

Club drugs and HIV Intersecting epidemics among MSM

Grant Colfax, MD
Director, HIV Prevention
HIV San Francisco Department of Public
Health

What's new?

- Update epidemiology of club-drug use and HIV
- Describe relationship between club-drug use and HIV risk
- Describe current and potential future HIV prevention research among MSM club-drug using populations
 - To decrease club-drug use
 - To decrease sexual risk associated with club-drug use

What are club drugs?

- According to NIDA: include 3,4 methylenedioxy-methamphetamine (MDMA, ecstasy), gamma hydroxybutyrate (GHB), ketamine, amphetamines.
- Due to their prevalence in the MSM community, will also include poppers (amyl nitrites).
- Club drugs are generally not injected, but ingested orally, nasally, or rectally.

Prevalence of club-drug use among MSM National HIV Behavioral Surveillance System Survey, 2003-2005

	Used drug	Used drug during sex
Poppers	29%	89%
Meth/stimulants	27%	66%
Ecstasy	29%	52%
Other club drug	12%	58%

Source: MMWR, 2006

Club-drug use is common among MSM, but most MSM are episodic users

Site	Meth use	
	Last 12 months	Weekly or more
San Francisco	21%	6%
New York	14%	3%
Los Angeles	13%	4%
Chicago	10%	2%

A primer on club drugs Ecstasy

- Causes increased release of serotonin
- Results in euphoria, increased energy, and feelings of intimacy.
- Effects include:
 - Dehydration, hyperthermia, tachycardia, rhabdomyolysis
 - Cognitive impairment associated with long-term use



Gamma-hydroxybutyrate (GHB)

- Closely related to CNS neurotransmitter GABA.
- Increases CNS dopamine, possibly via interactions with GABA receptors.
- Influences sleep cycles, core temperature.



GHB

- Effects include:
 - CNS depression: hypothermia, hypotonia, amnesia, respiratory depression.
 - Tonic-clonic seizures: include in differential
 - Bradycardia, hypotension.
 - Well-documented tolerance and withdrawal symptoms
 - Narrow therapeutic index makes overdoses frequent, especially if combined with alcohol, which impairs clearance

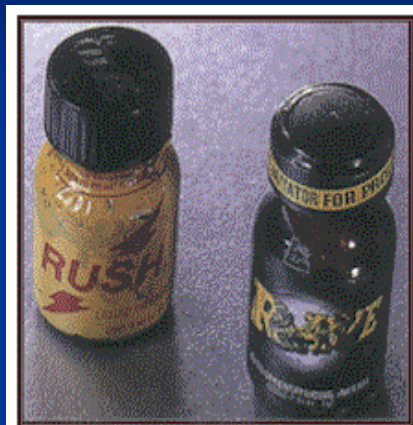
Ketamine

- Disassociative anesthetic
- Reduces excitatory amino aspartate activation in CNS
 - Hypertension, tachycardia, arrhythmias, amnesia
 - Respiratory depression, apnea.



Poppers

- Alkyl nitrates/nitrites
- Dilate smooth muscle, including increasing relaxation of anal sphincter.
- CNS effects include feeling “rush,” throbbing headaches, aura-like effects.
- Associated with anemia, decreased antibody and T-cell production, and increased tumor growth.
- Potentially fatal if combined with ED phosphodiesterase inhibitors (Viagra)



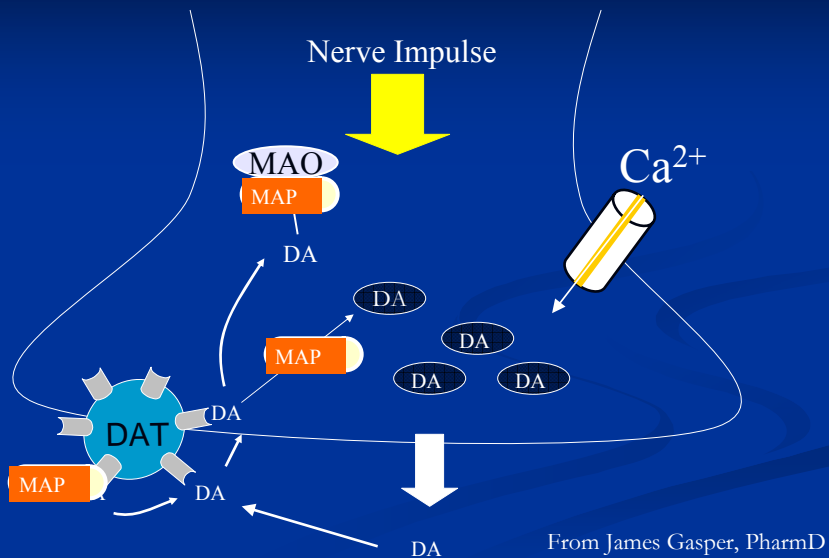
poppers

Methamphetamine

- Derived from ephedrine
- Short term effects:
increased energy, libido,
feelings of invulnerability
- Long-term effects:
depressed mood,
irritability, paranoia



DA Neurotransmission



Club drugs and HIV disease

- No studies have conclusively demonstrated that club drugs directly influence the progression of HIV disease.
 - Could club-drugs increase immune activation?
- Few data on adherence among club-drug users.
 - Adherence measures not validated among club-drug users.
- Potential interactions with ART: Ecstasy, GHB, ketamine, and meth are all partially cleared through p-450 system.

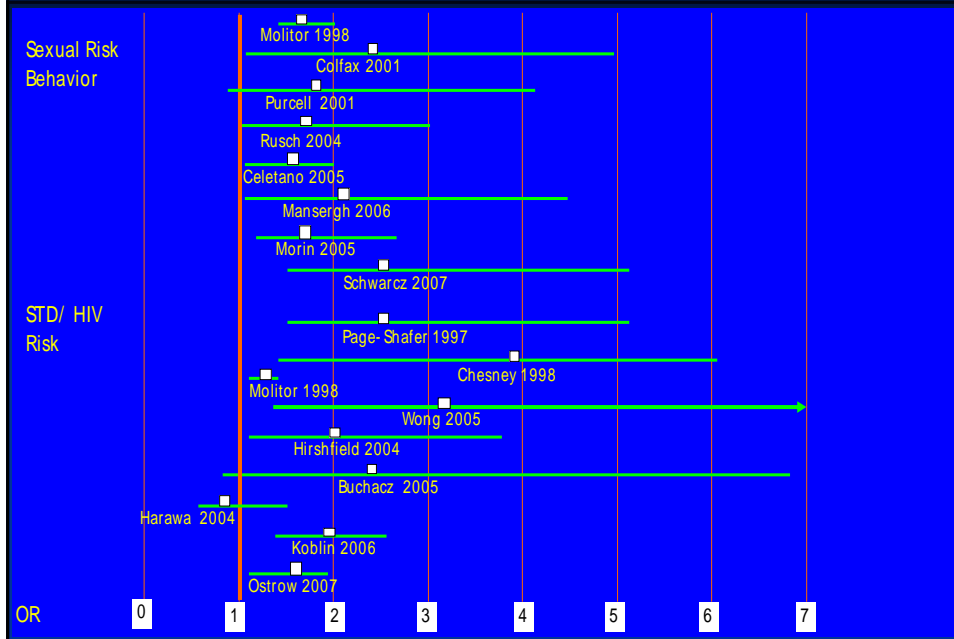
Club drugs and HIV risk

Non-injection substance use is associated with....

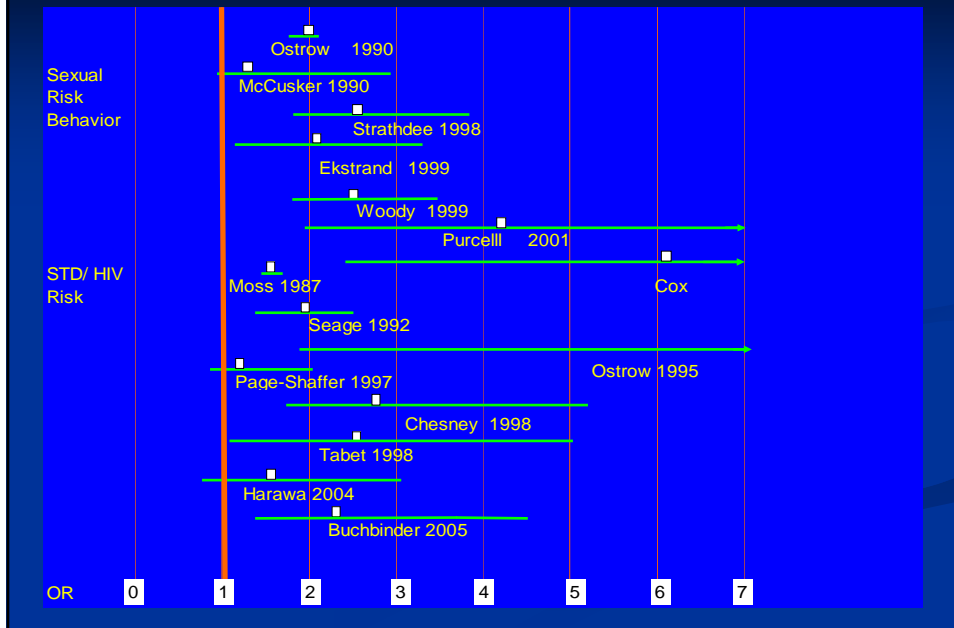
- ↑ Sex partners
- ↑ Unprotected sex
- ↑ Risk STDs
- ↑ Risk of HIV infection

....data most consistently show these associations with meth and popper...

Methamphetamine and HIV risk



Poppers and HIV risk



Methamphetamine and HIV seroconversion EXPLORE study results

Risk factor for HIV	AHR	95% CI	Attributable fraction
Methamphetamine use	1.9	1.4-2.6	16
URA with HIV+	3.4	2.2-5.1	18
URA with unknown status	2.8	2.1-3.8	28
Gonorrhea	2.5	1.4-4.2	4

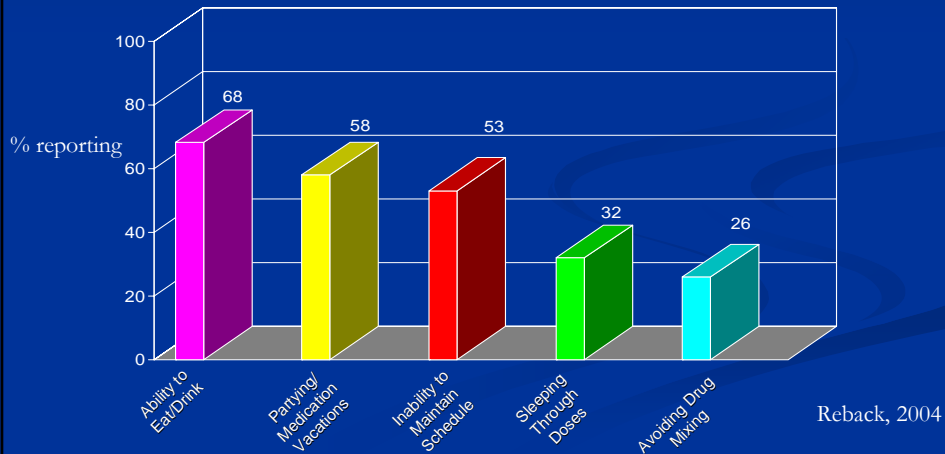
Koblin, Husnik, Colfax, et. al, AIDS 2006

How can club-drug use be independently associated with HIV infection?

- Unmeasured behavioral confounders
 - More traumatic sex
 - Partner selection
 - Higher viral loads
 - More likely to be HIV-positive
 - Biased reporting
- Direct biologic effects
 - Impaired T-cell responses
 - Pro-inflammatory
 - Increased viral load

Non-adherence due to methamphetamine use

- 100% of participants claimed that their meth use had an effect on adherence



Methamphetamine and primary drug resistance

- Methamphetamine in OPTIONS cohort, 1996-2005
 - 400 SF MSM with recent HIV infection
 - 27% reported meth use in 30 days prior to enrollment
 - In multivariate analysis, meth use associated with primary drug resistance (OR 2.8, 95% CI 1.1-7.0)
 - Driven by NNRTI resistance (OR 3.5, 95% CI 1.2-10.8)

Colfax, Hecht, Grant, et. al, AIDS 2007

Interventions for club-drug users

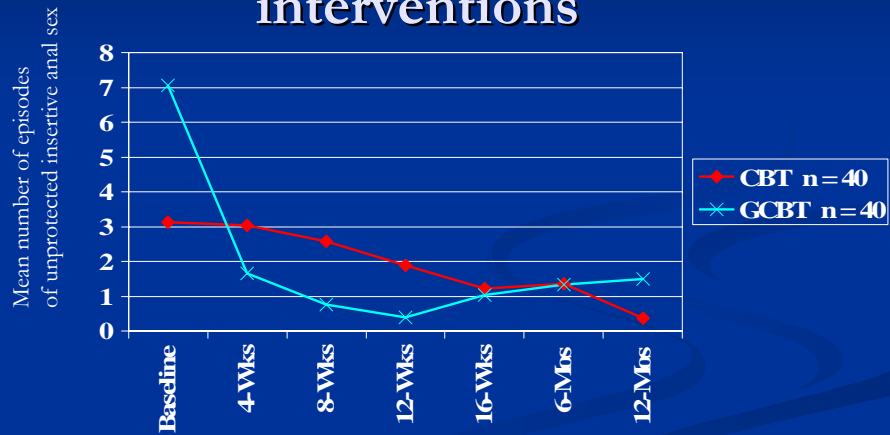
- Approaches
 - Counseling
 - Contingency management
 - Pharmacologic

Counseling for meth dependence is associated with reduced meth use

- MATRIX intervention
 - Meth-dependent persons in treatment programs
 - Abstinence-based, relapse prevention model
 - Primarily heterosexuals
- 56 behavioral sessions vs. standard outpatient treatment
- Compared with standard treatment:
 - Meth use decreased more in intervention during active phase
 - Similar reductions in meth use in standard and intervention arms at 6-month follow-up

Rawson, 2004

Risk behavior declines among MSM in meth behavioral interventions

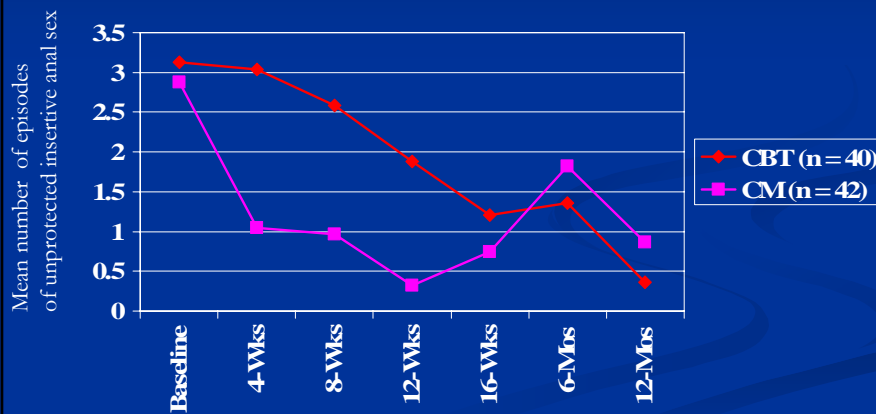


Shoptaw 2005

Contingency Management

- Provides positive reinforcement in form of vouchers for producing drug-free urine samples
 - Participants earn up to \$200-\$1,000 in vouchers
 - Observed urine samples collected 3x weekly
 - Reduces rates of heroin, cocaine, alcohol use

MSM in contingency management reduce risk



Shoptaw 2005

Will a behavioral risk-reduction approach work among club-drug using MSM?

- Project MIX
 - Non-treatment seeking MSM
 - Six group sessions vs. control
 - Primary outcome: sexual risk behavior
- ADAPT study
 - Targets episodic substance-using MSM
 - Based on risk-reduction intervention by Dilley et. al.
 - Single-session intervention examining self-justifications for episodic substance use

Behavioral interventions Challenges

- How efficacious are they?
 - To date, small sample sizes among SUMSM
 - Unknown what degree of behavior change is necessary to reduce HIV infection rates
- Generalizability
 - Can heavier drug users consistently engage in and re-learn healthier behaviors?
 - Behavioral interventions generally tested among treatment-seeking populations
- Feasibility

Pharmacologic treatment for methamphetamine users

- Pharmacologic treatments successful for heroin, tobacco, alcohol dependence.
- Can medications stabilize neurotransmitter levels among meth users, leading to reductions in meth use?
 - Will MSM meth users adhere to medications?
 - Are they willing to enroll in placebo-controlled studies?
 - Will they tolerate the side effects of medications?
- Failed or unpromising agents: sertraline, amlodipine, imipramine, dextroamphetamine

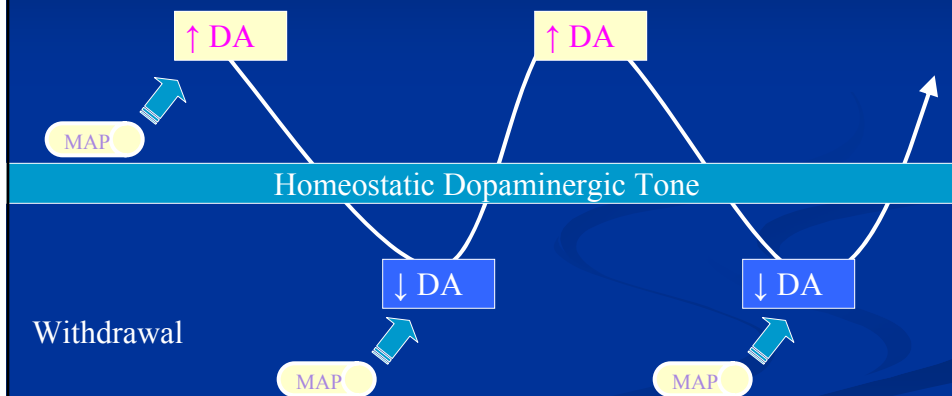
Methamphetamine users are deficient in dopamine



NIDA, 2005

Treatment Considerations: DA Dysfunction

Intoxication



Courtesy of James Gasper

Bupropion

- RCT of heterosexual, meth-dependent users
- 48% study completion
- GEE analysis: more bupropion participants had meth-free urine week ($p = .09$).
- Low/moderate meth users had significantly more meth-free weeks ($p = .05$)
- Trial among MSM in progress

Ahmed, in press, 2007

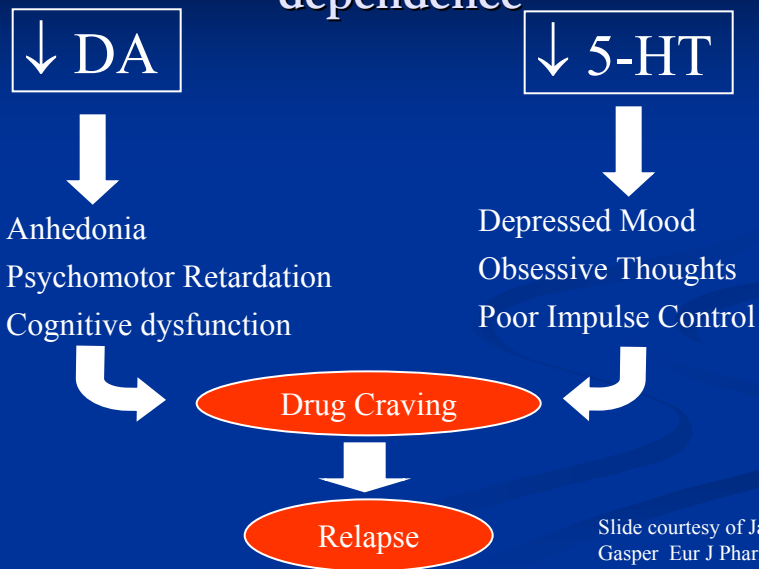
SFDPH: Medication studies among meth-dependent MSM



tweaked?
we may have an alternative.
415.554.9013

BUMP
San Francisco Department of Public Health

The Dual Deficit Model of drug dependence



Slide courtesy of James Gasper Eur J Pharm 2003;479:23-40

Dual-action drugs

- Mirtazapine (Remeron)
 - Another antidepressant
 - “Dual action” - - works on serotonergic and dopaminergic pathways
 - Small RCT in Thai meth-dependent persons
 - Mirtazapine reduced meth withdrawal symptoms
 - Independent of effects on depression

Source: Kongsakon 2005

Mirtazapine study SFDPH

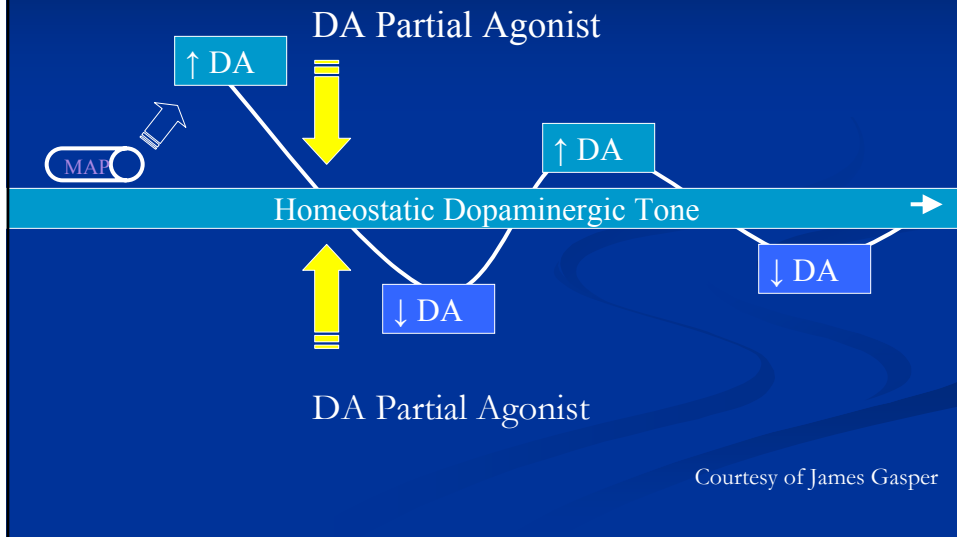
- RCT, double-blind, placebo-controlled
- 1:1 randomization
- N = 60 MSM
 - Currently enrolling
- Primary outcome: meth use, as detected via urine
- Secondary outcome: adherence, risk behavior

Pharmacologic approaches....

- Aripiprazole
 - “Atypical” antipsychotic
 - Relatively few side effects
 - D2 partial agonist
 - May prevent meth withdrawal
 - May decrease effects of meth use
 - Double-blind, drug discrimination studies show aripiprazole blocks meth’s effects compared with placebo

Sources: Lile 2005; De la Garza, 2005

Treatment Considerations: DA Dysfunction



hythiam
PROMETA[®]

Or have us call you.
CALL ME

HEALTHCARE PROFESSIONALS | LICENSEES

SEARCH

STAY IN TOUCH

We're here for you.
CALL TOLL FREE
1-866-321-6558

www.hythiam.com

Prometa

Which of the following is true?

1. Is a proven treatment for meth dependence
2. Is free
3. Is FDA approved
4. Has been marketed aggressively to vulnerable populations

Prometa approach

- Combination therapy with counseling
- Advocated for stimulant tx and alcohol use
- \$8,000 - \$15,000 per course
- 3 infusions followed by outpatient treatment - - for 23 days, followed by two additional infusions
- Medications: hydroxyzine, flumazenil, gabapentin, multivitamin

Could it work?

- Flumazenil: benzodiazapine antagonist; partial agonist at GABA receptors;
 - Stimulant users have high levels of GABA dysregulation.
 - Restoration of GABA tone = reduced craving
 - Anxiolytic
- Gabapentin: Works on glutamate
 - Glutamate circuits critical in the nucleus accumbens
 - Restoration of glutamatergic tone = reduced craving
- RCT in progress
 - NO conclusive data at this time
 - Shareholder company with profit motive
 - Heavily marketed to vulnerable populations
 - Off-label treatment at its worse

Pharmacologic interventions Challenges

- May need to be combined with behavioral therapy for greatest efficacy
 - But very intensive behavioral platforms may overwhelm any detectable drug effects
- Prior studies of other agents have been negative or inconclusive
- Side effects
- Duration
- Cost

Conclusions

- Club-drug use among MSM is common
 - High across many areas in US
 - Most use is episodic
- Meth, poppers associated with consistent increases risk for HIV infection
 - About double risk
 - Behavioral dis-inhibition
 - Plausible biologic mechanisms
- Critical need for continued testing of interventions
 - Meth users in behavioral interventions reduce risk
 - Some pharmacologic interventions for meth promising, but not proven
- Ask your patients if they are using club drugs
 - Refer for treatment
 - Substance use treatment
 - Risk-reduction counseling
 - Frequent HIV/STI testing!

Acknowledgements

- San Francisco Department of Public Health: David Bandy, Susan Buchbinder, Henry Raymond-Fisher, Jonathan Fuchs, Reggie Gage, James Gaspar, Abel Gonzalez, Robert Guzman, Jeff Klausner, Tim Matheson, Willi McFarland, Deirdre Santos, Susan Scheer, Sandy Schwarcz, Tory Sostillio
- UCSF: Bob Grant, Rick Hecht, Paula Lum, Meg Newman, Eric Vittinghoff
- UCLA: Cathy Reback, Steve Shoptaw
- CDC: Gordon Mansergh, David Purcell