The Changing Landscape of Marijuana (Cannabis): What’s Real and What’s Not

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APA Division 50
Clinical Forum 11/11/16
Disclosures - Budney

Funded by National Institute on Drug Abuse - NIH has supported my research and conference attendance for about 25 yrs

Copy of Slides, Articles, or Other:

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https://www.youtube.com/watch?v=o4W6cS_9xk
Reefer Madness
Goals / Conclusions

1. Characterize cannabis use, misuse, or addiction
   - substantial abuse potential and consequences
2. Clinical Epidemiology: Prevalence of Problems
   - comparable or greater than other substances; increasing?
3. Treatment Responsivity
   - “efficacious” treatments
   - but, limited efficacy, need more potent methods, extend reach
4. Describe the Changing Landscape
   - more potent products, alternative ways of use – increase risk?
   - therapeutic use / medical marijuana: Data are sorely lacking!!
DO YOU THINK...

• Cannabis has addictive potential?
• Cannabis withdrawal is clinically important?
• Quitting Cannabis is relatively easy?

• Cannabis has benefit for ADHD, PTSD, Anxiety?
• Cannabis has benefit for Epilepsy?
• Cannabis has therapeutic benefit for Pain?
• Cannabis use increases risk of psychosis?
DO YOU THINK …

- Vaping is a safe way to use Cannabis?
- Eating is a safe way to use Cannabis?
- Cannabis is as dangerous as Alcohol?
- We should legalize Cannabis?
  - Medical? Recreational? Just One, Both?
We Know that Cannabis Use Can Develop into an “Addiction”

Cannabis Use Disorder (CUD) is not qualitatively different from other SUDs
Evidence for Addictive Potential
Biological, Behavioral, Epidemiological

• Endogenous cannabinoid system in the CNS
• Effects of administration and cessation on the reward centers of the brain are similar to that of other drugs with addictive potential
• Functions as a reinforcer in the human laboratory
• People meet use disorder (“dependence”) criteria
• Evidence for a Withdrawal syndrome
• People seek help for CUD
• Difficult to quit; high rates of relapse
## How Does Cannabis Compare to Cocaine Dependence?

<table>
<thead>
<tr>
<th></th>
<th>Cannabis</th>
<th>Cocaine</th>
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</thead>
<tbody>
<tr>
<td># of DSM-III-R criteria</td>
<td>6.3 (1.8)</td>
<td>7.7 (1.2)*</td>
</tr>
<tr>
<td>Continued Use</td>
<td>97%</td>
<td>97%</td>
</tr>
<tr>
<td>Cut Down</td>
<td>86%</td>
<td>93%</td>
</tr>
<tr>
<td>Larger Amounts</td>
<td>80%</td>
<td>100%*</td>
</tr>
<tr>
<td>Excessive time</td>
<td>73%</td>
<td>87%*</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>75%</td>
<td>81%</td>
</tr>
<tr>
<td>Tolerance</td>
<td>63%</td>
<td>97%*</td>
</tr>
<tr>
<td>Reduced Activities</td>
<td>41%</td>
<td>87%*</td>
</tr>
</tbody>
</table>

*(Budney et al., 1998)*
Cannabis Use Disorder (CUD) Compared with other SUDs
Shmulewitz et al. 2015; Hasin et al. 2013; Budney, 2006

Over 30 International Population-based Studies

CUD highly similar to other disorders
- unidimensional construct (IRT analyses)
- full range of criterion are endorsed
- less severe than cocaine, opioid or alcohol
- most prevalent SUD behind alcohol & tobacco
Cannabis Withdrawal

Cannabis Withdrawal demonstrated in:

– Non-human studies (primate, rodent, dog)
– Human inpatient/outpatient laboratory studies
– Clinical survey studies

Budney et al. 2004
True Withdrawal Syndrome
(Hughes 1990)

• Reliable abstinence symptoms
• Not Rare
• Onset, with Transient Timecourse
• Pharmacological Specificity
• Clinical Importance
Cannabis Withdrawal
Onset and Timecourse
(Budney et al. 2003)
Pharmacological Specificity: Effect of oral THC (dronabinol) on Withdrawal

Budney, Vandrey et al, 2007
Cannabis & Tobacco Withdrawal
(Vandrey et al., 2005; Vandrey et al. 2008, Budney et al., 2009)
Clinical Importance of Cannabis WD

Use cannabis (or other substances) to relieve WD

Complain about WD; makes quitting difficult

# of WD symptoms predicts dependence severity

WD severity predicts rapid relapse (adolescents)

(Budney et al., 2006)
Cannabis Withdrawal Symptoms

1) irritability, anger, or increased aggression
2) nervousness or anxiety
3) sleep difficulty (insomnia)
4) decreased appetite or weight loss
5) restlessness
6) depressed mood
7) at least 1 physical symptom causing significant discomfort (stomach pain, shakiness/tremors, sweating, fever, chills, headache)
Cannabis Use Disorder is real.

When it occurs, it manifests much the same as other types of Substance Use Disorders.
What is the prevalence of CUD?

How often does CUD occur among users?
# NESARC 2002 vs. 2012

## Past Year Marijuana Use

Table 1. Past-Year Prevalence of Marijuana Use by Sociodemographic Characteristics, 2001-2013

<table>
<thead>
<tr>
<th>Sociodemographic Characteristics</th>
<th>NESARC Wave 1, 2001-2002</th>
<th>NESARC-III, 2012-2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4.1 (0.15)</td>
<td>9.5 (0.27)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>5.6 (0.24)</td>
<td>12.3 (0.40)</td>
</tr>
<tr>
<td>Female</td>
<td>2.6 (0.15)</td>
<td>6.9 (0.29)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>10.5 (0.47)</td>
<td>21.2 (0.67)</td>
</tr>
<tr>
<td>30-34</td>
<td>4.1 (0.24)</td>
<td>10.1 (0.41)</td>
</tr>
<tr>
<td>45-64</td>
<td>1.6 (0.15)</td>
<td>5.9 (0.28)</td>
</tr>
<tr>
<td>≥65</td>
<td>0.0 (0.02)</td>
<td>1.3 (0.22)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4.1 (0.17)</td>
<td>9.4 (0.34)</td>
</tr>
<tr>
<td>Black</td>
<td>4.7 (0.35)</td>
<td>12.7 (0.64)</td>
</tr>
<tr>
<td>Native American</td>
<td>7.0 (1.15)</td>
<td>17.1 (2.32)</td>
</tr>
<tr>
<td>Asian</td>
<td>3.1 (0.54)</td>
<td>5.0 (0.59)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3.3 (0.31)</td>
<td>8.4 (0.50)</td>
</tr>
</tbody>
</table>

Hasin et al. (2015)
## NESARC 2002 - 2012

### Rates of Past Year CUD

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2002</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 and older:</td>
<td>1.5%</td>
<td>2.9%</td>
</tr>
<tr>
<td>18-29 years:</td>
<td>4.4%</td>
<td>7.5%</td>
</tr>
<tr>
<td>30-44 years:</td>
<td>1.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td>45-64 years:</td>
<td>0.4%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>
NESARC 2012
Conditional Probability of Past Year CUD

(Hasin et al., 2015)
Prevalence of Cannabis Use and Conditional Probability of Use Disorders

NSDUH 2011
(Wu et al., 2013)
Prevalence of Use and Conditional Probability of Use Disorders x Race/Ethnicity

NSDUH 2011
(Wu et al., 2013)
Summary

• 50% increase in cannabis users over last decade
• Almost 50% increase in Cannabis Use Disorders
• Increase in CUD related to increased # of users?

However:
• NHSDU: only shows 12% increase
• MTF (youth): similarly lower rate of increase
What do we know about the prevalence of treatment seeking for CUD?
Treatment Admissions Primary Substance
2012 TEDS Data (12 and older)

% of Total Admissions

- Alcohol
- Marijuana
- Opiates
- Cocaine
- Stimulants

Year: 2002 vs 2012
Treatment Admissions Primary Substance
2012 TEDS Data (12 – 17 years)
Persons with CUD make up a substantial proportion of treatment admissions!
What do we know about how effective treatment is for CUD?
Pharmacotherapy / Medications

Potential Targets:
- Withdrawal symptoms: mood, sleep, anxiety
- CB1 receptor agonist substitution
- CB1 antagonists
- Opioid antagonists
- GABA and Glutamate (Gabapentin, NaC)
- Enzymatic targets (FAAH)

** No robust findings to date!**
<table>
<thead>
<tr>
<th>Study</th>
<th>Treatments</th>
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<tbody>
<tr>
<td>Stephens, et al. (1994)</td>
<td>SS, CBT</td>
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<tr>
<td>Stephens, et al. (2000)</td>
<td>MET, CBT</td>
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<tr>
<td>Budney et al. (2000)</td>
<td>MET, MET/CBT, MET/CBT/CM</td>
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<tr>
<td>Copeland et al. (2001)</td>
<td>MET/CBT</td>
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<tr>
<td>MTPG (2004)</td>
<td>MET, MET/CBT</td>
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<td>Budney et al. (2006)</td>
<td>MET/CBT, CM, MET/CBT/CM</td>
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<tr>
<td>Carroll et al. (2006)</td>
<td>MET/CBT, DC, MET/CBT/CM, DC/CM</td>
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<tr>
<td>Kadden et al. (2007)</td>
<td>MET/CBT, CM, MET/CBT/CM</td>
</tr>
<tr>
<td>Kay-Lambkin (2009, 2011)</td>
<td>MET/CBT (computerized)</td>
</tr>
<tr>
<td>Litt et al. (2013)</td>
<td>CaseM, CBT/CMabst, CBT/CMhmk</td>
</tr>
<tr>
<td>Hoch et al (2014)</td>
<td>CANDIS (MET/CBT/Problem Solving)</td>
</tr>
</tbody>
</table>
Motivational Incentives Enhance Point Prevalence Abstinence

(Budney et al. 2006); replicated in Carroll et al., 2006 and Kadden et al., 2007
Adolescent Treatment Literature

Family-based and group/individual behavioral interventions (Waldron 2008: review)

Waldron et al. FFT, CBT, combo
Liddle et al. MDFT
Henggeler et al. MST
Dennis et al./Godley et al. MET/CBT, ACRA, FSN
Kaminer et al. MET/CBT
Szapocznik et al. BSFT
Stanger, Budney et al. CM
Cannabis Youth Treatment Study
Abstinence at Discharge

(Dennis et al. 2004)
Incentives Enhance Abstinence Outcomes During but not Post Treatment

Stanger et al. 2015
CUD Treatment for Youth and Adults

Not yet identified effective Pharmacotherapy

Behavioral treatments are efficacious

Access to efficacious treatments is poor

Many people do not respond

Youth response appears lower than with adults?

Success in disadvantaged populations is low?

** Much room for Improvement
How Do We Improve?

Behavioral Science and Neuroscience Provide Targets

- Enhance Delivery Systems / Improve Access
- Endogenous Cannabinoid System; Withdrawal Syndrome
- Genetics
- Improve Brain Function / Impulsivity / Decision Making
- Innovative Incentive Programs
- Target Concurrent Tobacco Use
- Target Non-responders
- Innovative Use of Technology
- Extend Reach to Intervene with More Problem Users
What We Know About the Impact of the Changing Landscape of Cannabis Laws and Regulations

Potential for Positive and Negative Impact

- Higher Potency / New Products / New Delivery Systems
- Impact on Use, Attitudes, Perceived Risk
- Impact on Health, Public Safety
- Addiction / Problematic Use
- Science: Understanding of Cannabis
Legalization: “Medical” / “Recreational” (20-30 minutes)

Why is this important to Psychologists?

Unregulated Medicine? Populous Medicine?

Data-based; Empiricism

Approvals/Conditions

Nature of the Supportive Science

What’s real / what’s not?

Adverse Effects? What is tolerable?
A Changing Landscape of Cannabis Laws

• Medical marijuana legal in 28 states and DC
• Recreational marijuana legal in 8 states plus DC
• Both medical and recreational laws vary greatly by state
  – Approved medical conditions (in medically legal states)
  – Dispensaries allowed
  – Possession limits
  – Type of marijuana regulated (i.e. plant, edibles, concentrates)
• Legalization increases access to novel and potent forms of cannabis with little knowledge of consequences to public health
Reefer Madness
High Potency Cannabis Products
Reefer Madness
Edibles
Reefer Madness Devices
The “Farmacy” and the Market
EXPOs
Medical Cannabis Landscape:

What “should” you know before approving / prescribing cannabis for a medical or psychiatric condition?
Approved Medical Conditions across States

- Cachexia, cancer, chronic pain, epilepsy and other disorders characterized by seizures, glaucoma, HIV or AIDS, multiple sclerosis and other disorders characterized by muscle spasticity, and nausea, Hepatitis C, ALS, Crohn's disease, Alzheimer's disease, anorexia, arthritis, migraine, Parkinson's disease, posttraumatic stress disorder, decompensated cirrhosis, muscular dystrophy, severe fibromyalgia, spinal cord disease (including but not limited to arachnoiditis), Tarlov cysts, hydromyelia syringomyelia, Rheumatoid arthritis, fibrous dysplasia, spinal cord injury, traumatic brain injury and post concussion syndrome, Arnold-Chiari malformation and Syringomelia, Spinocerebellar Ataxia (SCA), Parkinson's Disease, Tourette Syndrome, Myoclonus, Dystonia, Reflex Sympathetic Dystrophy, RSD (Complex Regional Pain Syndromes Type I), Causalgia, CRPS (Complex Regional Pain Syndrome Type II), Neurofibromatosis, Chronic inflammatory Demyelinating Polyneuropathy, Chronic Inflammatory Demyelinating Polyneuropathy, Sjogren's Syndrome, Lupus, Interstitial Cystitis, Myasthenia Gravis, Hydrocephalus, nail-patella syndrome or residual limb pain; terminal illness with a life expectancy of under one year, one or more injuries that significantly interferes with daily activities as documented by the patient's provider, Huntington's disease.
Product / Medication / Drug / Herb

• What the medication is and its availability
• How much is needed (dose); schedule of dosing; course of treatment; tolerance?
• Its relative efficacy to safety profile; specific to the patient
• Available alternatives
Narrative review of the safety and efficacy of marijuana for the treatment of commonly state-approved medical and psychiatric disorders

Katherine A Belendiuk, Lisa L Baldini and Marcel O Bonn-Miller
Common conditions shared by > 80% of MML states:

- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Cachexia/wasting synd.
- Cancer
- Crohn’s disease
- Epilepsy and seizures
- Glaucoma,
- Hepatitis C
- HIV/AIDS,
- MS / muscle spasticity
- Severe & chronic pain - severe nausea.
- Severe & chronic pain
- Post-traumatic stress disorder (PTSD)

*... for the majority of these conditions, there is insufficient evidence to support the recommendation of medical marijuana at this time.*
Additional Suggested Reading:

Medical Marijuana: Review of the Science and Implications for Developmental-Behavioral Pediatric Practice


Suggested Reading:


*Neuropsychopharmacology, August 2015*

www.nature.com/npp/journal/vaop/naam/abs/npp2015251a.html
Medicinal Cannabis: Challenges and Needs

Cannabis studied in context of illicit not medical use

Cannabinoids more so than cannabis studied

Highly variable plant(s) over 100 “active” compounds

Education needed for clinicians and patients

Data needed to determine effects, side-effects & risks
Product? Potency? Dose? Route of Administration?

Basic Behavioral and Clinical Pharmacology

With Cannabis it’s all about THC dose …or is it?
  • Cannabidiol?
  • Over 100 compounds; over 70 phytocannabinoids

Potency / Dose Matter!
THC Potency

Lab studies have not gone above 8% THC, and only one study has gone that high.

- confiscated cannabis averaged 12.8% in 2012

Existing data on lab and epidemiological studies capture results from use of much lower THC levels than now used.

Need to learn more about higher % THC products!

Unlike alcohol, we do not have current norms on a standard dose (drink) and how much you can use before becoming “intoxicated”, or in medical danger.

Unlike alcohol – different methods of administration.
Cannabis plants have varying amounts of CBD

**Suggestive** data that it may *moderates effects of THC*
- Potential as an anxiolytic?
- Potential as an antipsychotic?
- Marketed (like marijuana) as a medication for multiple problems: e.g., epilepsy, SUDs!
- 1:1 ratio with THC in Sativex (approved medication)

Recent lab study suggests effects are not so clear?
- appeared almost inert when studied carefully in experienced cannabis users

Schubart et al. (2013); Neisink et al. (2013) Haney et al., (2015)
KanaVape is legal, natural and tasty

Developing a legal hemp vaporizer meant pushing the edge of science. True to the original plant while avoiding the combustion and smell, KanaVape brings you a premium CBD rich hemp e-liquid in a stylish vaporizer pen. Keep a clear mind and an active lifestyle with KanaVape – anytime, anywhere.
Summary: Potency / Product

- Cannabis is not just THC
- Cannabidiol ≠ Cannabis or Marijuana
- Need data on higher % THC
- Need data on Cannabidiol and THC/Cannabidiol
- Know little about how dose interacts with method of use
Are the Products What They Appear?
Vandrey et al. (2015)

- Edible cannabis products (N=75) purchased from medical dispensaries
- 3 quasi-randomly selected stores in San Francisco, Los Angeles, and Seattle
- State-approved patients given budget of $400 to purchase variety of products
<table>
<thead>
<tr>
<th></th>
<th>Accurate</th>
<th>Under</th>
<th>Over</th>
</tr>
</thead>
<tbody>
<tr>
<td>#, % Products</td>
<td>12 (17%)</td>
<td>17(23%)</td>
<td>45 (60%)</td>
</tr>
<tr>
<td>THC, mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- label</td>
<td>15 - 200</td>
<td>20 - 1000</td>
<td>2 - 325</td>
</tr>
<tr>
<td>- actual</td>
<td>15 - 183</td>
<td>34 - 1246</td>
<td>&lt;1 - 267</td>
</tr>
<tr>
<td>Discrepancy (Mean, SD) (Max)</td>
<td>-3 (4) 9</td>
<td>28 (13) 55</td>
<td>-47 (29) -99</td>
</tr>
</tbody>
</table>
Route of Administration

Smoking vs. **Vaping vs. Eating**

- onset, timecourse, euphoric effects, adverse effects
Vaping Devices

Differences between devices:

- Cost
- Temperature control
- Type of cannabis (i.e. plant vs. concentrate)
- Discretion
Other Vaping Devices

**Dabbing**

- Water pipe (generally made of glass)
- Uses blowtorch/nail to vape product
- Concentrates/oils/extracts

Many different custom devices (called dabs or oil rigs)
“Vaping” is the slang term for the vaporization of substances (e.g., flavors, nicotine, or cannabis products) whereby liquid, oil, or plant material is heated to a temperature that releases an aerosolized mixture of water vapor and active ingredients (e.g., nicotine in e-cigs and THC in cannabis), which is then inhaled.

Avoids combustion of the substance and the inhaling of smoke, which contains carbon monoxide and other by-products of combustion.
Vaping: Knowns and Unknowns

**Benefits**
- Clear harm reduction impact with respect to respiratory / lungs / carcinogenic factors.
- Facilitate use of cannabis for medical purposes (titrate, no combustible smoke, etc.).

**Concerns**
- Long-term effects of frequent vaping are unknown.
- May have a positive impact on cannabis initiation, problem development and maintenance?
  - Better tasting, more efficient high, more discreet use, combined with flavors or nicotine, attractive packaging, part of an evolving vaping culture, perceived as safe

(Budney et al., 2015 *Addiction*)
Youth Concerns: Vaping Culture

- FLAVORS, NICOTINE, CANNABIS, CAFFEINE
  - Earlier Initiation? Combine Products
  - Initiation by Youth at Lower Risk?
  - More frequent use?
  - More problematic use?
  - Health Concerns?
Edibles

- Onset much slower, eventually similar effects
  - “overdose” concerns
- Increase access and ease of use
- Discreet
- Reinforcing taste in addition to drug effect
Edibles: Concerns

Labels related to dose and onset of effects?

• Why are all these cannabis products needed?
  - alcohol lollipops, alcohol in chocolate?
  - caffeine???

• What is their purpose.... Marketing to youth, easier to ingest, sell as much as possible?

• Child protective packaging?

• Overdosing / Toxic Accidents
IMPACT ON PROBLEM DEVELOPMENT

Medical and Recreational Laws:
- Perceived Risk, Availability, New Products

Cannabis Products:
- Potency, Attraction, Reinforcing Efficacy

Delivery Devices:
- Safety, Efficiency

Advertising / Competition / Sales:
- Cost, Attraction, Nudging

Product Packaging / Labeling:
- Attraction, perception of risk or benefit
What We Know:
1. Cannabis has substantial addictive potential
2. CUD is common, resembles other SUDs, and may be increasing
3. Interventions for CUD have efficacy, but there is much room for improvement
4. Factors that influence the probability of CUD are similar to other SUDs
5. Changing Laws and Regulations will impact the development and prevalence of CUD
What We Still Need to Know:

1. How to translate knowledge into more effective CUD prevention and treatment – efficacy and dissemination

2. How to best communicate accurate information about cannabis use and its associated risks to the public

3. How to address the changing legal and regulatory systems to minimize impact on rates and consequences of CUD
The emerging legislation on cannabis in the US and elsewhere strongly indicates an urgent need for a major push for Cannabis Regulatory Science.
How Science Works
Silver Lining

- stimulating thoughtful and important science and discourse related to cannabis and drug policy
- more objective, thoughtful contemplation of pros and cons
- Perhaps More Effective Prevention Messaging?
- maybe develop some potent therapeutic compounds

In the end, more rational policy and regulation...
Take Home Messages

Science and Common Sense Policy is Needed Now More than Ever

Educate yourself through traditional means: read the scientific literature!

Also get on the Internet!
Funding and Support

NIDA research and training awards
NIAAA research awards

University of Vermont
University of Arkansas for Medical Sciences
Dartmouth College, Geisel School of Medicine
<table>
<thead>
<tr>
<th>Faculty/Trainees</th>
<th>Staff / Therapists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cathy Stanger</td>
<td>Patty Costello</td>
</tr>
<tr>
<td>Stephanie Fearer</td>
<td>Eliza Wessinger</td>
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<tr>
<td>Brent Moore</td>
<td>Gray Norton</td>
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<td>Ryan Vandrey</td>
<td>Leanna Delhey</td>
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<td>John Hughes</td>
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<td>Doris Ogden</td>
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<td>Warren Bickel</td>
<td>Jonathan Young</td>
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<td>Denise Walker</td>
<td>Heath Rocha</td>
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<tr>
<td>Roger Roffman</td>
<td>Andrea Meier</td>
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<tr>
<td>Bob Stephens</td>
<td>Merrie Vannucci</td>
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<tr>
<td>Pam Brown, Jen VanScoyoc</td>
<td>Marlo Lowe</td>
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<tr>
<td>Stacy Ryan</td>
<td>Bobby Ward</td>
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<tr>
<td>Amanda Elton / Clint Kilts</td>
<td>Sarah Clark</td>
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<td>Jody Kamon</td>
<td>Nancy Culbertson</td>
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<td>Dustin Lee, Jacob Borodovsky</td>
<td>Stanley See, Hao Yang</td>
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<td>Ben Crosier</td>
<td>Nick Tacke, Samantha Auty</td>
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<td>James Sargent</td>
<td>Jennifer Darsie</td>
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