G01: Look Who's Doing Research Now! What Does it Mean for Walgreens, Walmart, Etc., to Be Conducting Human Subjects Research?

Wednesday, December 6th, 2023 11:30AM-12:30PM

Speaker: Adam Samson, MS, PMP, CCRA, CCRC, CCDM – Head of Clinical Delivery Operations, Clinical Trials, Walgreens

Speaker: Mark A. Munger, Pharm.D., F.C.C.P., F.A.C.C., F.H.F.S.A., HF-Cert – Professor, Pharmacotherapy and Internal Medicine, University of Utah

PRIM&R

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PRIM&R PUBLIC RESPONSIBILITY IN MEDICINE AND RESEARCH

Mark A. Munger, Pharm.D.,

F.C.C.P., F.A.C.C., F.HF.S.A., HF-Cert, University of Utah, SLC, Utah

Dr. Munger graduated from Oregon State University with a B.S. in Pharmacy, received his Pharm.D. from the University of Illinois at Chicago and completed a Clinical Cardiovascular Pharmacology Research Fellowship from Case Western Reserve University School of Medicine in Cleveland, Ohio.

His current position is Professor of Pharmacotherapy and Adjunct Professor of Internal Medicine (Cardiology) at the University of Utah where he joined the faculty in 1991. He is a Fellow in the University Utah Academy of Health Science Educators.

Dr. Munger is a Fellow in the American College of Clinical Pharmacy, the American College of Cardiology, and the Heart Failure Society of America. He has served as Chairman, University of Utah Institutional Review Board for 7 years (1999-2006); Chairman and Member, Utah State Board of Pharmacy; Chairman, Utah State Department of Health Digital Health Commission; the Utah State Controlled Substances Advisory Board; and a past member of the Utah State Cannabinoid Product Safety Board.

His current research interests are repurposing and advancing drugs for new therapeutic indications and developing community pharmacy into an integrated model of healthcare delivery. He is the author of 270+ manuscripts and abstracts cited 28,000 times. He has been invited to present 150+ times nationally and internationally in human cardiovascular physiology and pharmacology, human research regulatory affairs and professional pharmacy matters.

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Disclosure: Mark A. Munger Pharm.D., F.C.C.P., F.A.C.C., F.H.F.S.A., HF-Cert

I have no relevant personal/professional/financial relationship(s) with respect to this educational activity

University of Utah Health: Professor, Pharmacotherapy and Internal Medicine (Cardiology)

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Learning Objectives

At the end of this presentation the participant should be able to:

- Summarize the healthcare problem of non-optimized drug therapy and the application to the study of community pharmacy implementation research;
- Understand domestic comparative research from the setting of community pharmacy-based implementation research; and
- Identify issues and concerns with community pharmacy implementation research to institutional research boards and federal/state/local regulations from a Principal Investigator perspective.

The Current Status of Drug Therapy in the U.S.

- 3,658 prescription drugs (20,000 Total Rx products)
- 100,000 over-the-counter (OTC) agents approved by U.S. Food and Drug Administration (FDA) on the U.S. marketplace.
- Nutraceutical products: $267 Billion (2019)
  - Functional food (probiotic and omega free fatty acid fortified foods, branded: ionized salts, wheat flour, and other functional food)
  - Functional beverages (fruits and vegetable juices and drinks, dairy and dairy alternative drinks, non-carbonated drinks [bottled water, tea, coffee] sports and energy drinks)
  - Dietary supplements (proteins and peptides, vitamins and minerals, herbals),
  - Personal care items

6 Billion Different Combinations

U.S. Food and Drug Administration Fact Sheet. https://www.fda.gov/about-fda/fda-basics/fact-sheet-fda-glance Accessed 07 08 2021
Regulation of OTC Medications. https://www.chpa.org/faqs-about-regulation-otc-medicines Accessed 07/08/2021
Natraceutical Market Size, Share and Trends Analysis 2022.

The Problem

A non-optimized medication therapy (NOMT) event is defined as an iatrogenic hazard or incident associated with medications[1]

NOMTs are a major healthcare crisis [1-5,8-9]

- $528.4 billion (2016). (15% of total US healthcare expenditures in 2020 [projected])[3]
- $14.85 additional cost for every prescription written in 2019 ($600 billion/4.38 billion prescriptions)

- The average cost of a patient NOMT who experiences a treatment failure, new medical problem, or both is $2481/event[3]
- Excess of 3.5 million physician office visits, 1 million emergency department (ED) visits, and 125,000 additional hospital admissions[6-7]

1. Besco K et al.Medication Misadventures I: Adverse Drug Reactions. In: *Drug Information: A Guide for Pharmacists, 6e*. McGraw-Hill;
2. To Err is Human: Errors in Health Care – A Leading Cause of Death and Injury. https://www.ncbi.nlm.nih.gov/books/NBK225187/ Accessed 12/24/2020
3. Watanabe JH, et al. *Ann Pharmacother* 2018;52(9);829-837.
4. Assiri GA, et al. *BMJ Open* 2018;8:e019101
5. Lin CW, et al. *Scientific Reports* (Nature) 2017;7.41035 DOI:10.1038.
6. Adverse Drug Events. https://health.gov/our-work/health-care-quality/adverse-drug-events Accessed 12/24/2020.
7. AHRQ National Scorecard on hospital-acquired conditions: updated baseline rates and preliminary results 2014-2017. Accessed 12/24/2020.
8. Dzau VJ, Shine KI. *JAMA* 2020;324(24):2489-90.
9. https://www.pgpf.org/blog/2020/04/why-are-americans-paying-more-for-healthcare

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HEALTH

Fenta

Life expectancy for men in U.S. falls to 73 years — six years less than for women, per study

the Globe

The 'l

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"The Opioid Epidemic, Mental Health, and Chronic Metabolic Diseases are Front and Center for lower Men's Life Expectancy"

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ADOBE

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The Call To Action

Medication Overload

- If current trends continue, **medication overload will be responsible for at least 4.6 million hospitalizations between 2020 and 2030** and will cost taxpayers, patients and families an estimated $62 Billion [1]

Adverse Drug Events (ADEs)

- The risk of an ADE increases 7-10% with each medication a patient takes[1]
- For **every dollar we spend on prescription medication, we spend more than another dollar trying to address problems caused by the medications**. ($528.4M – 16% of total health expenditures – in 2016) [2]

Growing Awareness & Urgency…

APhA

LOWN INSTITUTE

GTMRx Institute™ Get the medications right

World Health Organization

1. *Lown Institute Medication Overload: America's Other Drug Problem Link, 4/1/19*
2. *Watanabe, McInnis, Hirsch, Cost of Prescription Drug-Related Morbidity and Mortality, SAGE, UC San Diego Health, 2018*

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HEALTH · MEDICARE

CVS CEO sees changes coming 'faster than a freight train' for Medicare. She's betting billions she can build a new American health care system

BY FORTUNE EDITORS

October 10, 2023 at 10:42 AM MDT

Village Medical's "The New Way to Well" campaign, winner of the Best in Show Award in the 2023 Healthcare Marketing Impact Awards, highlights the primary care provider's efforts to differentiate itself from the current model of care.

A key part of the disruptor business model is more patient-centric care, which "The New Way to Well" campaign

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Artificial Intelligence Software

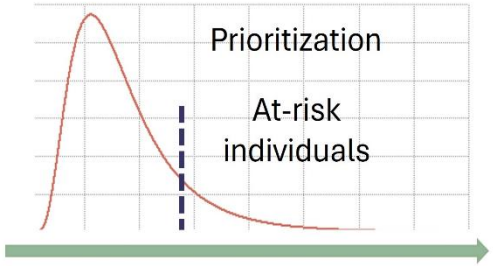
Identification of Pharmacokinetic, Pharmacodynamic and Pharmacogenomic Drug Problems

GalenusRx: Delivering Lifesaving Insights™

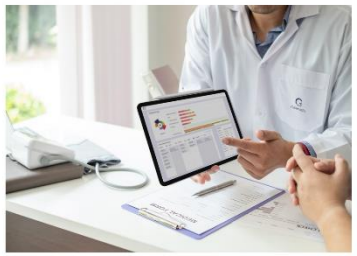
1-to-1 drug interaction software is more than four decades obsolete, and does not address complete drug regimens with complex polypharmacy

Our simultaneous multi-drug analysis using pharmacokinetics, pharmacodynamics and chronopharmacology addresses polypharmacy complexity

At the population level



At the individual level



Assessment of patient's condition by trained health care providers.

The Risk Score is Predictive of…

Outcome	Risk Score of 10	Risk Score of 20	Risk Score of 30
Outpatient Visits (Average # Per 100 Members in 2019)	717 (706, 728)	1,170 (1,152, 1,188)	1,622 (1,591, 1,654)
Hospital Admissions (Average # Per 100 Members in 2019)	21 (20, 22)	44 (43, 45)	67 (64, 69)
Days in Hospital (Average # Days Per Member in 2019)	1.2 (1.1, 1.2)	2.6 (2.4, 2.7)	3.9 (3.8, 4.1)
Days in Skilled Nursing Facility (SNF) (Average # Days Per Member in 2019)	2.2 (2.0, 2.3)	4.8 (4.5, 5.0)	7.4 (6.9, 7.8)
ADEs (Parts A and B) (% of Members with ≥1 ADE in 2019)	5.0 (4.8, 5.1)	9.3 (9.1, 9.6)	13.7 (13.3, 14.1)
Falls (Parts A and B) (% of Members with ≥1 Fall in 2019)	8.8 (8.6, 8.9)	15.3 (15.0, 15.6)	21.8 (21.3, 22.3)
Mortality (% of Members Who Died in 2019)	4.4 (4.3, 4.6)	7.8 (7.6, 8.1)	11.2 (10.7, 11.6)
Total Cost (Parts A/B) (Average $ Per Member in 2019)	$9,005 ($8,818, $9,193)	$16,574 ($16,267, $16,881)	$24,143 ($23,616, $24,670)

Increasing risk score is associated with poorer clinical outcomes and higher costs.

Source: PSM-Mortality-Q3Q4-2018_20201230 RMD for mortality; MRM_Story_Y18Y19_20201123 RMD for other outcomes

Cohort Criteria for Mortality: All members for whom death can be observed in 2019 and who have risk score information available in the second half of 2018. Members who became ineligible for the EMTM program partway through 2019 for a reason other than death are excluded.

Cohort Criteria for Other Outcomes: All members with uninterrupted eligibility for the 2019 EMTM program year

Sample: 184.258 for mortality; 195,541 for other outcomes

Note: For mortality, we examine the relationship between (a) the maximum risk score in the last six months of 2018 and (b) the likelihood of dying in 2019. For the remaining outcomes, we examine the relationship between (a) the maximum risk score in 2018 and (b) the corresponding outcome in 2018.

ESRD members are excluded.

Emergency Department (ED) visits have been removed due to a pending definition change.

Outcome Data AI Driven Software

Morbidity, Mortality and Economic Outcomes

Stein A, et al. Am J Manag Care. 2021 Sep;27(16 Suppl):S300-S308. doi: 10.37765/ajmc.2021.88755.

- 11,436 beneficiaries were targeted for Medication Safety Reviews (MSRs) in both 2018 and 2019.
  - Beneficiaries were, on average, 76.6 ± 10.0 years old.
- First MSR (N=4,384) outperformed Failure-to-Engage (patients who did not consent to be part of the study) (N=7,052) in:

  - Total medical costs (-$958/year [7.5% savings], P=0.042)
  - Hospitalizations (-3.9 admissions/100 beneficiaries/year [10% reduction], P=0.032)
  - ED visits (-6.2 visits/100 beneficiaries/year [10% reduction], P=0.014), and
  - Mortality (-2.1% deaths in 2019, P<0.001)
  - Outcomes remained significant after adjusting for baseline MRS and multi-morbidity.

  - **ROI: 4:1**
  - **50,000 patients enrolled (2 Harms Reported) (0.004%) No Litigation**

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Red=Professional/Clinical Judgement
Clinical Support System Overlap

Community Pharmacy part of TRAIL Program

Database Search for HFrEF 4 Pillars of Drug Therapy

Patients with MedWise™ Risk Score >15 with HFrEF

300 U.S. Community Pharmacies
1300 Engaged
vs. 1300 non-engaged

MedWise™ Fully Certified Pharmacists and Pharmacy Technicians (Training by Tabula Rasa HealthCare)

For urgent medications on new prescriptions, action plan and encounter should occur real-time by direct contact to hub pharmacists

Engaged

Failure to Engage

Encounter Scheduled

Med Reconciliation

With selected PGx Testing

UU IRB Approved Study and ICF

Med Reconciliation Sent to Hub #3

Information Transferred to Analytical Core for Survey and Review of Outcomes

Medication Safety Review at Hub

Action Plan Generated

Difference-in-difference Analysis on Year-to-Year Outcomes (Propensity Score Matching)

Action Plan Sent to Pharmacy and to Primary Physician

Academy of Family Physicians National Research Network (DARTNet Institute)

MedWise™ System:
Information System
Clinical Judgement of Pharmacist/M.D. Necessary

Hub M.D. Sign Off on Action Plan under CPA

Community Pharmacist
Professional Judgement
Med Reconciliation and Patient Interaction from Action Plan

Each Patient F/U 3 times (Initially, 3 and 6 months)

PRIM&RE ... MEDICINE AND RESEARCH

Future of Community Pharmacy Based Research

- Community Pharmacy Based Research
  - Will stay mainly recruiting for industry-sponsored or foundation-based research protocols for the near future;
  - With the increased need for racial equity in research recruiting (funding-dependent and/or regulatory requirements) – community pharmacy, especially in inner cities, will be increasing sought after to aid in recruitment.
    - Government-Funded Research
    - Foundation-Based Research
    - Industry-Sponsored Research (Bently-Edwards KL, et al. *Health Equity* 2022;6(1) doi:10.1089/heq2022.0042)
  - Why?? Pharmacies are currently the most frequently utilized healthcare delivery locations in the United States, as 89% of consumers live within 5 miles of a pharmacy and there are 61,715 community pharmacies nation-wide. https://www.pharmacytimes.com/view/study-88-9-of-us-population-lives-within-5-miles-of-a-community-pharmacy

Single IRB Model for Community Pharmacy Implementation Research
Research Team Perspective from prior IRB Chairman

- Meet with the Single IRB Site Administrators
  - Prior to meeting-have protocol development in place including:
    - Global investigative plan
    - Site selection criteria (approximate number of sites)
      - Positives and negatives of site selection
        - Experience in research (i.e. recruiting, consenting, data collection, adverse event reporting)
        - Remote Monitoring
    - Participant selection criteria
      - Positives and negatives of participant selection criteria
        - Diversity, inclusion, equity considerations
        - Reading/understanding/follow instructions/transportation/stressor capabilities (i.e. ICF, exposome)

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Single IRB Model for Community Pharmacy Implementation Research
Research Team Perspective

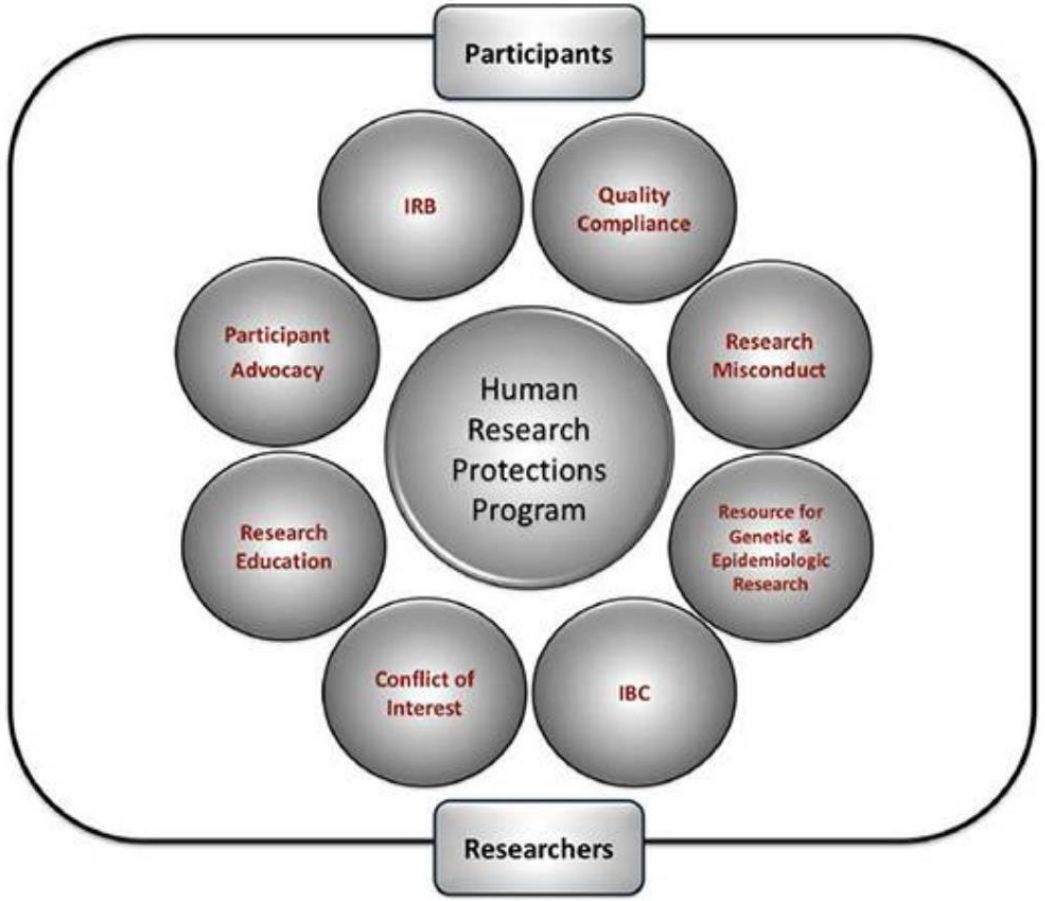
- Meet with the Single IRB Site Administrators
  - Prior to meeting-have protocol development in place including:
    - Consent Form Template
      - Universal ICF preference over individual ICFs at participating sites
      - Study specific information vs. site specific information-preferable for both to be the same
      - Research-related injury language
      - HIPPA-related language
    - Recruiting Documents – preferably similar across the study
    - Data and Safety Monitoring Plan
      - Lead Study Team
      - Participating Sites
      - Analytical Core Team

Single IRB Model for Community Pharmacy Implementation Research
Research Team Perspective

- **Understand what you do not know and ask for help!**
- University of Utah Data Coordinating Center
  - Project Director and Manager

Why??

- Reliance documents allow a SIRB to negotiate with other sites takes time and expertise;
- Human Research Protections Programs; and
  - Understanding the breadth and depth of these protections programs takes experience
- Lead site and participating sites are approved during initial submission, then can add sites via amendment.
- Budgeting; IRB Review Fees



Single IRB Model for Community Pharmacy Implementation Research
Research Team Perspective

- Given the complexities of multiple sites, regulatory approval, and protocol-driven methods a coordinated, comprehensive lead-team led, all-site training session is a must.
- This should include at a minimum:
  - Investigative Plan
  - Site-specific: Recruiting methods, informed consent process, data collection methods, adverse event reporting, and remote monitoring requirements.
  - Data and Safety Monitoring Plan

Summary Comments

- Given the complexity of drug therapy and need for increasing drug safety in the U.S. (world-wide), pharmacists will increasingly be responsible for the oversight of starting, monitoring, and discontinuing medications, in collaboration with the primary prescriber, (and consumer/research participant), across the healthcare system.
- Community pharmacy-based research, both practical (*building of knowledge useful to practice that adheres to the basic principles of scientific inquiry*) and implementation will become increasing necessary.
- The interaction between PRIM&R members and community pharmacy organizations will become more commonplace.
- Understanding from both parties to work *together* for a successful research outcome will be necessary and essential.