NARCOMS

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Characteristics Associated with Sustained Disease Progression in Previously Relapsed MS Patients

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Disclosures and acknowledgments

Stacey Cofield: Dr. Cofield serves on data safety monitoring committees for Orthotech Biotech and Medimmune. Dr. Cofield has received consulting fees from the American Shoulder and Elbow Society and Teva Neuroscience.

Jessica Marvel: Employee of Novartis Pharmaceuticals

Ruth Ann Marrie: (last two years) Pharma-funded research: Sanofi-Aventis Other sources of research funding: CIHR, PHAC, National Multiple Sclerosis Society, MS Society of Canada, MS Scientific Foundation, CMSC Foundation, Rx & D Health Research Foundation
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Gary R. Cutter: Dr. Cutter serves on data safety monitoring committees for Antisense Therapeutics Limited, Sanofi-Aventis, Bayhill Pharmaceuticals, Bayer Pharmaceuticals, BioMS Pharmaceuticals, Daichi-Sankyo, Glaxo Smith Klein Pharmaceuticals, Genmab Biopharmaceuticals, Medivation, Peptimmune, PTC Therapeutics, Teva, Vivus, NHLBI, NINDS, National MS Society; and receives consulting or speaking fees from Alexion, Accentia, Barofold, CibaVision, Biogen-Idec, Novartis, Consortium of MS Centers, Klein-Buendel Incorporated, Enzo Pharmaceuticals, Somnus Pharmaceuticals, Teva, Biogen Idec, Advanced Health Media, EMD Serono, EDJ Associates, Aegis Creative Marketing, Eli Lilly, UT Southwestern University, Klein Buendel, University of Illinois Health Policy Center, Somnus Therapeutics.

Yuliang Liu and Tuula Tyry: have nothing to disclose

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Background

- The emerging definition of secondary progressive multiple sclerosis (SPMS) is based on the concept that MS is a continuously destructive disease in which a declining course ensues once a threshold is reached.
- Disease management over the total course of MS requires better understanding of the nature and timing of the transition from the primarily relapsing-remitting to the predominantly progressive phase.
- NARCOMS allows for description of changes in disease progression as measured by the self-report PDDS

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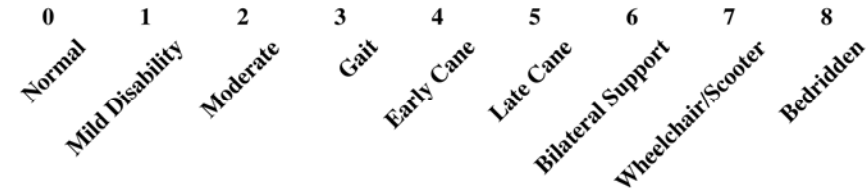
PDDS & Performance Scales

- The NARCOMS registry participants report disability using Patient-Determined Disease Steps (PDDS):



0	1	2	3	4	5	6	7	8
Mild symptoms, return to normal after an attack	Noticeable symptoms with small effect on my life	No limitations in my walking, significant problems limit daily activities	Do not need a cane, but might need assistance during an attack	Need assistance to walk as far as 3 blocks	Cane to walk 25 feet, scooter or wheelchair for further distances	Two canes, crutches or a walker, scooter or wheelchair for further distances	My main form of mobility is wheelchair .	Unable to sit in a wheelchair for more than one hour

Objectives

- To describe characteristics of RRMS Participants who have changes in their PDDS
- To estimate change in PDDS over 5-year period and total follow-up based on starting PDDS & covariates
- To determine patterns of PDDS changes and durability of changes

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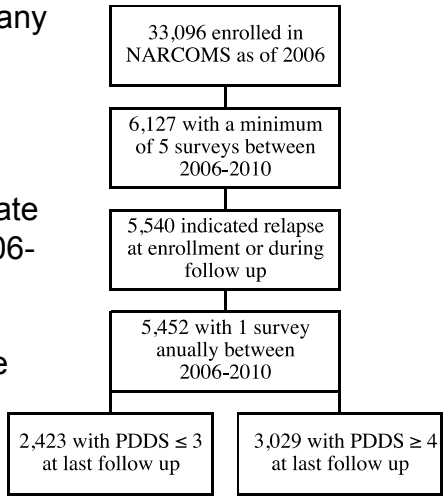
Participant Inclusion Criteria

- **RRMS:** Reported history of any relapse at enrollment or reported a relapse between 2006-2010
- Completed at least one update survey each year during 2006-2010
- US residency throughout the study period
- At least 18 years old



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Participant Characteristics

Characteristic	% Mean (Standard Deviation) (N*=5452)	Median (Inter quartile Range) (N*=5452)
Gender = Females	77.3%	
Age at Symptom Onset	30.2 (9.8) years	30 (23, 37)
Age at Diagnosis	37.9 (9.5) years	38 (31, 45)
Age in 2006	52.7 (10.0) years	53 (46, 59)
Time Since Enrollment	9.7 (2.3) years	10.2 (7.8, 11.1)
Disease Duration in 2006	9.0 (8.6) years	6.0 (2, 13.0)
PDDS in 2006	3.4 (2.3)	3 (1, 5)
PDDS in 2010	3.8 (2.4)	4 (1,6)
Total Relapses 2006-2010	3.6 (3.2)	3 (1,5)

*number varies slightly across characteristics due to missing values or bad dates

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Changes Over Time 2006-2010

Variable	Improve N=696 (12.8%)	No Change N=2956 (54.2%)	Worsen N=1799 (33.0%)	Total N=5451
Age in 2006	51.72	52.78	52.91	52.69
Disease Duration	7.65	9.42	8.73	8.97
Total Relapses	3.64	3.46	3.70	3.56
Rate of PDDS Change	-0.07	0.05	0.19	0.08
Mean Change in PDDS	-1.43	0	1.46	0.30
% w/Confirmed Change	11.6%	17.1%	92.2%	41.2%

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RAM7

Stability over Follow-Up

Enrollment PDDS	Final PDDS Score 2010			
	≤ 3 (2172)	≥ 4 (2810)	All	p-value
≤ 3 (2895)	68.5%	31.5%	58.1%	<0.0001
≥ 4 (2087)	9.1%	90.9%	41.9%	
Total	43.6%	56.4%		

- Cohort was selected to have a minimum follow-up time of 4 years between 2006-2010

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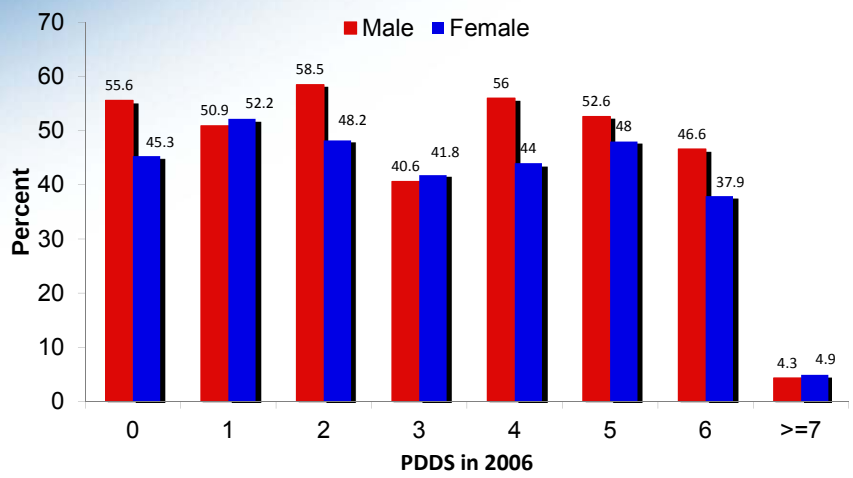
Percent with Confirmed PDDS Change

(Two Successive increases of 1 point > 2006 PDDS between 2006-2010)



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Slide 9

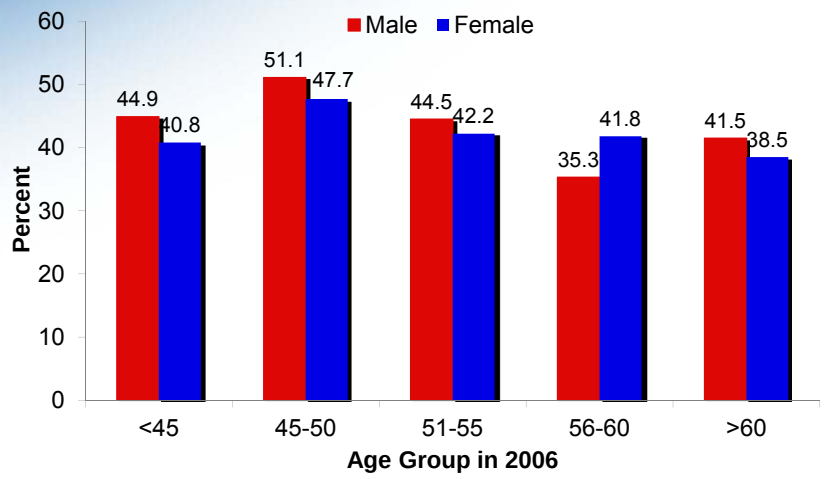
RAM7 would be ideal to know where people were in disease course - or do sens analysis with a virtual incident cohort to see how this holds up

Ruth Ann, 5/24/2014

SC3

Percent with Confirmed PDDS Change

(Two Successive increases of >=1 point over 2006 PDDS between 2006-2010)



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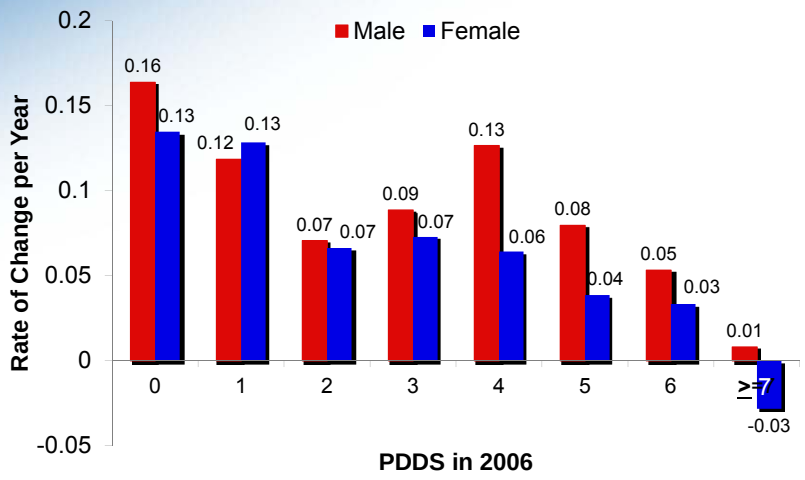
SC4

Annualized PDDS Rate of Change



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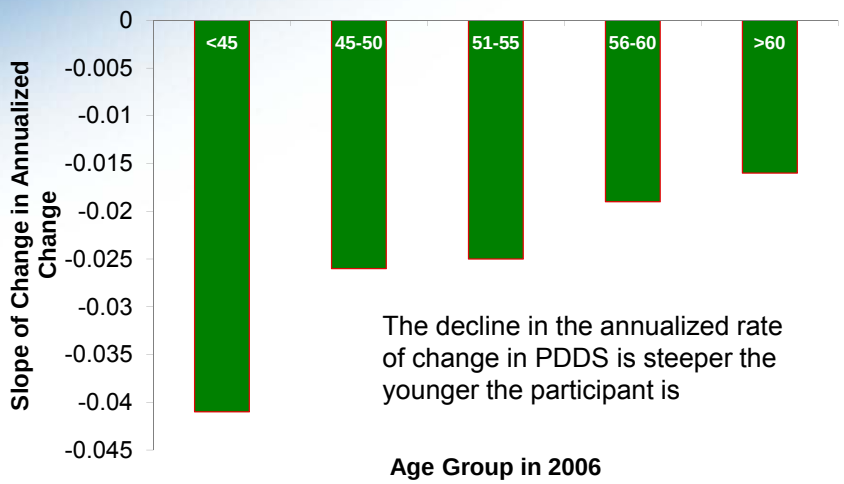
Slide 11

SC3 Same here, remove gridlines
Stacey Cofield, 5/24/2014

Slide 12

SC4 Same here, remove gridline and fix axis on 7 with a text box or something
Stacey Cofield, 5/24/2014

Effect of Age on the Rate of PDDS Change



The decline in the annualized rate of change in PDDS is steeper the younger the participant is

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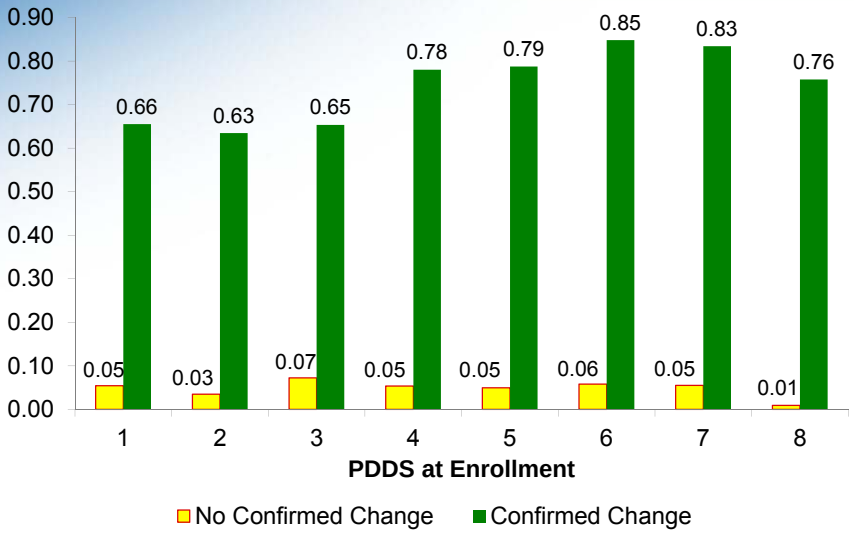
SC6

Durability of Confirmed PDDS Change
Percent With 1 point Change from Enrollment



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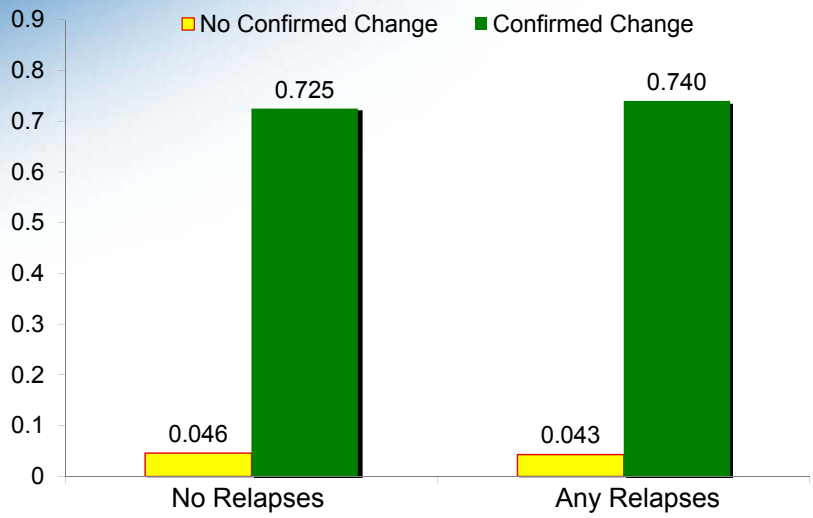
Slide 14

SC6 remove gridlines and what is red and blue? Is this male and female again?
Stacey Cofield, 5/24/2014

RAM5
SC7

Effect of Relapses on Durability of Confirmed PDDS Change Percent With 1 point Change from Enrollment



Relapses between 2006-2010

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Conclusions

- Over an average of almost 10 years, two thirds of those starting at or below PDDS 3 remained < 3
- Males change more than Females but the difference diminishes with age
- Annual rate of change in PDDS drops with age, that is, the effect of PDDS is greater at younger ages
- Durability of worsening increases with PDDS and is unaffected by relapses.
- Durability mirrors that reported by Lublin et.al. for EDSS

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Slide 15

RAM5 seems like a label may be missing here - for relapses vs. no relapses

why don't bars add to 100%
Ruth Ann, 5/24/2014

SC7 Wouls use different colors than red/blue since this is not by gender
Stacey Cofield, 5/24/2014

Thanks For Listening

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