Comparative Effectiveness Research: 
Role of Registries

Ruth Ann Marrie, MD, PhD
University of Manitoba

&

Gary Cutter, PhD
University of Alabama at Birmingham

Objectives

• To understand the purpose of comparative effectiveness research

• To understand the elements of a comparative effectiveness study

• To know what data sources may be available to conduct comparative effectiveness studies

• Understand importance of and approaches to knowledge translation for comparative effectiveness research
Comparative Effectiveness Research

• To inform health-care decisions
  – From the perspective of ? Patients, clinicians, payors

• Provides evidence regarding different treatment options:
  – Effectiveness
  – Benefits
  – Harms

• Treatment options that can be studied:
  – Drugs, devices, procedures, tests, ways of delivering health care

Comparative Effectiveness Research
Research for the Modern Medical Care System

• Outcomes Research
• Quality Improvement Research
• Effective use of the electronic Medical Record
In attempting to arrive at the truth, I have applied everywhere for information, but in scarcely an instance have I been able to obtain hospital records fit for any purposes of comparison. If they could be obtained, they would enable us to decide many other questions besides the one alluded to. They would show subscribers how their money was being spent, what amount of good was really being done with it, or whether the money was not doing mischief rather than good:

NIH? CMS? Institute of Medicine? Am Hosp Assoc?

No it was Florence Nightingale 1863

NOTES OR HOSPITALS.

FLORENCE NIGHTINGALE.

London:
Longman, Orme, Brown, Green, and Broom.
1863.
CE Studies

• Designs
  – Sequential
  – Adaptive
  – Futility

• Outcomes
  – Clinical
  – Imaging
  – Patient-reported

• Data sources

Limitations of Sequential Trials

• Requires rapid outcome
  – e.g. BMT engraftment
  – Oxygenation response to intervention
  – Too many MRIs in PEDs MS to be feasible

• May not enter boundary and can lead to larger sample sizes than fixed trials

• Assumes accrual is limitless and sequential with homogeneous population
Adaptive Designs
Little Word - Many Meanings

• Requires the trial to be conducted in incremental stages with access to the accumulated data and predefined decisions

• Adaptive design may adapt using:
  – Allocation Rule: how subjects are allocated to treatments
  – Sampling Rule: how many subjects are used in the next stage
  – Stopping Rule: when to stop the trial (for efficacy, for harm, for futility)
  – Decision Rule: how the next steps move forward

Interim analyses & adaptations are performed for many reasons

• To stop enrollment in the control arm so all future enrollment is in the test regimen.
• To stop all enrollment because of disappointing results.
• To increase enrollment to reach larger sample size.
• All such decision points must be planned and pre-specified.
• Extra burden on the monitoring and data management groups.
Interim Analyses or Adaptation entail careful planning of the protocol

• Exacting detail of the statistical design and analysis that can be fixed in advance is provided in the protocol:
  • number of interim analyses or adaptations
  • information rates (how much of the data are available)
  • stopping guidelines
  • Tests

• The time of the Interim Analysis is unknown to the investigators, if possible.

Futility Trials

• A Futility Design or Futility Trial is similar in some way to noninferiority trials or to equivalence studies
  – Assumes a negative outcome as the null hypothesis
    • Drug A is worse than B and tries to reject that hypothesis
    • Rather than convention of null be equal results.

• Often uses historical controls and single group trial to save time and patients
Why Do Futility Trials?

• **PRO**
  - Opportunity cost – spending $ on a futile trial is silly because $ could be spent on other trials
  - Ethically wrong to continue to recruit patients to trials with little hope of achieving helpful results

• **CON**
  - Well conducted trials provide valuable scientific evidence
  - The costs of designing futility trials with a planned futility analysis outweigh any savings
  - Will the result be believed and really save $$$

Outcomes

• **Clinical endpoints**
  - Currently / often used endpoints
  - Emerging endpoints

• **Imaging endpoints**
  - Current / often used endpoints
  - New endpoints

• **Patient-reported outcomes (PROs)**
Currently Used Clinical Endpoints

• Relapse rates
  – Annualized relapse rate
  – % relapse free
  – Time to first relapse

• EDSS disability progression
  – EDSS scale: most common disability scale in MS
  – Progression: 1.0-point ↑ in EDSS if < 5.5, or 0.5 point if ≥5.5
  – Usually time to 3-month confirmed progression
  – Sometimes time to 6-month confirmed disability progression
    (more robust end point, but shortens observation period)

• Multiple Sclerosis Functional Composite (MSFC)

Emerging Clinical Endpoints

• Composite dysconjugate endpoints
  – Change in EDSS or any component of MSFC

• Disease Activity Free Status (DAFS)
  – Absence of Change in EDSS, relapses, MRI activity

• Sustained improvement in EDSS

• Sustained reduction in disability / sustained accumulation of disability
  – Ratio of SRD/SAD (if ratio=1, benefit/risk in balance or random)

• Modifications in MSFC
  – Addition of vision component
  – Replaced Paced Auditory Serial Addition Test (PASAT) with Symbol Digit Modalities Test (SDMT)
Sustained Improvement in EDSS

- A ≥1.0 point decrease in EDSS score sustained for 12 weeks
- Utilized in post-hoc analysis of natalizumab AFFIRM study
  - Natalizumab increased the cumulative probability of improvement over 2 years by 69% versus placebo (P=0.006)
- Potential indicator of neurological improvement
- In AFFIRM, sustained improvement in EDSS correlated with quality of life measures (eg, SF-36)

AFFIRM = Natalizumab Safety and Efficacy in Relapsing Remitting Multiple Sclerosis


Example of Sustained Improvement in EDSS from Natalizumab Phase III AFFIRM Study

Supplemental Figure 1. Time to sustained improvement in physical disability, defined as a ≥1.0-point decrease in EDSS score sustained for 12 weeks, in patients with baseline EDSS scores ≤2.0. EDSS=Expanded Disability Status Scale; HR=hazard ratio; CI=confidence interval.

Adjusted HR=1.66 (95% CI: 1.16, 2.45) P=0.006

Natalizumab 29.9%
Placebo 18.7%

Weeks from baseline

Number of Patients at Risk
Placebo 263 189 175 158 147 117
Natalizumab 417 375 336 302 266 229

Potential Use of Composite (Combined) Clinical/MRI Endpoints

- Disease activity-free status (DAFS)\(^1\)
  - DAFS is a new endpoint, generally defined as:
    - Absence of any relapses or any confirmed accumulation of disability, and
    - Absence of new MRI activity (no new T2 lesions, and no new Gd+ lesions)
  - Should be calculated over a defined time period (e.g., 2-yr, 3-yr)
  - Application in MS phase III clinical trials (post-hoc analyses)

<table>
<thead>
<tr>
<th>Study</th>
<th>% DAFS (2 yrs), Active agent</th>
<th>% DAFS (2 yrs), Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natalizumab (AFFIRM)</td>
<td>37</td>
<td>7</td>
</tr>
<tr>
<td>Cladribine (CLARITY)</td>
<td>44-46</td>
<td>16</td>
</tr>
<tr>
<td>Fingolimod (FREEDOMS)</td>
<td>32.7-37.5</td>
<td>12.9</td>
</tr>
</tbody>
</table>

- In above studies, despite marked reduction of ARR vs placebo, %DAFS was below 50%, leaving room for increases in efficacy
- May be very relevant outcome for Head to Head Trials
- May also be relevant for SPMS and PPMS studies


Currently Used Imaging Endpoints

- At present, most imaging endpoints in trials are based on conventional MRI techniques
- Measures of neurodegeneration\(^1\)
  - Brain volume / atrophy (e.g., brain parenchymal fraction [BPF])
    - Atrophy rates in grey matter may differ from rates in white matter
  - T1 Hypointense lesions (“Black holes”)
    - Limitation: definition is qualitative\(^2\)
    - Evolution of “black holes”
- Measures of inflammatory component of disease\(^1\)
  - Gadolinium-enhancing T1 lesions
  - T2/FLAIR hyperintense lesions
    - Measures cumulative lesion burden

\(^1\) Sicotte NL. Neurotherapeutics. 2011;8(1):54-62.
\(^2\) Inglese M. J Neurol Sci. 2011;311 S1:S16-S23.
Emerging Imaging Endpoints

• Non-conventional MRI techniques
  – Proton magnetic resonance spectroscopy (1H-MRS)
  – Magnetization transfer ratio (MTR) imaging
  – Diffusion tensor imaging
  – Functional MRI (fMRI)

• Other imaging endpoints
  – Optical coherence tomography (OCT)
    • RNFL
    • Other measures of retina/disc


PROs: SF-36 Quality of Life

• Measures patient health-related quality of life (physical & mental)
• Generic, validated & multiple languages
• Generalized to be used for any disease, not just MS
  – Thus, may not properly weigh domains important for MS patients
• Endpoint in ALLEGRO (laquinimod) and DEFINE (BG-12) phase III studies, among others
• Can complement EDSS

SF-36: Mean Changes from BG-12 Phase III DEFINE Study

Mean change from baseline to 2 yrs in physical component summary (PCS) of SF-36

Mean change from baseline to 2 yrs in mental component summary (MCS) of SF-36

• After 2 years of BG-12 therapy, patients in the BG-12 group (both doses) had significantly higher PCS (physical well being) and MCS (mental well being) scores vs placebo


Other Patient-Reported Outcomes

- Modified Fatigue Impact Scale (MFIS)
  - Used in the laquinimod ALLEGRO phase III study
  - Laquinimod produced a significant improvement in fatigue vs placebo

- Guy’s Neurology Disability Scale (GNDS) / UK Neurological Disability Scale (UKNDS)
  - MS-specific scale; takes into account cognitive issues, and fatigue
  - Many validation studies show high reliability
  - However, designed for use in clinical practice not research trials
  - Moderate responsiveness to clinical change

- MS Quality of Life-54 (MS-QOL-54)
  - Validated, acceptable test-retest reliability; limited inclusion of visual and bladder/bowel function

- Functional Assessment of MS (FAMS)
  - Good internal consistency; but almost omits visual, sexual, bladder, and bowel measures

- Patient Determined Disease Steps (PDDS)
  - A self reported EDSS, extensively used in the NARCOMS Registry

Example Published CE Study

- **Objective**: assess relapse rates in patients with active MS initiating fingolimod, IFN or GA
- **Data source**: US PharMetrics Plus database
- **Population**: 525 MS patients who initiated fingolimod, IFN, GA between Oct 1, 2010 and Mar 31, 2011 and had relapse in prior year
- **Outcome**: Relapses – claims-based algorithm
  
  (inpatient visit with a primary ICD-9-CM diagnosis code of 340, or both an outpatient visit with a diagnosis code of 340 and oral or intravenous corticosteroid use within 7 days of the outpatient visit)

CE Study Results

- **Treatment**  
  - Fingolimod 128 31.3% 0.50  
  - IFN/GA 397 34.0% 0.55

  - Baseline differences: age, use of another DMT, number of relapses pre-treatment
  - Adjusting for baseline differences odds of having relapse 52% ↓ with fingolimod OR 0.48; 0.28-0.84
  
  - 50% ↓ ARR OR 0.50; 0.34-0.75
Cost Effectiveness Analyses Does Not Equal Cost Benefit Analyses

• CEA is based on an assessment of the ratio of the financial cost to a unit of measure
  – Cost per relapse
  – Cost per sustained progression
  – Cost per Quality Adjusted Life Year

• CBA less widely used:
  – ratio or difference of two costs, the cost or Euro value of the event or outcome
  – Means putting a cost in Euros on the outcome, which is sometimes the value of a life!

CEA vs. CBA

Cost-Effectiveness Ratio = Total Cost / Units of Effectiveness

Cost-Benefit-Analysis often uses:

Net Benefits = Total Benefits – Total Cost

What is the Dollar value of a relapse prevented?

If MS Therapy ↓ mortality, what is the value of that life saved?
Simplified Process
Steps in Cost - Effectiveness & Cost - Benefit Analysis

• Set the framework for the analysis
• Decide whose costs & benefits should be recognized
• Identify and categorize costs and benefits
• Project costs & benefits over the life of the program
• Monetize (place a dollar value on) costs
• Quantify benefits in terms of units of effectiveness (for CEA), or monetize benefits (for CBA)
• Discount costs & benefits to obtain present values
• Compute a cost - effectiveness ratio (for CEA) or a net present value (for CBA)
• Perform sensitivity analysis
• Make a recommendation where appropriate

Costing Treatments Using Markov Chains
### Following the Cohort Over Time

<table>
<thead>
<tr>
<th>Time 1</th>
<th>By Time 2</th>
<th>By Time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Relapse</td>
<td>Relapse</td>
</tr>
<tr>
<td>No Relapse</td>
<td>0.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Relapse</td>
<td>0.6</td>
<td>0.4</td>
</tr>
</tbody>
</table>

- Of those who started with no relapses by Time point 2, 20% would have relapses and 40% of those who had relapses during Time 1 would have relapses.

- Of those with no relapses seen at Time 2, 24% would have relapses by time 3 because that group is a mixture of the lower and higher risk populations from the prior interval (relapsed at time 1).

### Using the Markov Chain we can estimate the total number of relapses by Year & over longer periods

- **Treatment A**
  - How many people have 0, 1, 2, ... relapses
  - What is the cost of a relapse
  - What is the cost of side effects in those with relapses and those without relapses
  - Repeat for Treatment B

- **Treatment A**
  - How many people have 0, 1, 2, ... relapses
  - What is the cost of a relapse
  - What is the cost of side effects in those with relapses and those without relapses
  - Repeat for Treatment B

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Adding up the Costs

• Total cost in Treatment A is the sum of the cost of the relapses and their treatment plus the cost of the side effects of treatment plus….

• Total cost in Treatment B is the sum of the cost of the relapses and their treatment plus the cost of the side effects of treatment plus….

Quality Adjusted Life Years (QALY): National Institute for Health and Care Excellence (NICE)

• Measures of benefit of treatment used in cost-effectiveness analyses can be based on:
  – ‘natural’ units, e.g. years of life gained
  – value-based measures, e.g. Quality Adjusted Life Years (QALYs).

• Number of QALYs gained by using a treatment is a measure of its benefit in terms of improvements in:
  – the quality of life of patients (including physical performance, pain, distress and psychological improvements as well as changes in survival) summed over a period of time.
  – It therefore incorporates the value of changes in both morbidity and mortality, where these exist.
In the particular case of MS*

- Natural units which capture specific aspects of the impact of MS:
  - relapses avoided
  - delaying progression to wheelchair dependency

- No units which capture both the impact on relapses & the full impact of progression

- One measure used is the Area under the EDSS curve – how long at various steps

*NICE technology appraisal guidance Issued: January 2002
TA32 Beta interferon and glatiramer acetate for the treatment of multiple sclerosis

How a QALY is calculated

- Patient x has MS: If she continues receiving Treatment A → will live 1 year & quality of life = 0.4 (0 or below = worst possible health, 1= best possible health)

- If she receives Treatment B → will live 1 year, 3 months (1.25 years), with a quality of life = 0.6.

- Compare treatments in terms of QALYs gained:
  - Treatment A: 1 (year's extra life) x 0.4 = 0.4 QALY
  - Treatment B: 1.25 (1 year, 3 months extra life) x 0.6 = 0.75 QALY
Then We Compare the Cost per QALY Gained!

- Therefore, Treatment B leads to 0.35 more QALYs (0.75 - 0.4 QALY = 0.35 QALYs).
- Cost of Treatment A is 100,000 per year & Treatment B costs 120,000.
- Difference in treatment costs is divided by the QALYs gained (0.35) = cost per QALY.
- So Treatment B costs 20,000/0.35 = $57,142.86 per QALY gained.

The Other Side of the Benefit/ Risk Equation

- Adverse event reporting system (AERS)
  - Case reports (spontaneous reports)/ Med Watch
- Literature
- Epidemiology Studies
  - Registries
  - Sponsor conducted
  - Observational studies most common
  - Estimation of frequency/rates of events
Postmarketing Safety Information
Spontaneous Reports

- After approval, there are requirements for reporting safety data to FDA
- Serious unexpected events: 15 calendar days
- Other events periodically depending on time product on market (e.g., quarterly for first three years and annually thereafter)

“Serious” Adverse Events (at any dose)

- Death
- Life Threatening
- Disability (persistent or significant)
- Congenital Anomaly
- Hospitalization (initial or prolonged)
- Unexpected “not in the label”
Limitations of Case Reports

- No denominator to assess rate
- Bias toward abnormal outcomes
- Uncertain value for common events
  - e.g., migraine, spontaneous abortion
- Information often incomplete
- Underreporting is problematic
  - e.g., knowledge, time, fear of reprisal

When are case reports helpful?

- Biologically plausible event
  - e.g., pharmacology, confirms animal data
- Pattern is suggested
- Confounders ruled out
- Dose, timing and other exposures known
- Rechallenge/Dechallenge
Data Mining

Valuable information in Data Warehouses, EMRs, Insurance Databases

Data Sources for CE Studies

• Administrative data

• Clinical registries & databases

• Electronic medical records
Administrative Data I

• Result from:
  – delivery of health care services
  – reimbursement for health care services
  – enrolment into health insurance plans

• Sources:
  – Government
    • E.g. Medicare, Medicaid
  – Private (commercial insurance) organizations

Administrative Data II

• Personal identification number
• Demographic information
  – Date of birth, sex, region of residence [e.g. postal code, zipcode]
  – Generally lack race/ethnicity (although not universal)
• Date of service
  – E.g. dates of hospital admission and discharge
• Diagnostic & procedure codes for service
• Some datasets capture:
  – prescription claims eg. medications prescribed
  – Site of service delivery
  – Who delivered the service
Recording Diagnoses

- Many jurisdictions use a version of International Classification of Disease (ICD) codes
  - Detail of coding may vary e.g. number of digits
  - At 3 digit level not specific e.g. bipolar disorder (296.4) is the same as depressive disorder (296.3)

- Some customized codes
  - E.g. Clinical Practice Research Database uses READ codes but these can be mapped to ICD-10 codes

Socioeconomic Status

- Not explicitly captured

- An important potential confounder in many studies as strongly associated with health care utilization

- Geocoding of residence data (e.g. zipcode) to census data allows use of ecologic, area-based measures of socioeconomic status
Potential Outcomes

• Health care utilization
  – Number of hospital days
  – Reasons for hospitalization (based on dx codes)
  – Resource use during hospitalizations
  – Hospital mortality
  – Number of physician visits
  – Types of physicians seen (e.g. specialists)
  – Diagnostic testing (e.g. # MRIs, not results)
  – Medication use & related adverse events

Strengths & Limitations

• In some jurisdictions, population-based
  – E.g. Canada, Scandinavian countries, Taiwan
• Large sample size
• Accessible
• Less costly than primary data collection
• Not collected for research
  – Not validated
  – Coding biases may affect utility of data
  – Lack clinical data
    • E.g. MS course, disability
    • Linkage to other data sources (if possible) may address these deficiencies
US Data Sources

• Medicare
• Medicaid
• Kaiser Permanente
• Indian Health Service National Data Repository
• IMS LifeLink PharMetrics Plus Database
• United HealthCare Database
• ….

Medicare

• Nationwide health insurance program for
  – people aged ≥65 yrs (98% of this pop’ n)
  – people <65 with certain disabilities
  – people with End-Stage Renal Disease
  – over 45 million beneficiaries enrolled
• Custodians: Department of Health and Human Services, Centers for Medicare & Medicaid Services (CMS).
• Dx coding: Hospital/Physician claims, ICD-9-CM
• Linkable: cancer registry, VA, NDI
• Data access/ cost: Research Data Assistance Center (ResDAC) resdac@umn.edu.
Medicare Claims for MS Studies

• Feasibility analysis: data 2004 to 2008
• Large no.: 6,680 MS patients aged 20-85 yrs
  – Among them, ~30% were 20-49 years of age, 30% 50-59 years, 25% 60-69 years, & those ≥70 years accounted for the remaining 15%.
• Useful for many different study questions
• Part D data since 2006 → unique opportunity to comparatively examine the use & comparative safety of DMTs.

IMS LifeLink PharMetrics plus Database

• Integrated claims database of >100 commercial health plans in US
• Custodians: IMS Health
• Database:
  – Inpatient/outpatient diagnoses & procedures
  – Prescriptions
  – Costs of services
  – Place of service…
• Dx: ICD-9-CM
• Contact: IMSeservice@imshealth.com
Kaiser Permanente Northern California

- Covers KP members (>3 million as of Dec 2012)
- Custodian: Comprehensive Clinical Research Unit within KPNC
- Database
  - Demographics
  - Hospitalizations
  - Ambulatory care
  - Pharmacy
  - Geocoded to census data
- Dx: ICD-9
- Contact: Maureen.B.Fitzpatrick@kp.org

Clinical Registries/ Databases

- Multiple examples
  - Danish MS Register, National Swedish MS Register, Italian MS Database Network, MSBase, New York State MS Consortium Database
- Vary widely in data collected and coverage
- E.g., Danish MS Register
  - All MS patients in Denmark since 1948
  - Years of onset & diagnosis, presenting symptom, course of disease, DSS, MRI/CSF/EP results
  - Linkage to national administrative datasets
The NARCOMS Registry

- NARCOMS = The North American Consortium of Multiple Sclerosis Project
- Begun by the Consortium of Multiple Sclerosis Centers (CMSC) in 1993
- Patient self-report registry
- Goal: to facilitate MS-related research
- Enrollment began 1996
- Semi-annual update questionnaires began 2000

Validation of Diagnosis

- Randomly sampled typical / atypical groups (n =109)
- 52 consented → weighted response rate: 76.3 ± 4.5

- Based on medical records review, physician survey, or physician interview (n=48, weighted %)

Definite MS 98.9 ± 1.1
## NARCOMS: Data Collected

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Age at symptom onset</td>
</tr>
<tr>
<td>Sex</td>
<td>Year of diagnosis</td>
</tr>
<tr>
<td>Race</td>
<td>Relapses</td>
</tr>
<tr>
<td>Education</td>
<td>Hospitalizations</td>
</tr>
<tr>
<td>Annual income</td>
<td>Family history</td>
</tr>
<tr>
<td>Insurance status</td>
<td>Quality of life (SF-12)</td>
</tr>
<tr>
<td>Marital status</td>
<td>Employment status</td>
</tr>
<tr>
<td>Twin status</td>
<td>Treatment</td>
</tr>
<tr>
<td></td>
<td>Disability status</td>
</tr>
</tbody>
</table>

## What if you want to use NARCOMS for a comparative effectiveness (or any other) study?

- Contact person
- Types of collaborations
- Steps to getting a collaboration going
Overview & Process

I Overview

• Range of services
• Range of collaborators
• Confidentiality and research agreements
• Cost structure

II Process guidelines

• Initial request
• Review and discussion
• Proposal
• …then what?

Range of Services

1. Recruitment assistance
   – IRB approved studies (observational & interventional)
   – Target population selected based on inclusion/exclusion criteria and proximity to study site(s)
   – One-time notifications sent by mail or online

2. Data-collection collaboration
   – By mail or online
   – IRB approved studies only, no marketing research

3. Data access or analysis
   – Limited de-identified data sets for secondary data analysis
   – Analyses and reports on a specific topic or research question
Range of Collaborators

1. CMSC members and member clinics
2. Other clinician-researchers
3. Academic collaborators
4. Non-profit organizations
5. Government agencies
6. Research and recruitment companies
7. Pharmaceutical industry

Confidentiality & Research Agreements

• Program director → confidential disclosure agreement on behalf of NARCOMS when requested (e.g. prior to discussion on clinical trial sites or study protocols)
• Recruitment projects do not require a research agreement (N.B.: may be needed to obtain a purchase order)
• Academic collaborators need to sign either a confidentiality agreement or a research agreement depending on the scope of the project, determined based on the proposal submitted
• Research Agreement with the CMSC/NARCOMS is required for projects with commercial parties, mainly to document data ownership and publication rights
  • Project specific agreement OR
  • Master Service Agreement + task orders

www.NARCOMS.org
Cost Structure of Projects

- NARCOMS is only partially funded by CMSC & thus operates on a cost recovery basis
- Fee structure follows guidelines provided by CMSC & takes into account nature of proposed projects
- Different fees are applicable to
  - Commercial parties
  - Academic collaborators
  - Post-graduate students
  - CMSC member clinics
- Donations and unrestricted grants are always welcome but must be routed through the CMSC

STEP 1. Initial Request

- [http://narcoms.org/researcherinforform](http://narcoms.org/researcherinforform)
  - Start early (before submitting to IRB or funding source)
  - Fill out all applicable sections, including the preferred time frame for the project
Step 2. Feasibility Review

NARCOMS will contact you to discuss:

- Nature and purpose of the project
  - No marketing surveys
  - Potential overlap with other projects (topic or timing)
- Anticipated timeframe
- Availability of participants /data
- Preliminary budget estimate

www.NARCOMS.org

Step 3. Proposal Submission

- Academic collaborators:
  - Complete the NARCOMS proposal form
  - Executive Committee review
  - Provide IRB and other documents when requested

- Commercial parties:
  - NARCOMS will submit a formal research proposal & budget estimate based on discussions with the PI at the company
  - NARCOMS will initiate the research agreement process in collaboration with the CMSC attorney

www.NARCOMS.org
....then what?

- We will work with you throughout the process
- Recruitment projects - cover letter, best query criteria, description of methods for publication
- Data collection projects - survey design, pilot study, IRB proposal, analysis plan
- Data access and analysis projects - data cleaning & mapping, data analysis & linking, abstract submission, poster preparation
- Publication review or shared authorship
- Collaboration with the authors on a brief article for NARCOMS Now after peer-reviewed publication
- Brainstorming on your next project …

www.NARCOMS.org

Research Summary

- Start early, get NARCOMS involved during the planning process before locking into a budget or timeline
- Submit a request, get feasibility reviewed before completing the proposal form
- Plan and prepare for publications!

www.NARCOMS.org
Knowledge Translation

• Dynamic and iterative process that includes synthesis, dissemination, exchange, and ethically-sound application of knowledge to improve health
• The creation of new knowledge often does not on its own lead to widespread implementation or impacts on health

End of Grant KT

• Goals: raising awareness & promoting action
• Identify the knowledge users and their role in decision-making related to research findings
• Any activity aimed at diffusing, disseminating or applying the results of a research project
  – Conference presentations
  – Publications in peer-reviewed journals
  – Publications for lay public → websites, creative media
  – Workshops
  – Television, radio, print
• Tailor to the particular group of knowledge users
### Integrated KT

- Applies principles of KT to entire research process
- Involve knowledge users as equal partners with researchers → lead to research that is more relevant, useful to the knowledge users
  - Refinement of research questions
  - Selection of methodology
  - Data collection & tools development
  - Selection of outcome measures
  - Interpretation of findings
  - Dissemination of results
- Aka participatory action research, Mode 2 research

### The NARCOMS Approach to KT

- **Audiences**
  - Participants
  - Clinicians
  - Researchers

- **Vehicles**
  - Magazine
  - Conference presentations
  - Scientific publications
  - Website
Participants: NARCOMS Now

- NARCOMS participants receive a publication while they are actively completing surveys (~15,000 annually)
- Previously received MSQR (United Spinal)
- 2011: large-size newsletter, 8-12 pages per issue
- 2012: launch of NARCOMS Now, named by the participants

www.NARCOMS.org/NARCOMSNow

NARCOMS Now Issues

http://www.narcoms.org/narcomsnow/previousissues
NARCOMS Now & Your Research

- One goal of NARCOMS is to relay NARCOMS research results back to the participants

- Once a manuscript has been published, your research is eligible for a feature in NARCOMS Now as either:
  - An interview by our Media Specialist
  - An edited, layman perspective article

- NARCOMS Now also includes highlights and previews of upcoming or ongoing research

www.NARCOMS.org/NARCOMSNow

NARCOMS Now Content

- Every issue has a theme and regular content
- Letter from the Director
- **MS Reflections**: column by an MD (interview or submitted)
- **Feature Focus**: two focus articles related to the theme, translated to Spanish
- **Snapshot**: Results from the NARCOMS database
- **NARCOMS Messenger**: Updates from NARCOMS
- **MS News**: Global MS news
- **Faces of NARCOMS**: a personal story from a participant

www.NARCOMS.org/NARCOMSNow
Clinicians & Researchers

- Information provided by NARCOMS participants
- 60+ published manuscripts
- 130+ conference posters, platforms, workshops and short courses (like this one!)
- Published in varied international journals
- Presented at global MS and Neurology conferences

NARCOMS Publication Areas

- **Symptoms include:** Bladder, Cognitive, Depression, Disability, Dizziness, Fatigue, Mobility, Pain, Sensory, Spasticity, Vision
- **Comorbidities include:** Cancer, Vascular, Fibromyalgia, Psychiatric
- **Other topic areas:** Diagnosis, Health Information & Literacy, Reproductive Health, Sexual Intimacy, Smoking

![Chart showing publication areas]
Some examples

Treatment Discontinuation and Disease Progression with Injectable Disease-Modifying Therapies
Findings from the North American Research Committee on Multiple Sclerosis Database
Robert J. Fox, MD; Amber R. Saher, MPH; Tuula Tyrry, PhD; Jennifer Sun, MS; Xiaojun You, PhD; Genevieve Laforet, MD, PhD; Denise Campagnolo, MD, MS
Injectable first-line disease-modifying therapies (DMTs) for multiple sclerosis (MS) are generally prescribed for continuous use. Accordingly, the various factors that influence patient persistence with treatment and that can lead some patients to switch medications or discontinue treatment may affect clinical outcomes. Using data from the North American Research Committee on Multiple Sclerosis

Another One

Impact of Mobility Impairment on Indirect Costs and Health-Related Quality of Life in Multiple Sclerosis
Craig J. Coleman1,2, Matthew F. Sidovar3, Matthew S. Roberts3, Christine Kohn1
1Department of Pharmacy Practice, University of Connecticut School of Pharmacy, Storrs, Connecticut, United States of America; 2Department of Pharmacy, Hartford Hospital, Hartford, Connecticut, United States of America; 3Clinical Development and Medical Affairs, Amgen Therapeutics, Inc., Amgen, New York, United States of America

Abstract
This study was conducted to estimate the indirect costs and health-related quality of life (HRQoL) (utilities) of multiple sclerosis (MS) patients in the United States (US), and to determine the impact of worsening mobility on these parameters. In collaboration with the North American Research Committee on Multiple Sclerosis (NARCOMS) registry we conducted a cross-sectional study of participants who completed the biannual update and supplemental spring 2010 survey. Demographic, employment status, income, mobility impairment, and health utility data were collected from a sample of registry participants who met the study criteria and agreed to participate in the supplemental Mobility Study. Mean annual indirect costs per participant in 2011 US$ and mean utilities for the population and for cohorts reporting different levels of mobility impairment were calculated.
Conclusion

• Comparative effectiveness
  – Many approaches
  – Real world

• Multiple potential data sources for secondary analysis
  – Administrative data
  – Clinical databases & registries
  – NARCOMS!

• Knowledge translation is key

Tuula Tyry, PhD
Program Manager, NARCOMS
Tuula.Tyry@DignityHealth.org
(602) 406 3072
NARCOMS Contact Information

• **Website:** www.NARCOMS.org

• **Magazine:**
  www.NARCOMS.org/NARCOMSNow

• **Telephone:** 1-800-253-7884 (toll free US)

• **Email:** MSRegistry@narcoms.org

• **For Researchers:**
  www.narcoms.org/contact

Questions?