




## 48<sup>th</sup> Annual Meeting

### SCCM and ACEP Meeting Summaries


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*Navigating the Oceans of Opportunity*



## Society of Critical Care Medicine (SCCM)

- **Largest multidisciplinary organization dedicated to the practice of critical care**
  - Nearly 16,000 members in over 100 countries
- **Variety of activities to promote patient care, education and research**
  - Research support and networking
  - Guidelines and LearnICU
  - Webinars





## Disclosure

- I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation




## SCCM Website

## Objectives

- Review opportunities for involvement in focused specialty organizations like the Society of Critical Care Medicine (SCCM) and the American College of Emergency Physicians (ACEP)
- Discuss therapeutic updates from the 2014 SCCM Annual Congress in the areas of drug shortages, pulmonary hypertension, delirium, alcohol withdrawal and stress ulcer prophylaxis
- Describe therapeutic updates from the ACEP meeting in areas of rapid sequence intubation, top articles of EM and toxicology
- Apply meeting updates and recent significant critical care and emergency medicine literature to pharmacy practice



## Clinical Pharmacy and Pharmacology Section

- **SCCM members with a special interest in pharmacy or pharmacology**
  - One of the most active sections in SCCM
- **Opportunities for involvement**
  - Research Support
  - Mentor/Mentee Programs
  - Journal Club
  - Visiting Clinical Professor Program
  - Quarterly Newsletter

## SCCM Annual Congress



- Offers large variety of critical care focused programming for multi-professional CE
  - Poster Sessions, Oral Abstracts
  - Pro-Con Debates, Plenary Sessions
  - Formal CE Lectures
- Networking
  - Clinical Pharmacy and Pharmacology Section Events
- Next Annual Congress
  - Phoenix, Arizona
  - January 2015

Society of  
Critical Care Medicine

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## Government Action!



- Food and Drug Administration Safety and Innovation Act (FDASIA) – signed 7/9/2012
  - Requires notification of FDA 6 months prior to discontinuation or interruption of production
    - Life-supporting or sustaining therapies
    - Emergency care medications
    - Medications for treatment or prevention of debilitating disease
  - Allows expedited review of product from new manufacturer if shortage occurring

FDA. Strategic plan for preventing and mitigating drug shortages. Available at: [www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf](http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf). Published Oct 2013. Accessed 18 May 2014.

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## Drug Shortages



- Causes
  - Regulatory
  - Economics
    - Inelastic supply and demand
  - Industry
  - Supply Chain
- Market issues
  - Lack of redundancy in production
  - “Just in time” production
  - No reward in market for quality



Lewin J, Mallow-Corbett S. Drug Shortages: Lessons Learned. Presented at SCCM 43<sup>rd</sup> Annual Congress; January 2014; San Francisco, CA.

Woodcock J, et al. *Clin Pharmacol Ther.* 2013;93(2):170-176.

Image from <http://www.sato.org/publications/commentary/understanding-asstx-holiday>.

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## Compounded Alternatives



- Drug Quality and Security Act – signed 11/27/13
  - Compounding pharmacy can become “outsourcing facility”
    - Subject to FDA inspections and current good manufacturing processes
    - Reporting requirements for adverse events, etc.

FDA. Compounding. Available at: <http://www.fda.gov/drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/>. Updated 23 April 2014. Accessed 18 May 2014.

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## We're Out of What?



- Risks
  - Lack of familiarity with alternative products
    - Medication errors increase
  - Lack of built-in safety checks
    - Automated systems – CPOE, ADCs
  - Removal of clinicians from patient care activities
  - Delays in care
- Benefits
  - Impetus for change in clinical practices

CPOE = Computerized Provider Order Entry

ADC = Automated Dispensing Cabinet

Kaakeh R, et al. *Am J Health-Syst Pharm.* 2011;68:1811-1819.

McLaughlin M, et al. *J Manag Care Pharm.* 2013;19(9):783-788.

Kaur K, et al. *Am J Health-Syst Pharm.* 2013;70:1533-1537.

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## Available Resources



- SCCM website → LearnICU → Knowledge Areas → Pharmacology → Drug Shortages
- ASHP website:
  - <http://www.ashp.org/menu/DrugShortages.aspx>
- FDA website:
  - <http://www.fda.gov/Drugs/drugsafety/DrugShortages/default.htm>
- Wholesaler or manufacturer
- Group Purchasing Organization (GPO)

Lewin J, Mallow-Corbett S. Drug Shortages: Lessons Learned. Presented at SCCM 43<sup>rd</sup> Annual Congress; January 2014; San Francisco, CA.

Kaakeh R, et al. *Am J Health-Syst Pharm.* 2011;68:1811-1819.

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## Pulmonary Hypertension

- Three new FDA approvals
  - Riociguat (Adempas®) – 10/2013
  - Macitentan (Opsumit®) – 10/2013
  - Treprostinil (Orenitram®) – 12/2013
- REMS programs for two of those medications – female patients only
  - Adempas® REMS
  - Opsumit® REMS

Dzierba A. Pulmonary Hypertension: Medications and Novel Therapies. Presented at SCCM 42<sup>nd</sup> Annual Congress, January 2014, San Francisco, CA.  
Adempas [package insert], Bayer HealthCare Pharmaceuticals Inc.; 2014.  
Opsumit [package insert], Actelion Pharmaceuticals US Inc.; 2013.

REMS = Risk Evaluation and Mitigation Strategy

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## FREEDOM-M

**Design and Population**

- Multicenter RCT
- PAH with baseline 6MWD between 100-450 m on no other PAH therapy

**Intervention**

- Oral extended-release treprostinil starting at 0.25 – 1 mg PO BID (max 12 mg BID)
- Placebo

**Results**

- Significant increase in 6MWD at 12 weeks
- Possible association between dose and 6MWD treatment effect

17 Jing ZC, et al. *Circulation*. 2013;127:624-633.

## PATENT-1

**Design and Population**

- Multicenter RCT
- PAH patients with mPAP ≥ 25 mmHg, mean PVR of > 300 dynes\*sec\*cm<sup>-5</sup> and 6MWD 150-450 m

**Intervention**

- Placebo
- Riociguat to max 2.5 mg PO TID
- Riociguat to max 1.5 mg PO TID

**Results**

- Significant change in 6MWD at end of week 12
- Significant change in all but the quality of life secondary outcomes

mPAP = mean pulmonary arterial pressure, PVR = pulmonary vascular resistance  
6MWD = 6 minute walk distance Ghofrani HA, et al. *New Engl J Med*. 2013;369:330-340.

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## Updated PAH Guidelines

INITIAL THERAPY WITH PAH APPROVED DRUGS				
Recommendation	Evidence*	WHO-FC II	WHO-FC III	WHO-FC IV
I	A or B	Ambrisentan Bosentan Macitentan†‡ Riociguat† Sildenafil† Tadalafil†	Ambrisentan Bosentan Epoprostenol i.v. Iloprost inhaled Macitentan†‡ Riociguat† Sildenafil† Tadalafil† Treprostinil s.c., inhaled†	Epoprostenol i.v.
IIa	C		Iloprost i.v.† Treprostinil i.v.	Ambrisentan, Bosentan Iloprost inhaled and i.v† Macitentan†‡ Riociguat† Sildenafil†, Tadalafil† Treprostinil s.c., i.v., inhaled†
IIb	B		Bosprost†	
	C		Initial Combination Therapy	Initial Combination Therapy

\*Level of evidence is based on the WHO-FC of the majority of the patients of the studies.  
†Approved only by the FDA (macitentan, riociguat, treprostinil inhaled); in New Zealand (iloprost i.v.); in Japan and S. Korea (bosprost).  
‡ Positive opinion for approval of the CHMP of EMA

Note: Sequential combination therapy now has a Class IA recommendation for patients with inadequate response to monotherapy.

18 Galie N, et al. *J Am Coll Cardiol*. 2013;62:D60-72.

## SERAPHIN

**Design and Population**

- Multicenter RCT
- PAH patients with 6MWD > 50 m and in functional class II, III or IV

**Intervention**

- Macitentan 3 mg or 10 mg PO daily
- Placebo

**Results**

- Significant reduction in morbidity and mortality over median 115 weeks
- First oral agent to use clinical outcome for study endpoint instead of 6MWD

Pulido T, et al. *New Engl J Med*. 2013;369:809-818.

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## Literature Updates

## Delirium



- **Key feature: altered attention or consciousness**
- **ICD-10 diagnostic criteria for delirium**
- **Assessment tools**
  - CAM-ICU
  - ICDS
- **ABCDE Bundle**
  - Balas MC, et al. *Crit Care Med.* 2014;42:1024-1036.
  - Balas MC, et al. *Crit Care Nurse.* 2012;32(2):35-48.

Kapinos G, Girard T, Rabinstein A. Delirium and Encephalopathy in the ICU. Presented at SCCM 43<sup>rd</sup> Annual Congress; January 2014; San Francisco, CA.  
The ICD-10 Classification of Mental and Behavioural Disorders. Diagnostic criteria for research. Geneva, World Health Organization, 1993.

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## The Battle Continues



- **Which agent?**
  - **Ideal agent**
    - Effective, safe, minimal interactions, diverse administration options, economic justification
  - **Multiple meta-analyses**
    - Need to assess risk of bias in individual trials
    - Levy, et al. 1997 – much higher bleed rate
      - Never replicated
    - Weight of each individual study within the meta-analysis impacts overall result

Alhazzani W, et al. *Crit Care Med.* 2013;41:693-705.  
Barkun AN, et al. *Am J Gastroenterol.* 2012;107(4):507-520.  
Lin PC, et al. *Crit Care Med.* 2010;38(4):1197-1205.  
Pongprasobchai S, et al. *J Med Assoc Thai.* 2009;92(5):632-637.

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## Alcohol Withdrawal



- **Dexmedetomidine and AWS**
  - Single-center RCT evaluating DEX as adjunct to symptom-triggered lorazepam
  - Low-dose (0.4 mcg/kg/hr), high-dose (1.2 mcg/kg/hr) or placebo (N=8 per group)
  - Significant difference in lorazepam use in the 24 hours post-study drug initiation (-56 mg v. -8 mg, p=0.037)
    - No statistically significant difference in lorazepam use at 7 days
  - May decrease BZD exposure, but further study needed
- **Review articles**
  - Awissi DK, et al. *Intensive Care Med.* 2013;39(1):16-30.
  - Ungur LA, et al. *Alcohol Clin Exp Res.* 2013;37(4):675-686.

AWS = Alcohol Withdrawal Syndrome  
BZD = Benzodiazepine

Roberts R. Substance Withdrawal. Presented at SCCM 43<sup>rd</sup> Annual Congress; January 2014; San Francisco, CA.  
Mueller SW, et al. *Crit Care Med.* 2014;42:1131-1139.

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## Summary



- **Drug shortages continue to impact pharmacy practice in significant ways**
  - Communication is key to error avoidance
- **Pulmonary hypertension treatment continues to evolve with more options and more patient-friendly therapies**
- **Delirium remains a significant concern with early management key to success**
- **Alcohol withdrawal management with adjuncts to benzodiazepines currently of significant interest**
- **Stress ulcer prophylaxis – focus is starting to move back to right population v. right agent**

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## Stress Ulcer Prophylaxis



- **Which patients?**
  - Fewer than generally thought
  - Bleeding definitions are key in studies
    - Decreasing rates over time (estimated 2-4%)
  - Risk factors
    - Most commonly cited:
      - Mechanical ventilation > 48 hours
      - Coagulopathy
    - Others:
      - Hepatic failure, chronic renal failure, H. pylori, traumatic brain injury, burns, spinal cord injury, high dose steroids

Cook D, Bruno J, Buckley M. Stop Stressing Over Stress Ulcers. Presented at SCCM 43<sup>rd</sup> Annual Congress; January 2014; San Francisco, CA.

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## American College of Emergency Physicians (ACEP)



- **ACEP supports quality emergency care and promotes the interests of emergency physicians.**
- **Founded in 1968**
  - 1970 - First EM residency
  - 1979 - Emergency medicine recognized as a specialty by AMA & ABMS
- **>32,000 members**
  - Only physicians can be members
  - Reach out to pharmacy groups when writing policies & statements

American College of  
Emergency Physicians®  
ADVANCING EMERGENCY CARE

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## ACEP Values

Through continuing professional education, patient advocacy at all levels, public information and research, ACEP strives to uphold these values:

- Quality emergency care is a fundamental individual right and should be available to all who seek it.
- There is a body of knowledge unique to emergency medicine that requires continuing refinement and development.
- Quality emergency medicine is best practiced by qualified, credentialed emergency physicians.
- The best interests of the patient are served when emergency physicians practice in a fair, equitable, and supportive environment.
- The emergency physician has the responsibility to play the lead role in the definition, evaluation and improvement of quality emergency care.

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## ACEP Website



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## Benefits from ACEP


- **Career and Practice Management Resources**
  - Annals of Emergency Medicine
  - Scientific Assembly
  - Practice Resources
    - Guidelines
    - Statements
    - Links
- **Leadership and Networking Resources**
  - Sections
  - Leadership & Advocacy Meeting



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## Scientific Assembly

- Offers large variety of emergency medical care focused programming
  - Formal CME Lectures
  - Poster sessions
- Section Meetings
- Networking
- Future Scientific Assemblies
  - 2014 Chicago, IL Oct 27<sup>th</sup> – 30<sup>th</sup>
  - 2015 Boston, MA Oct 26<sup>th</sup> – 29<sup>th</sup>



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## Sections



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## Networking Lunch with EM Pharmacists

- 3<sup>rd</sup> year
- 15 pharmacists
  - Others couldn't make due to conflicts
- Meet face-to-face
  - Great for residents networking
- Discussion
  - Different practices & models
  - Issues & needs
  - New services
  - Resident & student involvement

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## Opening Session: Boston Bombings



- Panel of physicians, nurses and first responders
  - Reviewed event and each role
  - Medical providers at scene
    - Pharmacists at tents & hospitals
- Key points
  - Scene
    - Bystanders helping at scene
    - Medical professionals & supplies available
    - Good distribution of patients to healthcare facilities



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## Rapid Sequence Intubation



### Ketamine

- 2 case reports of cardiac arrest after RSI
  - Both in septic shock
  - 2 and 2.4 mg/kg doses
  - Bradycardia to asystole or PEA
- Cardiovascular stimulation
  - Sympathomimetic effect
  - Inhibition of norepinephrine re-uptake
  - Negative inotropic effects
    - Normally overridden
    - Catecholamine stores depleted – may increase effect

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Dewhurst E, et al. *J Inten Care Med.*2013;28(6):375-9.

## Opening Session: Boston Bombings



- Key Points
  - Hospital
    - Clearing EDs of current patients
      - Psychiatric care patients were still in ED even after the incident
    - Create “micro zones”
      - Prevent overwhelming both providers & patients
      - Improve communication
    - Early identification
    - Debriefing – variable
      - Patient advocacy groups
      - Rescue animal visits



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## Steroids & Pressors in Cardiac Arrest



### Design and Population

- Multicenter RCT in Greece
- 268 consecutive pts in cardiac arrest requiring epi

### Intervention

- Vasopressin 20 units + 1mg epinephrine Q 3 min for 1<sup>st</sup> 5 cycles + 40 mg methylprednisolone with first dose
- Stress dose steroids with ROSC
- Saline / 1mg epinephrine

### Results

- Higher ROSC (83.9% vs 65.9%; OR = 2.98)
- Higher hospital discharge w/ CPC 1 or 2 (14% vs 5%; NNT = 11)
- Higher discharge w/ CPC in VSE shock group (21% vs 8%; NNT = 8)

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Mentzelopoulos SD, et al. *JAMA.*2013;310(3):270-9.

## Rapid Sequence Intubation



### Etomidate Discussion

1. Meta-analysis of RCT & observational studies
  - Jan 1950 – Feb 2012
  - 865 & 1303 subjects included
  - Results
    - Increased all-cause mortality: pRR = 1.2
    - Increased likelihood for adrenal insufficiency: pRR = 1.33
2. Large retrospective cohort from eICU database
  - 2014 ICU patients with sepsis
    - 1102 patients receive single-dose etomidate
    - 912 patients receive other induction agent
  - No difference in mortality, duration of mechanical ventilation, hospital or ICU duration

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Pearl RG. *Ann Internal Med.* 2013;158(19):JC2-10.  
McPhee LC et al. *Crit Care Med* 2013;41(3):774-783

## Diagnostic Accuracy of Nitroglycerin



- Systematic review – 5 included articles
  - 1978 adults in ED with CP
- Sensitivity = 0.52 & Specificity = 0.49
- OR = 1.2 (95% CI 0.97-1.5)
- Not good indicator for coronary cause of pain
- GI cocktail is also not good for diagnostics!

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Grailey K, et al. *Emerg Med J.* 2012;29(3):173-6.  
Dickinson MW. *J Emerg Med.*1996;14(2):245-6.

## Marijuana: Changes in Medicine & Social Use



### Reviewed articles on evidence in marijuana in medicine

#### Pain

- Neuropathic pain – Journal of Pain 2008
  - N=38
  - High-dose (7%), low-dose (3.5%) or placebo cannabis
  - Response but minimal difference between doses
- Neuropathic pain in HIV adjunctive therapy - Neuropsychopharm 2009
  - N=34
  - Double-blind, placebo, cross-over
  - 30% decrease in pain

Wilsley B, et al. *Journ Pain*. 2008;9(6):506-521.  
Ellis RJ, et al. *Neuropsychopharm*. 2009;34(3):672-80.

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## New Drugs of Abuse



### Large increase in new drugs!

- “Crocodile bites”
  - Desomorphine - Krokodil
  - Made from codeine in Eastern EU
- Cannabinoid Hyperemesis Syndrome
  - Chronic N/V
  - Relieved by hot showers
  - Length of hyperemesis dependent on use & duration
- Clean Kill
  - Toilet cleaner + plant food = hydrogen sulfite
  - Death pretty quick when in enclosed setting
  - Make sure caregivers are safe
  - Treat with sodium nitrite



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## Marijuana: Changes in Medicine & Social Use



#### N/V & cachexia:

- Data mainly in animals
- Cannabinoid hyperemesis

#### Adverse Effects:

- Stroke
  - Increased risk
  - All but 1 patient also smoked cigarettes
- Psychosis
- Overdose

Coutts AA, Izzo AA. *Cur Opin Pharm*. 2004;4:572-579.  
Simonetto DA, et al. *Mayo Clin Proc*. 2012;87(2):114-119.  
Barber PA, et al. *Stroke*. 2013;44(8):2327-9.

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## New Drugs of Abuse



#### Methoxetamine (MXE)

- Dopamine blocker
- Large pupils, staring off
- Acts like Ketamine but longer duration
- Case just published in *Annals of Emerg* 2012
- Treat complications

#### Phenazepam- whiffing zannie

- Old benzo in Russia
- Delayed onset, peaks at 4 hrs, half-life of 60 hrs + active metabolite
- Fatalities in UK
- Doesn't show up on drug screen even with benzos

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## Marijuana: Changes in Medicine & Social Use



### Discussion

- Need for more research
  - #1 drug currently used
  - 20% of California population has card
- Side effects & adverse reactions
  - Not for everyone
  - Cannabinoid Hyperemesis Syndrome
- Levels
  - What is a safe level to drive
  - Colorado & Washington – 5 ng/mL
- Ethical conflict
  - Writing a prescription for smoking
  - Alternative methods????

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## Other Great Topics



- Cardiology
  - Advanced ECG - Dysrhythmias & Syncope – Mattu
  - Heart failure
- Pregnancy emergencies
- Pediatrics
  - Procedural sedation
- Toxicology
- Wilderness & travel
  - Infections from abroad
  - Survival
  - Altitude diseases (AMS, HAPE, HACE)
- Leadership

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## Summary



- ❑ Disasters can create learning environments, including ways to handle large influx of patients & debriefing
- ❑ Ketamine & etomidate literature continues to expand with patient specific considerations
- ❑ Medications are still secondary to CPR in cardiac arrest, but steroids may play a role in the future
- ❑ Marijuana's role in medicine should continue to be evaluated but may have a role in n/v & pain control
- ❑ New drugs of abuse will continue to grow in numbers, all providers & parents should work to keep informed

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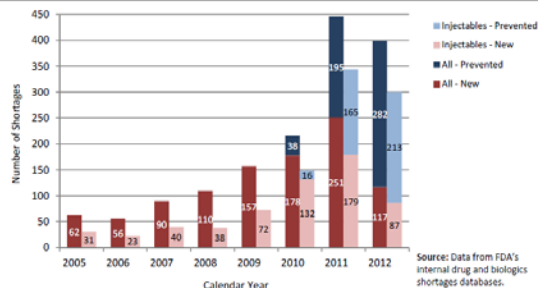
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*Navigating the Oceans of Opportunity*

## Impact of Increased FDA Involvement



FDA. Strategic plan for preventing and mitigating drug shortages. Available at: [www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf](http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf). Published Oct 2013. Accessed 18 May 2014.