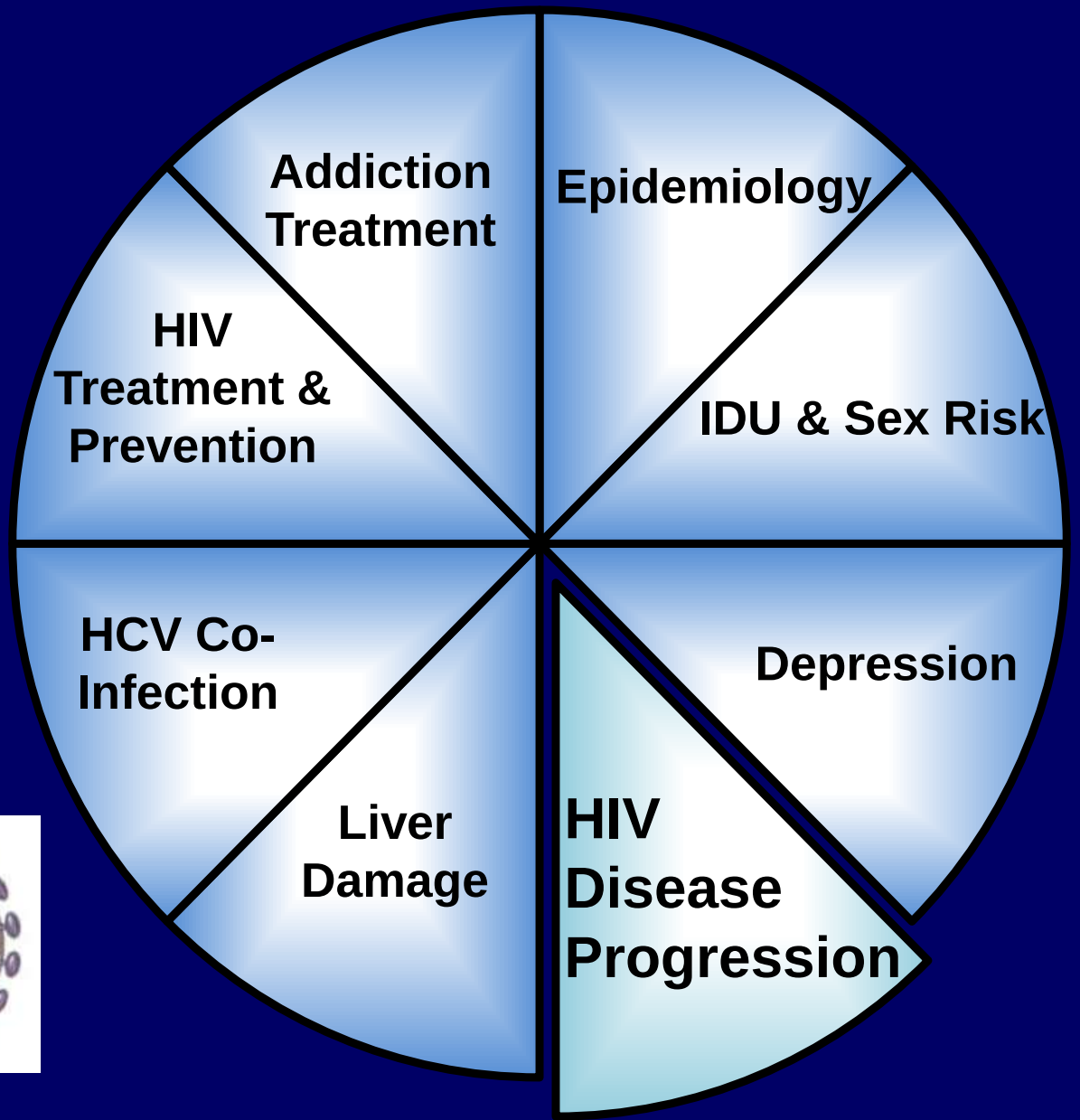
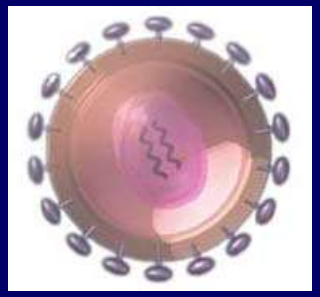
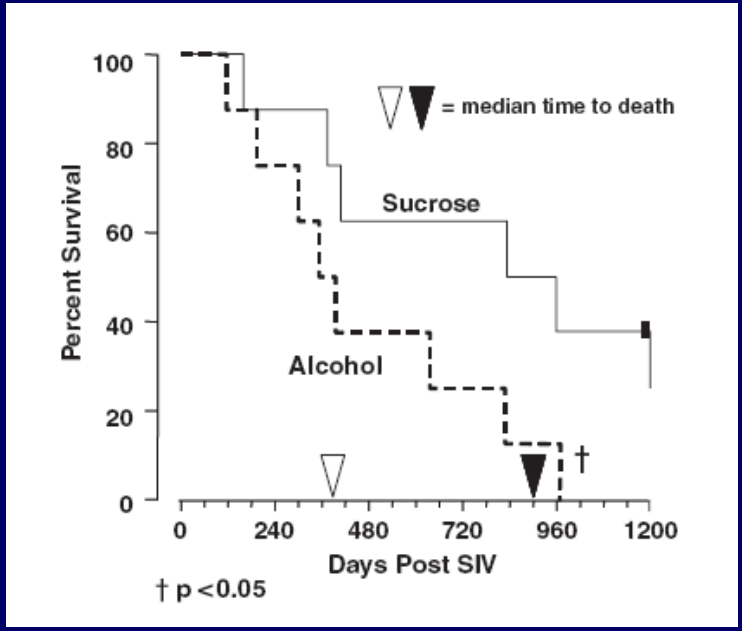




Alcohol and HIV Disease Progression

- Macaques (n=16): IV alcohol vs. sucrose at time of SIV infection
  - Higher viral set point (448 vs. 362 copies/mL; *p<0.05*)
  - Shorter time to death (374 vs. 900 days; *p<0.05)*



Bagby, Zhang, Purcell, Didier, Nelson. *ACER*. 2006;30:1781-1790.

Alcohol and HIV Disease Progression

- Pre-HAART (MACS): no association found*
- Post-HAART:
  - Hopkins† (n=1711): alcohol associated with
    - Worse ART adherence (AOR 0.46; CI: 0.34 – 0.63)
    - Less viral suppression (AOR 0.76; CI:0.57-0.99)
  - HIV-LIVE‡ (n=240): Heavy alcohol use associated with lower CD4 cell count in patients NOT on ART
    - Adjusted mean decrease of 49 cells/μl compared with abstinence (p=0.03)
- Possible mechanism:
  - Immune activation, increased GI bacterial translocation, interaction with ART metabolism§

* Kaslow, Blackwelder, Ostrow, et al. *JAMA*. 1989;261:3424-3429.
† Chander, Lau, Moore. *J AIDS*. 2006;43:411-417.
‡ Samet, Cheng, Libman, Nunes, Alperen, Saitz. *J AIDS.* 2007;46:194-199.
§ Hahn, Samet. *Curr HIV/AIDS Rep*. 2010;7:226-233.

Drug Use and HIV Disease Progression

- Hopkins* (n=1,851): Heroin and cocaine use and risk of opportunistic infections (OIs)

	OR	95% CI
Nonuser	**1.0**	
Intermittent user, abstinent	**1.4**	**1.0 - 1.9**
Intermittent user, active	**2.3**	**1.5 – 3.0**
Persistent user	**2.1**	**1.4 – 3.1**

Active drug use associated with HIV disease progression

* Lucas, Griswold, Gebo, Keruly, Chaisson, Moore. *Am J Epidemiology.* 2006;163:412-420

Cocaine and HIV Disease Progression

- HIV-infected non-injecting drug users (n=222)
- Crack cocaine users (n=110):
  - More likely to have a CD4 ≤ 200 cells/ml (OR 2.14, CI 1.08-4.25)
  - Higher HVL
  - Of those on ART, less likely suppress HVL
  - Of those not on ART (n=53), increased RR of CD4 decline < 200 (HR 3.9, CI 1.1-14.9)

Baum, Rafie, Lai, Sales, Page, Campa. *J AIDS*. 2009;50:93-99.

Tobacco and HIV Disease Progression

- HIV-LIVE cohort (n=462)
  - No significant association between CD4 or HVL and smoking status
  - True for the range of tobacco use compared to non-smokers

Kabali, Cheng, Brooks, Bridden, Horsbugh, Samet. *AIDS Care*. 2011;23:1-10.

Mortality and Substance Use

- HIV-LIVE (n=595), short-term mortality associated with*:
  - Heroin or cocaine use (HR 2.4, CI 1.1-5.3)
  - Homelessness (HR 2.9, CI 1.3-6.4)
  - No association with heavy alcohol use (HR 0.6, CI 0.2-1.4)
- Johns Hopkins HIV Clinical Cohort 1997-2006, (n=1030 women)†
  - Heavy drinking associated with increased mortality (HR 1.4, CI 1.0-1.97)
- Antiretroviral Therapy Cohort Collaboration 2001-2008 (n=44,043),§ mortality associated with:
  - IDU (RR 2.08, CI 1.91-2.26)

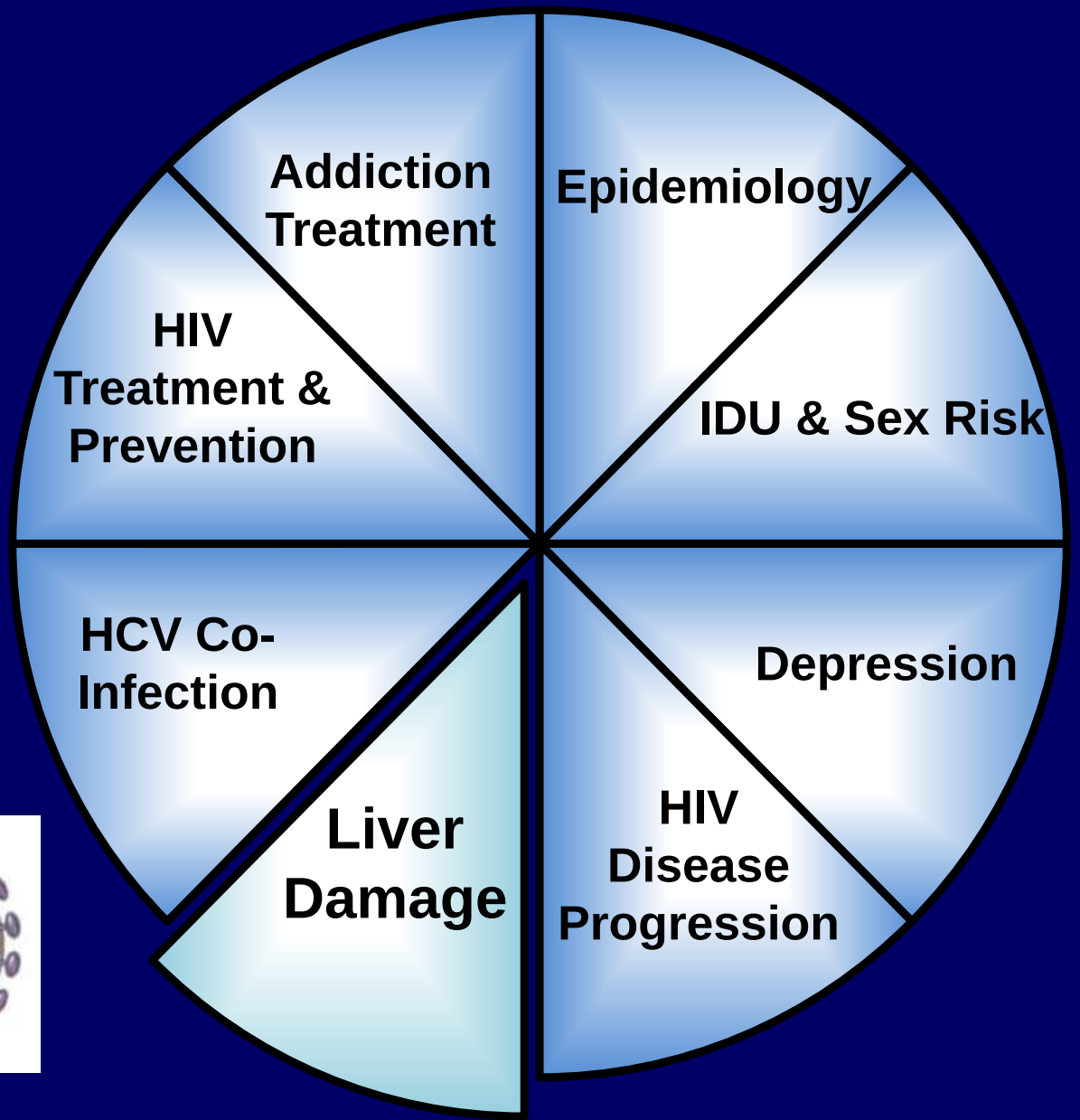
* Walley, Cheng, Libman, et al. *AIDS*. 2008; 22:415-420.
† Neblett, Hutton, Lau, McCaul, Moore, Chander. *J Women's Health*. 2011; 20:279-286.
§ Murray, Hogg, Lima, et al. *HIV Med*. 2012;13:89-97.

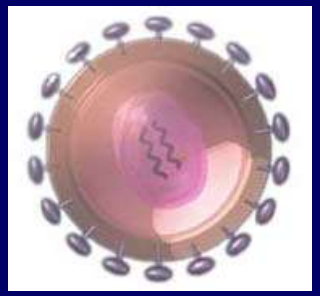
IDU, HIV, and Mortality

- IDUs have the worst life expectancy among all transmission categories
- IDU life expectancy post-dx in the US (2005):
  - Male: 15.2 years (CI 14.8-15.5)
  - Female : 15.9 years (CI 15.1-16.6)
- IDU life expectancy almost half compared to those with sexual transmission risk

Harrison, Song, Zhang. *J AIDS*. 2010;53:124-130.

Alcohol, Drug Use, and HIV





Alcohol Use Associated with Significant Liver Disease in HIV-Infected Persons

- Swiss HIV Cohort: Mono-infected patients (n=3,365)*
  - Hazardous alcohol use (>40g/day females; >60g/day males) associated with elevated ALT levels (OR 1.83; CI 1.19-2.80)
- Johns Hopkins HIV Clinical Cohort: Mono-infected patients (n=696)†
  - Hazardous drinking (>14 drinks/wk) associated with significant liver disease – APRI[1] (adjusted RRR: 3.72; 95% CI: 1.40-9.87)

[1] APRI= $\frac{\text{AST level / upper limit of normal}}{\text{Platelet count } (10^9/\text{L})}$; APRI >1.5 identifies significant liver disease

* Kovari, Ledergerber, Battegay, et al. *Clin Infect Dis.* 2010;50:502-511.
† Chaudhry, Sulkowski, Chander, Moore. *HIV Medicine.* 2009;10:133-142.

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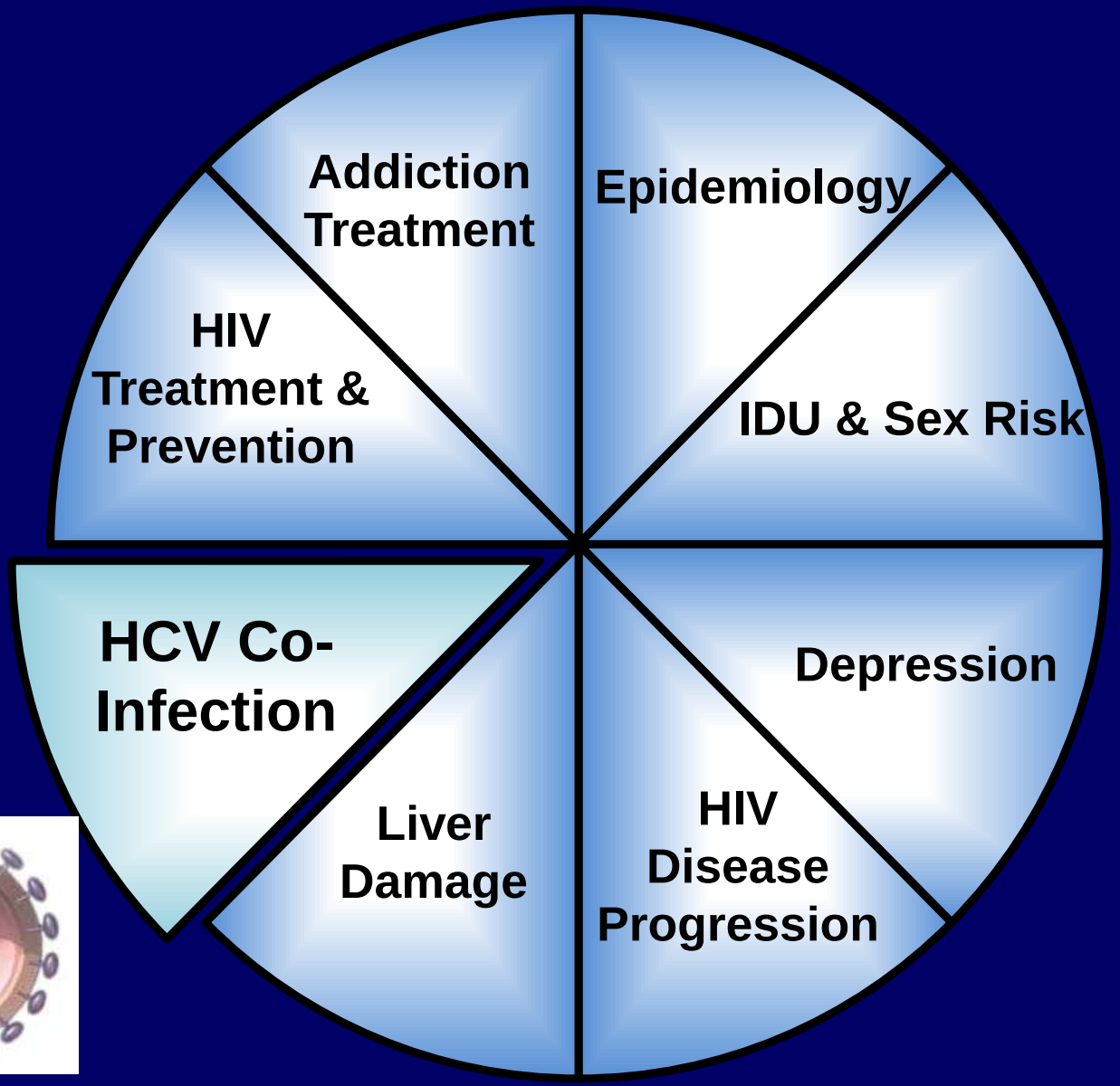
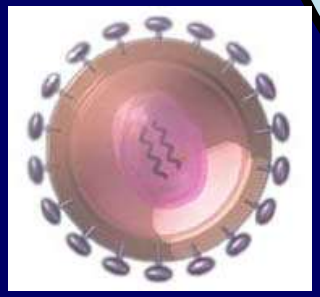
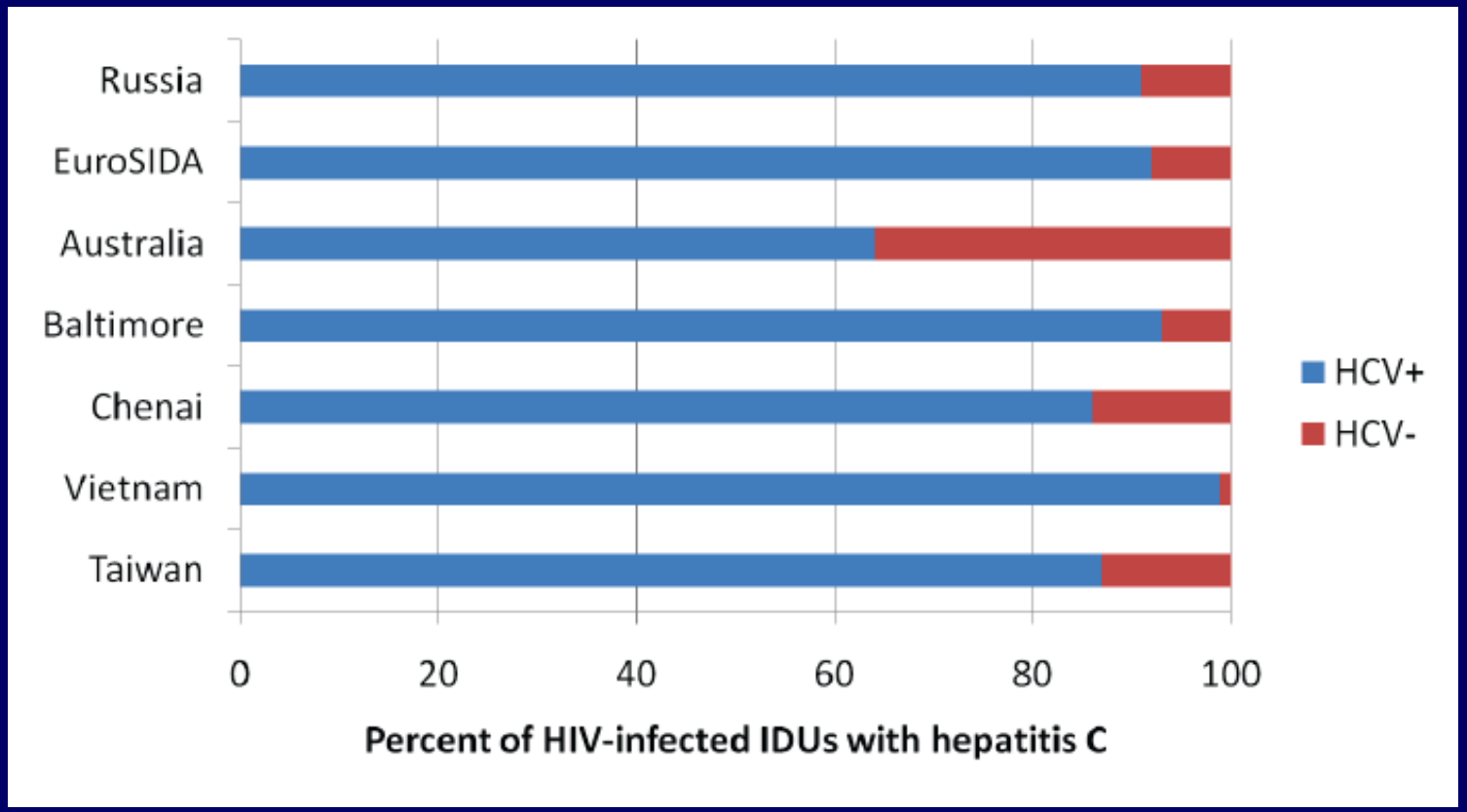




HCV Prevalence in HIV+ IDUs



Thomas, Leoutsakas, Zabransky, Kumar. *J Int AIDS Soc.* 2011;14:22.

Alcohol Use and Liver Function in HIV/HCV-infected Persons

- In co-infected persons in HIV-LIVE cohort (n=200), risky drinking was associated with elevated
  - AST (62.2 vs. 51.4 U/L; adjusted ratio of means 1.2, CI [1.07, 1.37], p=0.003)
  - ALT (51.3 vs. 41.6 U/L; adjusted ratio of means 1.2, CI [1.07, 1.42], p=0.004)
- In mono-infected persons (n=197), risky drinking was not associated with elevated AST or ALT levels

Tsui, Cheng, Libman, et al. *J Stud Alcohol Drugs.* 2013;74:266-70.

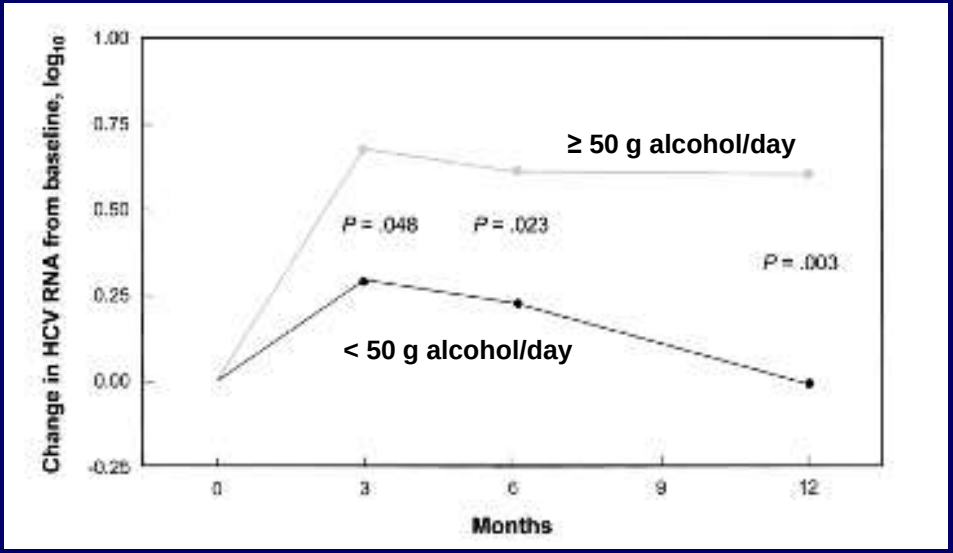
Alcohol Use among HIV/HCV-infected Persons

- HIV-LIVE (n=400)
- Those told about HCV diagnosis were more likely to report
  - Abstinence (AOR 1.60, CI 1.13 - 2.27)
  - Not drinking unhealthy amounts (AOR 1.46, CI 1.01 - 2.11)
- Awareness of HCV diagnosis associated with greater abstinence from alcohol and less unhealthy amounts of drinking

Tsui, Saitz, Cheng, et al. *J Gen Intern Med.* 2007;22:822-825.

Impact of Alcohol Use on HCV VL

- HIV/HCV co-infected persons on ART (n=44)*
  - Alcohol use (≥ 50 g/day) associated with increases in HCV RNA (>0.6 $\log_{10}$ IU/mL; p=0.04)



  - HCV RNA not associated with HCV disease progression
  - However HCV RNA is related to treatment outcomes

*Cooper, Cameron. *Clin Infect Dis*. 2005;41(Suppl 1):S105-S109.

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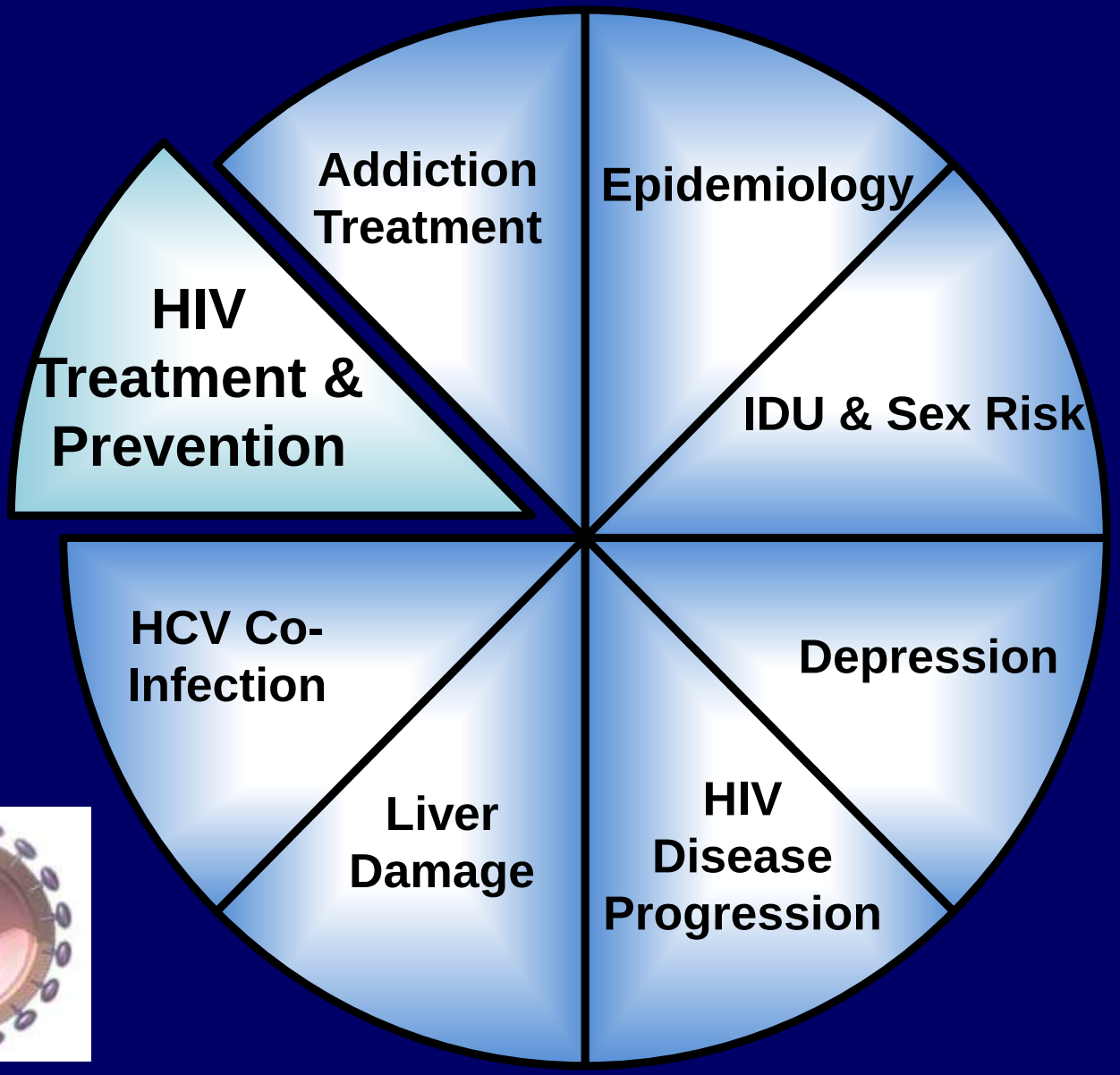
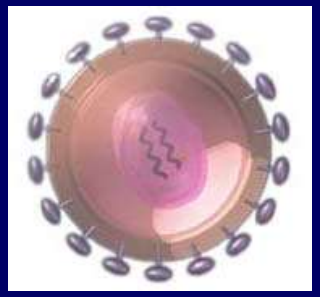




Presenting to Medical Care

Model of entry into HIV medical care*

- Entry into care in two New England clinics, 1994-1996 (n=189)†
  - 39% delayed >1 year, 32% >2 years, and 18% >5 years
  - IDU (p<0.001) and history of alcohol problems in men (p=0.03) associated with delay
- Entry into care in 18 states, 2000-2004 (n=3,942)‡
  - 28% delayed medical care for > 3 months
  - IDU associated with delay (OR 1.4, CI 1.08-1.82)

* Samet, Freedberg, Savetsky, Sullivan, Stein. *AIDS*. 2001;15:77-85.
† Samet, Freedberg, Stein, et al. *Arch Intern Med*. 1998;158:734-740.
‡ Reed, Hanson, McNaghten, et al. *AIDS Patient Care STDS.* 2009;23:765-773.

IDUs and HIV Treatment Engagement

- Global review of ART coverage for IDUs
  - In the five countries* with the largest IDU HIV epidemics, IDUs make up 67% of HIV cases, but only 25% of those receiving ART
  - Barriers to HIV Treatment Engagement of IDUs
    - Stigmatization of IDUs in health care setings
    - Separation of addiction and HIV care systems
    - Active IDU is contraindication for ART
    - No HIV treatment for prisoners

* China, Vietnam, Russia, Ukraine, Malaysia

Wolfe, Carrieri, Shepard. *The Lancet*. 2010;376:355-366.

IDUs and HIV Treatment Engagement

"The doctor said that I had to deal with one thing first, and then the other. Because I had told her straight that I used drugs. So, she said that I had to quit first and then take care of the rest. But how? … I'm actually afraid to discuss this issue of how to combine therapy and drugs. I don't even want to ask the doctor… The doctor gave me such a look that I understood I'm kind of not entitled to ever feel good if I use drugs. So I made my conclusions. She made it clear to me that I had to deal with one thing first, then with the other."

- Elena

Rhodes, Sarang. *Addiction.* 2012;107:1827-1836.

Alcohol and ART adherence

- Meta-Analysis of 40 studies and over 25,000 participants*
  - Risky or dependent drinkers were less adherent than non-problem drinkers or abstainers
    (OR 0.5, CI 0.4 -0.6)
- Study of African-Americans about beliefs of alcohol and ART (n=82)†
  - "Alcohol and ART do not mix." (85%)
  - "I will not take my meds if I have been drinking." (51%)
- Study of HIV-infected drinkers (n=178) showed that participants who endorse toxicity beliefs are:‡
  - More likely to miss medications on drinking days (OR 2.90 CI 1.09–7.68)
  - More likely to have VL>75 copies/mL (50% vs. 33%, p=0.02)

* Hendershot, Stoner, Pantalone, Simoni. *JAIDS*. 2009. 52:180-202.
† Sankar, Wunderlich, Neufeld, Luborsky. *AIDS Behav*. 2007;11:195–203.
‡ Kalichman, Grebler, Amaral, et al. *J Gen Intern Med.* 2012 [Epub ahead of print].

Efforts to Improve ART Adherence

Two RCTs to improve ART adherence among hazardous drinkers with motivational interviewing

- ADHERE (n=151)*
  - 4 session intervention
  - No significant differences in medication adherence, CD4 count, VL, or alcohol consumption
- Hazardous drinkers in New York City (n=143)†
  - 8 session intervention
  - Significant differences in VL, CD4 count at 3 months, but not 6 months

* Samet, Horton, Meli, et al. *Antivir Ther.* 2005;10:83-93.

† Parsons, Golub, Rosof, Holder. *J AIDS.* 2007;46:443-450.

IDUs and ART Adherence

- HIV-infected persons (n=578) first prescribed ART between 1996-2000*
  - Classified as current IDU, former IDU, or non drug user
  - Current IDUs were less likely to suppress their HVL compared to non-drug users
  - Former IDUs were NOT less likely suppress HVL compared to non-drug users
- Similar findings in Swiss Cohort between 1997-2006 (n=8669)†
- Improvement in achievement of 95% adherence among Vancouver IDUs – 19% (1996) vs. 66% (2009)‡

* Palepu, Tyndall, Yip, O'Shaughnessy, Hogg, Montaner. *JAIDS*. 2003;32:522-526.
† Weber, Huber, Rickenbach, et al. *HIV Med*. 2009;10:407-416.
‡ Mann, Milloy, Kerr, et al. *HIV Med.* 2012;13:596-601.

Changes in Sex and Drug Risk Behaviors After ART Initiation

Community-based cohort study of HIV-infected IDUs (n=362)

- ART initiation associated with reduction in likelihood of unprotected sex (OR 0.25, CI 0.19-0.32)
- Odds of any injection drug use reduced (OR 0.62, CI 0.51-0.75)
- However, needle sharing increased among persistent injectors

Fu, Westergaard, Lau, et al. *AIDS.* 2012;26:2383-91.

Integrated Opioid Agonist Treatment (OAT) & Directly Observed Therapy (DOT)

- RCT compared DOT to standard of care
- 12 methadone OAT clinics in the Bronx (n=77); 24-week follow-up
- DOT group at 24 weeks
  - Better adherence (86% vs. 56%, $p<0.0001$)
  - More likely to have undetectable viral load (OR 3.1, CI 1.1-5.4)

Berg, Litwin, Li, et al. *Drug Alcohol Depend*. 2011;113:192-199.

Treatment Options

- History of prior drug use is an insufficient reason for withholding ART
- Usually, it is possible to support active drug users such that acceptable ART adherence levels are achieved
  - Requires coordination of drug treatment, medical and psychiatric care, and harm reduction services (e.g., syringe exchange)

Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*. Department of Health and Human Services. January 10, 2011; 1–166. Available at http://www.aidsinfo.nih.gov/ContentFiles/ AdultandAdolescentGL.pdf. Accessed 06/11/13.

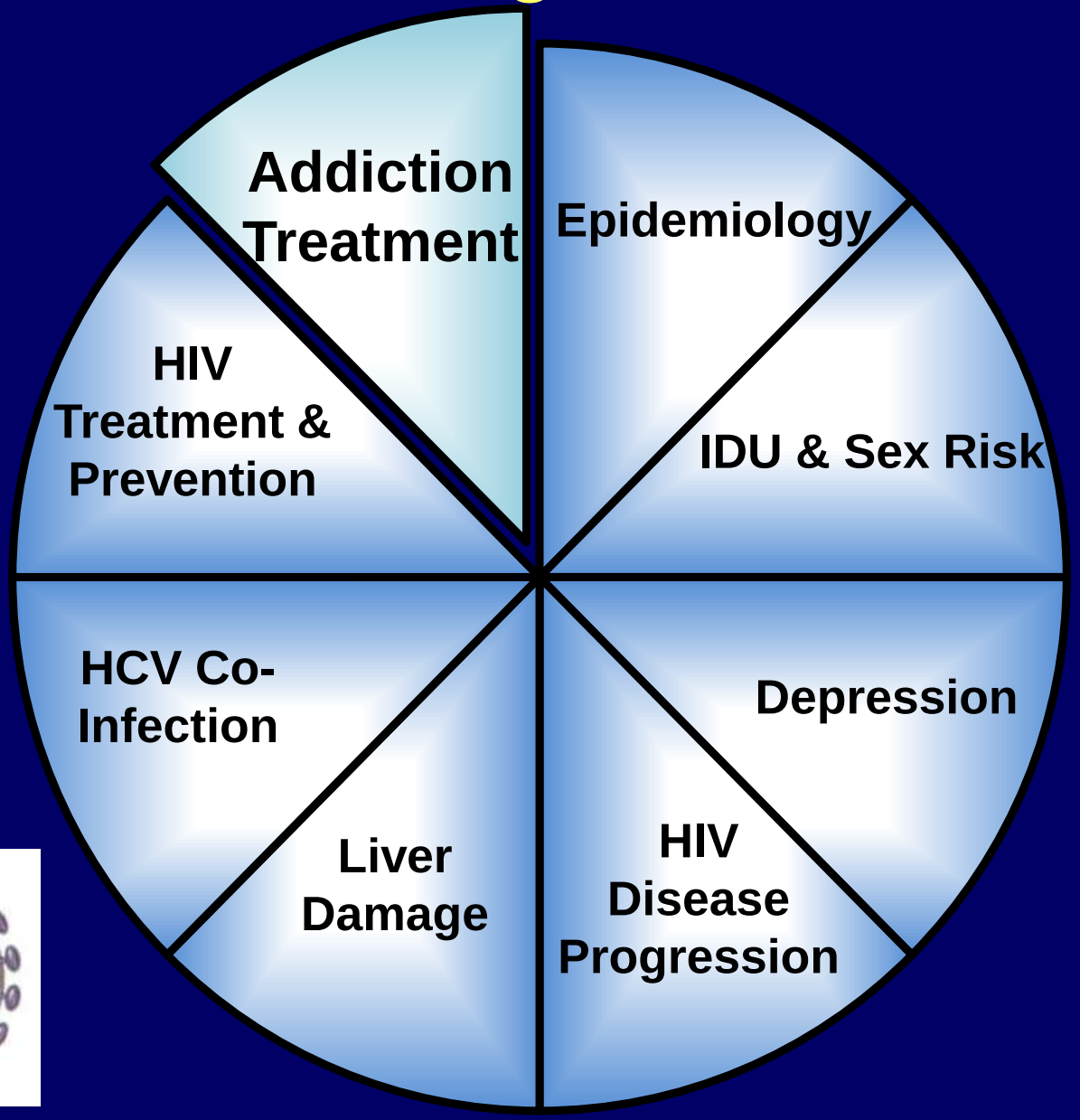
PRe-Exposure Prophylaxis (PREP) in IDUs

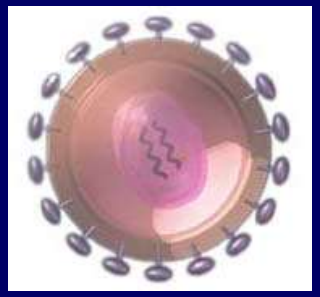
- RCT of tenofovir in IDUs enrolled in methadone clinics in Thailand (n=2413)
- Participants chose either daily DOT or monthly visits and could switch at monthly visits
- Tenofovir significantly associated with reduction in HIV incidence

	Tenofovir	Placebo	% Reduction (95% CI)
Infections/person years	17/4843	33/4823	48.9 (9.6-72.2)

Choopanya K, Martin M, Suntharasamai P, et al. *Lancet.* 2013;381:2083–90.

Alcohol, Drug Use, and HIV





Behavior Change After Testing HIV Positive

- HIV Cost and Services Utilization Study (HCSUS) sample of HIV-infected persons in medical care in 1996 (n=2,864)*
  - 80% of substance users quit or cut down drug use since diagnosis
  - Persons with CD4 counts <50 at some point were also more likely to quit or reduce substance use

- IDUs in the Ukraine (n=1,798), after testing positive for HIV:†
  - Less unprotected sex (OR 0.6, CI 0.4-0.7)

* Collins, Kanouse, Gifford, et al. *Health Psychol*. 2001;20:351-60.
† Booth, Lehman, Dvoryak, Brewster, Sinitsyna. *Addiction*. 2009;104:1864-1873.

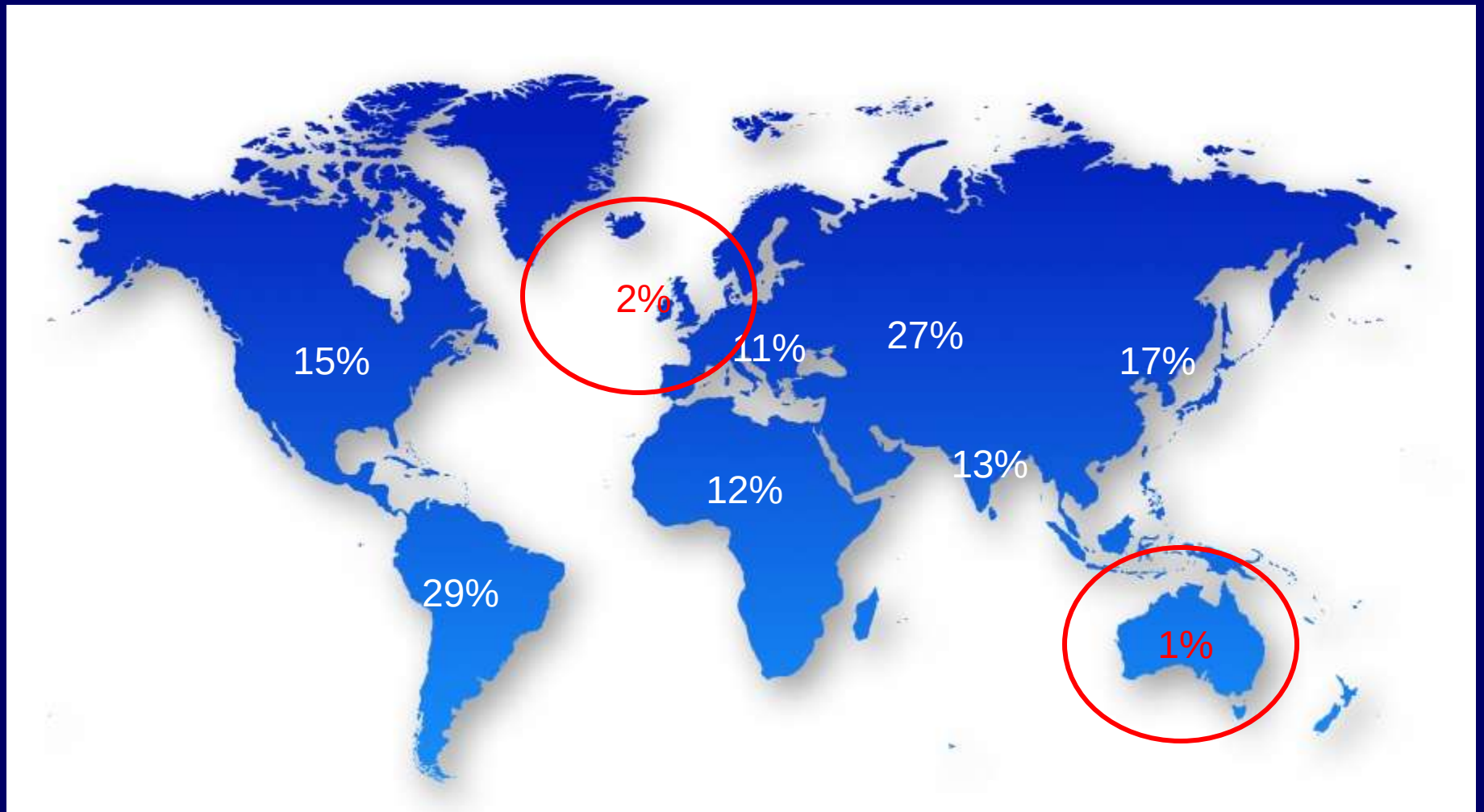
Needle Exchange Program (NEP)

- Review of 42 studies from 1989-1999 among IDUs*
  - Decrease in HIV risk behavior
  - Decrease in HIV seroconversion

- Review of 7 international studies from 1991-2001†
  - Cost-effective
  - Feasible to implement internationally
  - Applicable to special populations

* Gibson, Flynn, Perales. *AIDS*. 2001;15:1329-1341.
† Wodak, Cooney. *Substance Use & Misuse*. 2006;41:777-813.

Global HIV Prevalence Among IDUs



*Mathers, Degenhardt, Phillips, et al. Lancet. 2008;372:1733-1745.

Availability of Syringe Distribution and Exchange

- Great Britain and Australia have some of the lowest HIV prevalence rates among IDUs (~2%[*] and ~1%[†])
- Reflects early adoption of harm reduction measures (c. 1986)[†]
    - Needle exchange programs
    - Opioid agonist treatment

[*] Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.
[†] Wodak, Maher. *NSW Public Health Bulletin*. 2010;21:69-73.

Addiction Pharmacotherapy

- Heroin*
  - Methadone
  - Buprenorphine
  - Injectable naltrexone
- Alcohol*
  - Naltrexone
  - Acamprosate
  - Disulfiram
- Cocaine: none (only investigational†)
  - Modafinil
  - GABA-ergic compounds (e.g. vigabatrin, topiramate)
  - Disulfiram
  - Vaccine (TA-CD)
- Methamphetamine: no medications

* Bruce, Kresina, McCance-Katz. *AIDS*. 2010; 24:331-340.
† Kampman. *Curr Psychiatry Rep*. 2010; 12:441-447.

Addressing Addiction in HIV Care

- HIV-infected adults (n=951) receiving care at 14 sites*
  - 71% using substances; 24% receiving substance use treatment
  - Less than half reported discussing substance use issues with HIV care provider
- Need for providers to address substance use problems
- Audio-tapes of physician-patient encounters (n=413)†
- Quality of patient-provider communication
  - Good for illicit drug users
  - Worse for those with unhealthy alcohol use (shorter visit length, fewer activating/engaging and psychosocial counseling statements)

* Korthuis, Josephs, Fleishman, et al. *J Subst Abuse Treat*. 2008;35:294-303.
† Korthuis, Saha, Chander, et al. *AIDS Behav*. 2011;15:832-841.

OAT & HIV Outcomes

- HIV-infected Vancouver IDUs on ART, 1996-2003 (n=278)*
  - Methadone OAT associated with
    - Good adherence (OR 1.5; 95% CI 1.2-2.0)
    - HIV RNA suppression (OR 1.3, CI 1.0-1.8)
    - CD4 cell count rise (OR 1.6, CI 1.3-2.0)
- Prospective cohort of ART-naïve, HIV-infected IDUs in Vancouver, 1996-2008 (n=231)†
  - Methadone OAT associated with
    - Earlier ART initiation (RH 1.6, CI 1.2-2.3)

* Palepu, Tyndall, Joy, et al. *Drug Alcohol Depend*. 2006;188-194.
† Uhlmann, Milloy, Kerr, et al. *Addiction*. 2010;105:907-913.

OAT and HIV Transmission

- Meta-analysis of studies that assessed methadone OAT and HIV incidence in IDUs (n=9 studies)
- OAT associated with 54% reduction in risk of acquiring HIV (RR 0.46, CI 0.32-0.67)
- Methadone detoxification treatment not associated with decrease in risk (RR 1.54, CI 1.05-2.26)

MacArthur, Minozzi, Martin, et al. *BMJ.* 2012;345:e5945.

Buprenorphine OAT

- Advantage of buprenorphine OAT*
  - Efficacy and retention comparable to methadone
  - Milder withdrawal symptoms
  - Very low risk of overdose
  - Decreased risk of abuse and diversion with *buprenorphine/naloxone (bup/nal)*
- Can be effectively delivered in primary care (e.g. a collaborative nurse care-manager model†)

* Johnson, Chutuape, Strain, Walsh, Stitzer, Bigelow. *New Engl J Med*. 2000; 343:1290-1297.
† Alford, LaBelle, Kretsch, et al. *Arch Intern Med*. 2011; 171:425-431.

Buprenorphine OAT

- Longitudinal analysis of HIV+ patients on *bup/nal* (n=166)
  - *bup/nal* associated with significant reductions in HIV sex and drug-related risk behaviors from baseline to 12 and 24 weeks

	BL	12 wks.	24 wks.	P value
IDU in past 3 months	37%	12%	7%	< 0.001
Sex while “high”	64%	13%	15%	< 0.001

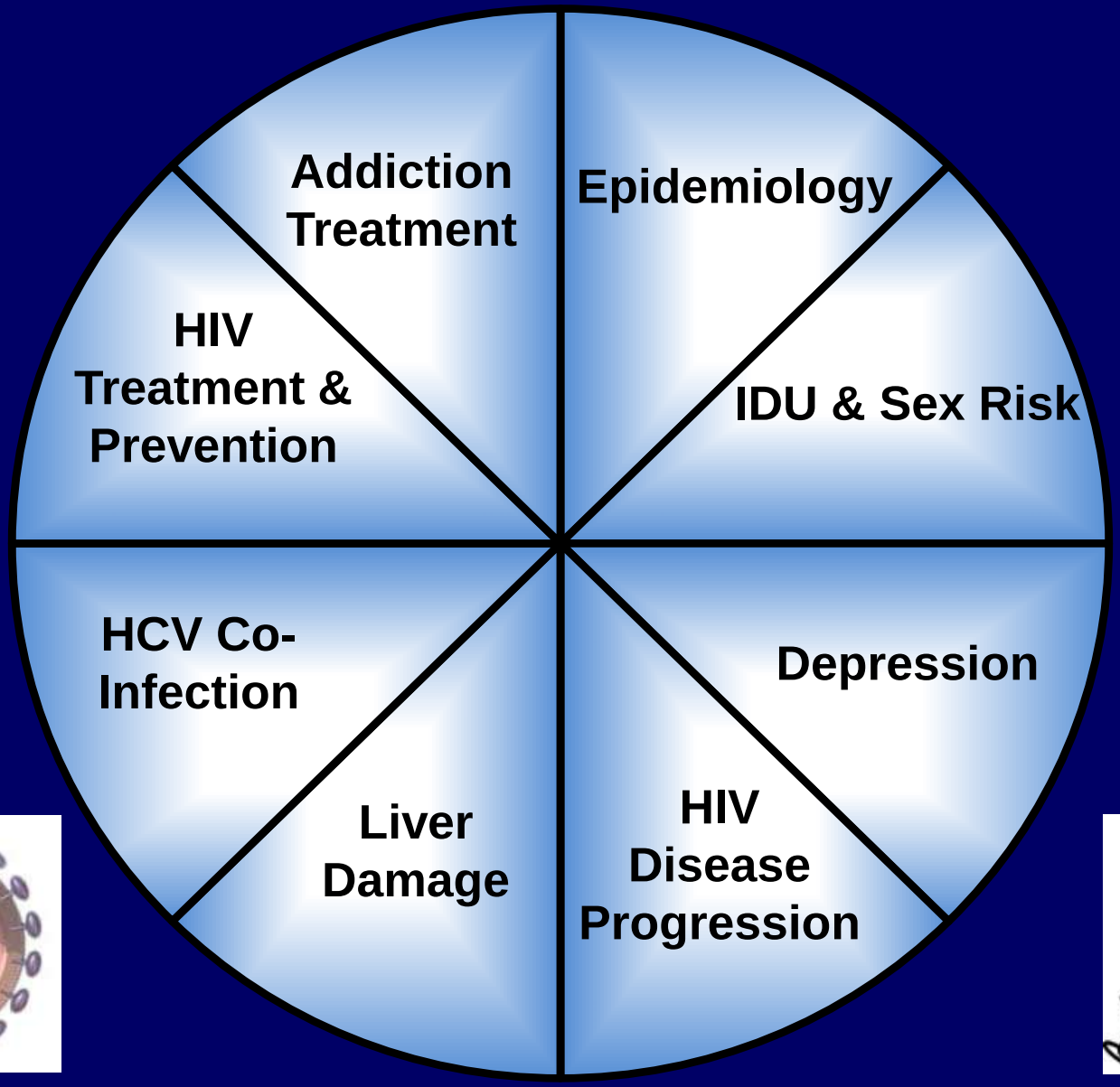
Sullivan, Moore, Chawarski, et al. *J Subst Abuse Treat.* 2008;35:87-92.

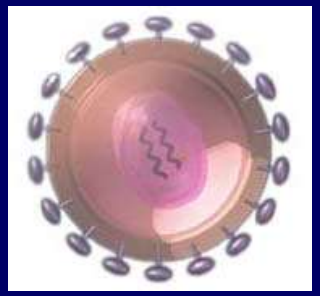
Drug Interactions: ART and Addiction Pharmacotherapy

- IDUs receiving ART and OAT (n=120)*
  - Median methadone dose increase:
    - 20 mg/d ($p<0.001$) with nevirapine
    - 7.5 mg/d ($p=0.004$) with efavirenz
  - No significant increase required for patients on ritonavir-boosted lopinavir
- Buprenorphine had no effect on early and newer protease inhibitors (early PIs n=30†) (newer PIs n=21‡)

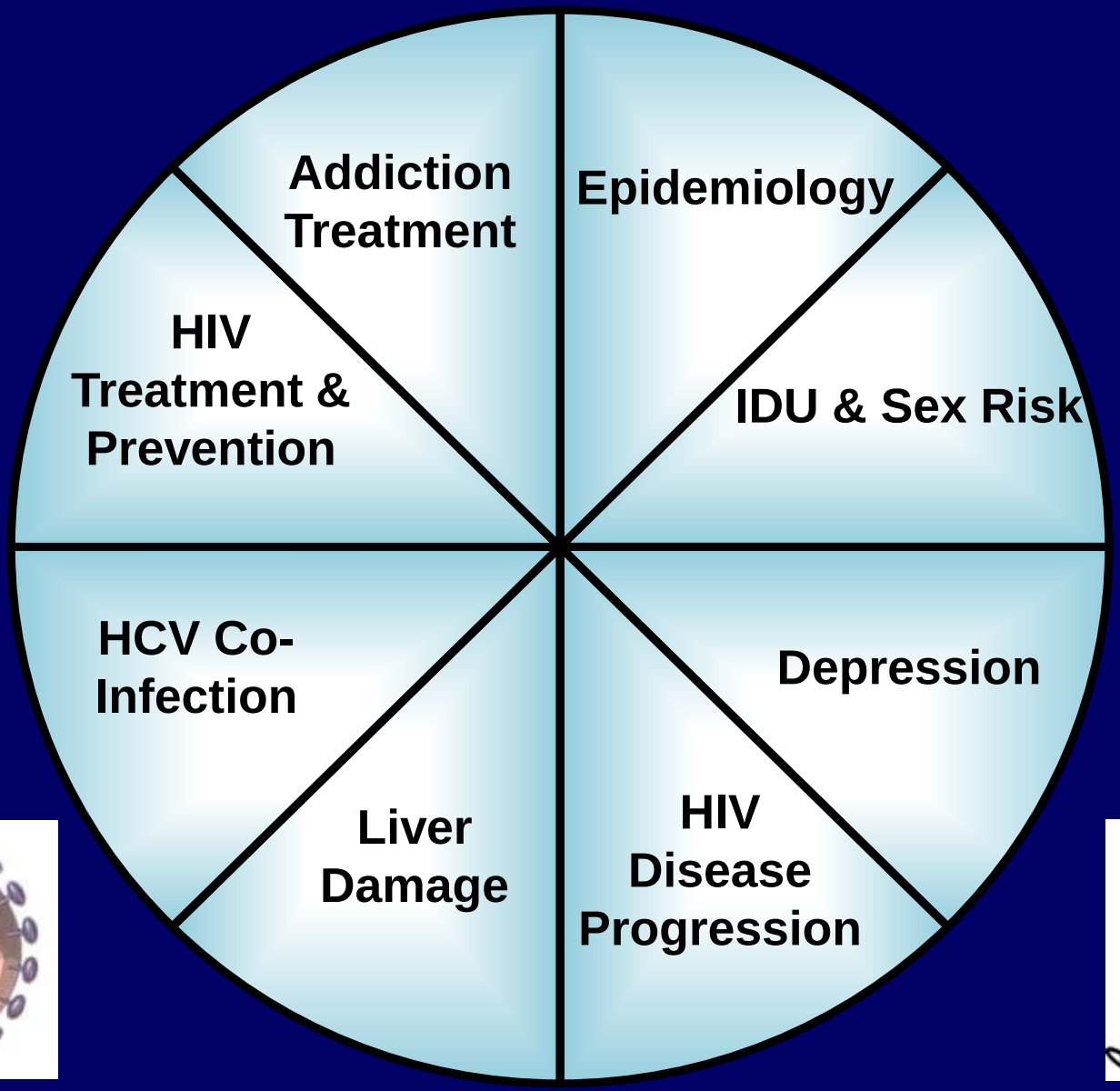
* Tossonian, Raffa, Grebely, et al. *JAIDS*. 2007;45:324-327.
† McCance-Katz, Moody, Smith, et al. *CID*. 2006;43:S235-246.
‡ Gruber, Rainey, Moody, et al. *CID*. 2012;54:414-423.

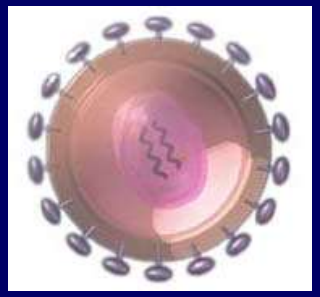
Alcohol, Drug Use, and HIV





Alcohol, Drug Use, and HIV

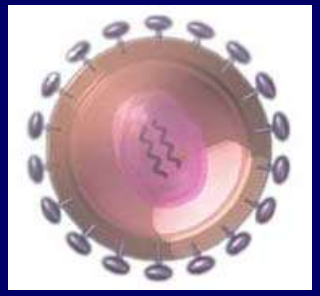




Alcohol, Drug Use, and HIV

Current Research Studies:

- LINC
- URBAN ARCH
- ZINC



LINC

- **L**inking **I**nfectious and **N**arcology **C**are
- R01 DA032082 (07/2011 - 04/2016)
- RCT of a behavioral and structural intervention to support and motivate HIV-infected Russian IDUs to engage in HIV medical care (n=350)
- Outcomes:
  - Initiation of HIV care
  - Retention in HIV care
  - Receipt of *quality* HIV care
  - HIV disease progression

Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS

URBAN ARCH Theme:

Examine the consequences of alcohol on HIV disease and mitigate its harmful effects.

www.urbanarch.org

Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS

- Uganda Cohort: Does heavy alcohol consumption accelerate HIV disease progression in ART-naïve HIV-infected individuals?
  - PI: Judith Hahn (U01 AA020776)
  - Prospective Cohort (n=650)
  - Biomarkers: CD4, HIV VL, PEth (n=250 - IL-6, sCD14)
  - Status: 307 enrolled (6/13)

Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS

- Boston Cohort: Is alcohol use associated with decreased bone density among HIV-infected drug users?
  - PI: Richard Saitz (U01 AA020784)
  - Prospective Cohort (n=250)
  - Biomarkers: CD4, HIV VL, PEth, vit D
  - Bone mineral densitometry
  - High resolution peripheral quantitative CT

  Status: 81 enrolled (6/13)

- Concurrent double-blind placebo-controlled RCT (n=100):
  - Can high-dose buprenorphine/naloxone (32mg) reduce heavy drinking days compared to standard-dose (16mg) at 3 months?

Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS

- Russia Cohort: Is heavy alcohol use associated with elevated inflammatory markers in ART-naïve HIV-infected individuals?
  - PI: Jeffrey Samet (U01 AA020780)
  - Prospective Cohort (n=250)
  - Biomarkers: sCD14, D-dimer, CD4, IL-6
  - Status: 61 enrolled (6/13)

ZINC

- Zinc for INflammation and Chronic disease in HIV (ZINC)
- Multiple PIs: Matthew Freiberg and Jeffrey Samet
- Double-blind RCT to assess the efficacy of zinc supplementation among 250 HIV-infected Russian ART-naïve heavy drinkers
  - Improve markers of mortality (VACS index)
  - Slow HIV disease progression (CD4 cell count)
  - Improve markers of acute MI risk (Reynolds score)
  - Decrease microbial translocation and inflammation (biomarkers)
- 2012-2017
- NIAAA (U01 AA021989)

International Research Team

Uganda Team

- Judy Hahn, PhD, MA
- Nneka Emenyonu, MPH
- Peter Hunt, MD
- Winnie Muyindike, MBChB, MMED
- Robin Fatch, MPH
- Starley Shade, PhD

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- Natasha Bushara, MD

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- David Fiellin, MD

URBAN ARCH Consortium
~ April 2013 ~