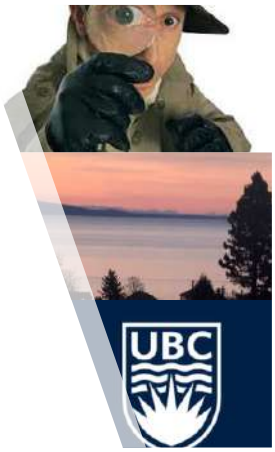
Research in Clinical Practice: From Finger on the Pulse to Publication

- Ted Rosenberg MD MSc
  trosenberg@hometeammedical.ca
- Margaret McGregor MD MHSc
  mrgret@mail.ubc.ca
- Morgan Price- MD PhD
  morgan.price@ubc.ca

Department of Family Practice
UBC



1

Key Points/ Learning Objectives

- Primary care – is an untapped (environmentally friendly) gold mine for new knowledge and Clinical Research
- Research starts with one observation and a question
- There are many resources to support primary care research
- Research is a Journey with value for physicians, teams and patient care regardless of disembarkation point

2

Embrace the Journey

3

Publication is only One Destination Along the Way

4

Disclosure

- Clinical Assistant Professor Dept. of Family Medicine and Community Geriatrics
- Conflict of Interest – None Identified
- Managing Potential Bias – None Identified
- (Full time Clinician and Curious and Amateur Sleuth)

5

Format

- "Case Study'
  - Clinical Case from my practice that led to a published Epidemiological Study
  - Use this case to illustrate the steps in a research cycle
- Hope that people will share their experience and tips……..

Focus will be on "hypothesis generating" clinical research – **not** on mining large administrative data sets and RCTs

6

Clinical Interventions in Aging

ORIGINAL RESEARCH

The relationship of SSRI and SNRI usage with interstitial lung disease and bronchiectasis in an elderly population: a case–control study

Ted Rosenberg[1]
Rory Lastimer[1]
Patrick Montgomery[1]
Christian Wiens[2]
Liran Levy[3]

[1]Department of Family Medicine, University of British Columbia and Island Medical Program, Victoria, BC, [2]Home Town Medical Services, Victoria, BC, [3]Division of Geriatric Medicine, University of British Columbia, Victoria, BC, [4]Geriatric Psychiatry, University of British Columbia, Victoria, BC, [5]Lung Transplant Program, Toronto General Hospital, Toronto, ON, Canada

Clin Interv Aging. 2017; 12: 1977–1984. doi: 10.2147/CIA.S144263

7

Index Case

- 92 year woman living in a retirement home
- Quit smoking – age 57
- PMHx: severe OA , HTN, Gout . P. Neuropathy, Depression
- Medications: venlafaxine , valsartan, acebutalol, nifedipine, ecasa, zopiclone
- Time Line
  - **June 2010**
    - Unexplained progressive fatigue and SOBOE
    - Bilateral crackles to mid lungs- rest normal, including JVP
    - O2 Sat 88% rest and 85% with walking
    - BNP 927
    - CXR –mild interstitial edema
    - CT- Apical and basilar scarring and central bronchiectasis
    - Echo - Pulm. artery pressure 58 and LVEF 60%
    - Respirologist – "Idiopathic ILD -no DX" . Started on Continuous O2 started

8

Index Case

- **Dec. 22.2014**
  - SOB , fatigue and mobility worse- moved to care section of retirement home in 2013
  - Daughters called because she was more depressed , cranky and withdrawn over the month
  - Appeared depressed, more irritable than normal, not sleeping as well
  - Venlafaxine (started 2004) was increased from 37.5 OD to 75mg OD

9

Index Case

- **Dec 24rd 2014**
  - Call from daughter- "I think mom is dying"
    - Can't get off the chair without 2 people helping
    - Severe SOB and fatigue
  - Exam
    - Alert, no confusion. Did not appear to have the flu. No cough
    - BP 102/68 HR 68 afebrile, O2 sat. 2l/m- 87% rest and 80% with walking a few feet with walker
    - Diffuse coarse Velcro Crackles in all lung zones
    - JVP 3cm +1 Edema. BNP 1,741. CXR diffuse pulmonary fibrosis
  - Refused to go to hospital
  - Medications reviewed:
    - Only change was Venlafaxine. –" Epocrates" –possible cause of ILD
    - Quick "google" Lit review Case reports of assoc. with ILD.
    - Venlafaxine stopped.
    - O2 increased to 4.5 L/M to get to 91% sat

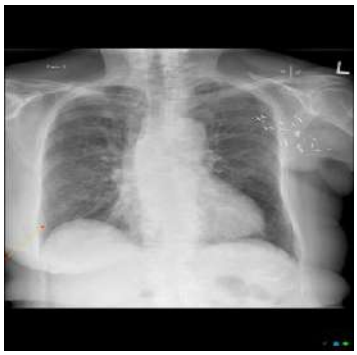
10

Index Case

- **48-72 hours later**
  - SOB much better
  - Fatigue much better
  - Walking in hallway in building and O2 sat>90% on 2l/m
  - "Felt better than had in long time"

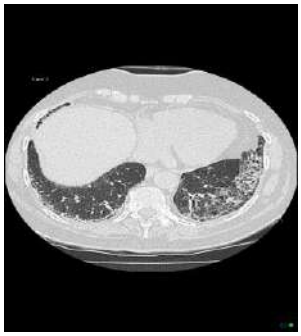
11

Case 1 CXR



12

Case #1- Honeycombing and Traction Bronchiectasis



13

Step 1 Clarify the Question

- Can Venlafaxine cause Lung Disease?

14

Step 2 Curiosity….. What do other Travellers Report? Jan.2015-Mar.2015

- Called Respirologist and Geri-psychiatrist
  - ’never heard of it” but advised to check:
  - Pneumotox website (www.pneumotox.com)

Found the following were associated with ILD:

- Most SSRIs
- SNRIs
- TCAD

- Email to Library- Quick Literature review- ~ 20 published case reports

15

Step 3 Review of Practice March 2015-June 2015

- Review other cases in practice with ILD and bronchiectasis
  - 5 people – severe symptomatic chronic ILD/ bronchiectasis
  - All on chronic SSRIs and SNRI
- Carefully took them off drugs and 4/5 improved symptomatically-
  - Cough/wheezing and dyspnea
  - Later found cessation of frequent “exacerbations of COPD”

16

Summary

- **5 patients whose lung disease improved off SSRI/SNRIs**
- **Not on my radar or specialists**
- **Lit Review**
  - **Antidepressant use has increased 400% in western countries in the past decade**
    - **Mostly SSRI/SNRI**
  - **Prevalence, Incidence and Mortality from ILD are increasing for unknown reasons**
- **Are they associated?**

17

Step 4- Plan Your Itinerary

Some Helpful Travel Resources

- **Research proposal**
  - What is question(s)- are SSRI /SNRI associated with ILD/Bronchiectasis
  - Do an audit of all the active patients in our practice-n=~300 EMR
    - Data on Clinical Status
    - Data on Anti-depressant and medication exposure
- **Study Design- Standard Criteria The EQUATOR network**
  (Enhancing the QUAlity and Transparency Of health Research). BMJ or JAMA author Hub
  https://authors.bmj.com/before-you-submit/clear-reporting-methodology/
  - Case reports and series- descriptive studies
  - Systematic reviews-PRISMA guidelines
  - Quality Improvement- SQUIRE guidelines
  - **Observational studies- : STROBE guidelines**
    - Cross sectional
    - **Case –control**
    - Cohort Studies
  - Diagnostic Accuracy - STARD guidelines
  - RCT - CONSORT guidelines
- **Reference Manager-**

18

Step 5
Travel Companions

- **Research Team**
  - **Technical Expertise**
    - Database Query from Oscar EMR-SQL-Rory Lattimer
    - Research methods – have MSc and training in Epid.
    - Stats – “ ”
  - **Subject Matter Expertise**
    - Geriatric Psychiatrist- Christian Wiens
    - Respirology- Liran Levy University of Toronto
    - Geriatric Medicine/Research-Pat Montgomery

19

Case Series and Case-Control Study

Study population – Entire practice

Case definition – people with radiological ILD/Bronchiectasis- CXR/CT Chest

Measure Exposure

- Query drug database in Oscar EMR
- Define standard exposure – equivalent to 10mg of citalopram. Calculate person-months exposure

Capture and control confounding variables – eg. smoking, age, Data

- Extraction and audit technique- SQL – OSCAR EMR into Excel
- Data cleaning- e.g. duplicate files, different names for same drug
- Data Management and confidentiality

Data analysis

20

Statistics
Cheap and Easy

NCSS 11
Data Analysis

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Epi Info™

21

Funding

- Our Study- Self Funded – "Cost of Doing Business"
- Other Funding – Grants: Faculty/Dept/Grants/Philanth.
  - Research Assistant/Student project
  - Proposal
  - Execution
  - Presentation –conference
  - Publication
- Other Costs- Personal Time

22

Funding opportunities & challenges

Opportunities:
- ✓ funded research training
- ✓ academic DFPs
- ✓ provincial funding agencies
- ✓ CIHR/ SSHRC
- ✓ targeted RFPs related to your topic

Challenges:
- ✓ administrative burden
- ✓ budget
- ✓ community and stakeholder engagement

23

Before you travel

24

Step – 6
Ethics Review

- Good idea to get this if you are looking at publication or presentation at conference
- **TCPS 2: CORE — Tutorial – on research ethics**
- May get Waiver of Informed Consent for most Audits/QA-QI. Still need Ethics review for publication.
- Needed written consent for the index Case Report/ Prospective studies
- Will take minimum of 2-4 hours to complete Ethics Approval on-line not including requirements for changes

25

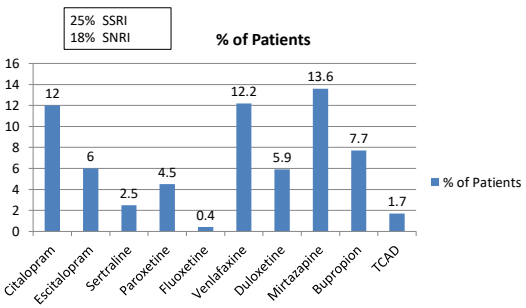
Travel requires patience…….

26

2016 Audit and Analysis- 3 months

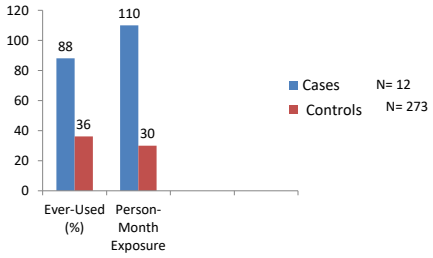
27

Antidepressant use by Type



28

Key Results:
SSRI/SNRI Exposure by Case Status



OR 8.79, 95% CI 2.40-32.2 (p=0.001)

29

Step 8
Preliminary Presentations

- **Rounds**- 2016 – useful feedback
  - Family Medicine Research
  - Geriatrics- invited Respirology
  - General Psychiatry
- **Conference** - IAGG/GSA – World Congress on Gerontology- July 2017
  - Poster Presentation
  - "Peer-reviewed -Late Breaking Research"
- **Publication** – Nov. 2017

30

Step 9
Completing Research
"**Getting to Base Camp**"

31

Peer - Review

32

Attempts at Peer –Review Publication "Our Study"

- **Journal of America Geriatric Society**- no review
- **BMJ** – letter - interesting- not large enough
- **CMAJ**-
  - Went to review
  - not large enough- want multiple sites and population based for this type of study
- **Clinical interventions on Aging**- Accepted

33

Pre-Prints and Pre-Review

- **A Preprint is a full draft of a research paper that is shared publicly before it has been peer reviewed.**
  - Author Certify – Ethics, COI etc
  - Have "Editors – Affiliates" to screen for poor quality
  - Not Typeset /Easily removed/Disclaimer –not peer -reviewed
  - Public Review and feedback
  - Increased visibility - Altimetrics
  - Given DOI- so can be cited even if not published in peer review
- Many journals like the BMJ allow pre-prints
- medRxiv (Pronounced "Med-Archive")- posted on Free server
  https://www.medrxiv.org/

34

Predatory Journals

- Directory of Open Access Journals (DOAJ)
- Journal Citation Reports (**JCR**) database tracked all **impact factors**
- Bealls List of Predatory Journals
  https://beallslist.weebly.com/

35

What if not Published?
Do you really need to "Summit"?

36

Embrace the Journey: Something to be gained every step of the way

- **Improved -Patient Care**
- **Helping Team**
- **Learning and skills**
  - ILD/Bronchiectasis
  - Drug induced lung toxicity
  - Help 1 patient
  - Change my practice-better care
  - Research methodology
  - Public Health issue – increased RX and incidence
- **Opportunity for Collaboration** with different disciplines
- **Sharing Ideas** – emails from conference
- **Leave it as a Pre-Print**
- **Interesting and unanticipated** – side trips

37

Good Stories to Share……

38

Plan your Next Trip…..

- **Population Based Historical Cohort Study**
- Link – Provincial Pharmacare, Hospital and Radiology Databases
- New Exposure to Drug
- Relative Risk/Hazard Ratio of ILD/Bronchiectasis over 10 years

39

Please fill out your session evaluation now!

Complete a session evaluation one of two ways:

- FMF app
- Fmf.cfpc.ca

Session #: **T329**

Session Name:

Clinical Research: moving from finger on the pulse to publication

YOUR FEEDBACK IS IMPORTANT TO US!

40