PALLIATIVE CARE RESEARCH COOPERATIVE GROUP

PCRC Data Repository Study Summary

TITLE: **Statin Discontinuation Randomized Control Trial**		
PRINCIPLE INVESTIGATOR(S):	**Jean S. Kutner, MD MSPH** **Amy Abernethy, MD**	SITE(S) (if applicable): • **University of Colorado, Denver** • **Duke University Medical Center** • **Four Seasons Hospice and Palliative Care** • **University of North Carolina, Chapel Hill** • **University of Alabama, Birmingham** • **University of Wisconsin Hospital and Clinics** • **San Diego Hospice and the Institute for Palliative Medicine** • **Northwestern University** • **Mayo Clinic** • **Mount Sinai School of Medicine** • **Kaiser Permanente** • **Western Reserve** • **Washington University** • **Beth Israel Medical Center** • **Capital Caring**
COORDINATING SITE:	**University of Colorado, Denver** **Duke University Medical Center**	
STUDY PERIOD		
START:	**2011-06-03**	
LAST SUBJECT CONTACT:	**2013-07-05**	

OBJECTIVES:

<u>Specific Aim:</u> The study will be conducted within subjects who have a life limiting illness who are on lipid lowering agents (HMG Co-A reductase inhibitors a.k.a. statins) prescribed for primary or secondary prevention of hyperlipidemia. Among such subjects, we aim to determine if there is a difference in the proportion of subjects who die within 60 days of enrollment between subjects who are discontinued on statins vs. maintained on statins.

<u>Hypothesis:</u> The proportion who die in the group that is discontinued from statins is not significantly less than the proportion who die in the group that is maintained on statins.

PARTICIPANTS		
	ENROLLMENT	ELIGIBILITY CRITERIA
Patients:	**381**	**INCLUSION:** • **age > 18 years old;** • **have an advanced life-limiting illness;** • **have a life expectancy of >1 months, AND exhibit declining function status, defined as a reduction in Australia-modified Karnofsky Performance Status (AKPS) 22 score to <80% in the previous 3 months;** • **be on a statin medication for primary or secondary prevention of cardiovascular disease for >= 3 months;** • **have adequately intact cognitive status to provide informed consent and complete the baseline assessment, as**

		evidenced by a Short Portable Mental Status Questionnaire (SPMSQ)23 score of >=6; • **provide informed consent;** • **speak and read English at or above a grade 5 level (per patient or caregiver report)** **EXCLUSION:** • **primary treating physician/care provider estimates their life expectancy as <1 month;** • **under the care of a primary treating physician/primary care provider who is unwilling to have the patient enrolled;** • **not consenting;** • **having known active cardiovascular disease or sufficient risk of active cardiovascular disease to require ongoing therapy with statin drugs, in the opinion of the treating physician;** • **exhibiting obvious symptoms of myositis, known liver function test (LFT) abnormalities of >2.5x the upper limit of normal (ULN), known creatine kinase (CK) abnormalities of >2.5x ULN, or other contraindications to continuing statins, in the opinion of the treating physician**
Informal Caregivers:	**n/a**	**n/a**
Health Care Providers:	**n/a**	**n/a**

METHODOLOGY:

The study was a multicenter, 2-arm, parallel-group, unblinded, non-inferiority, randomized controlled trial of participants in palliative care. Participants were randomized to either discontinue or continue on their statin medication. A stratified block randomization was used to randomize participants in a 1:1 ratio to the treatment arms. The stratification variables were study site and cardiovascular disease history (2 levels: yes vs. no), and block sizes of 2, 4, and 6 were randomly generated. The effects of medication cessation on patient's mental health and perceived QOL were aimed to be studied, so patients were not blinded as to assess the full impact of discontinuing a statin in the real-world setting.

INTERVENTION (if applicable):

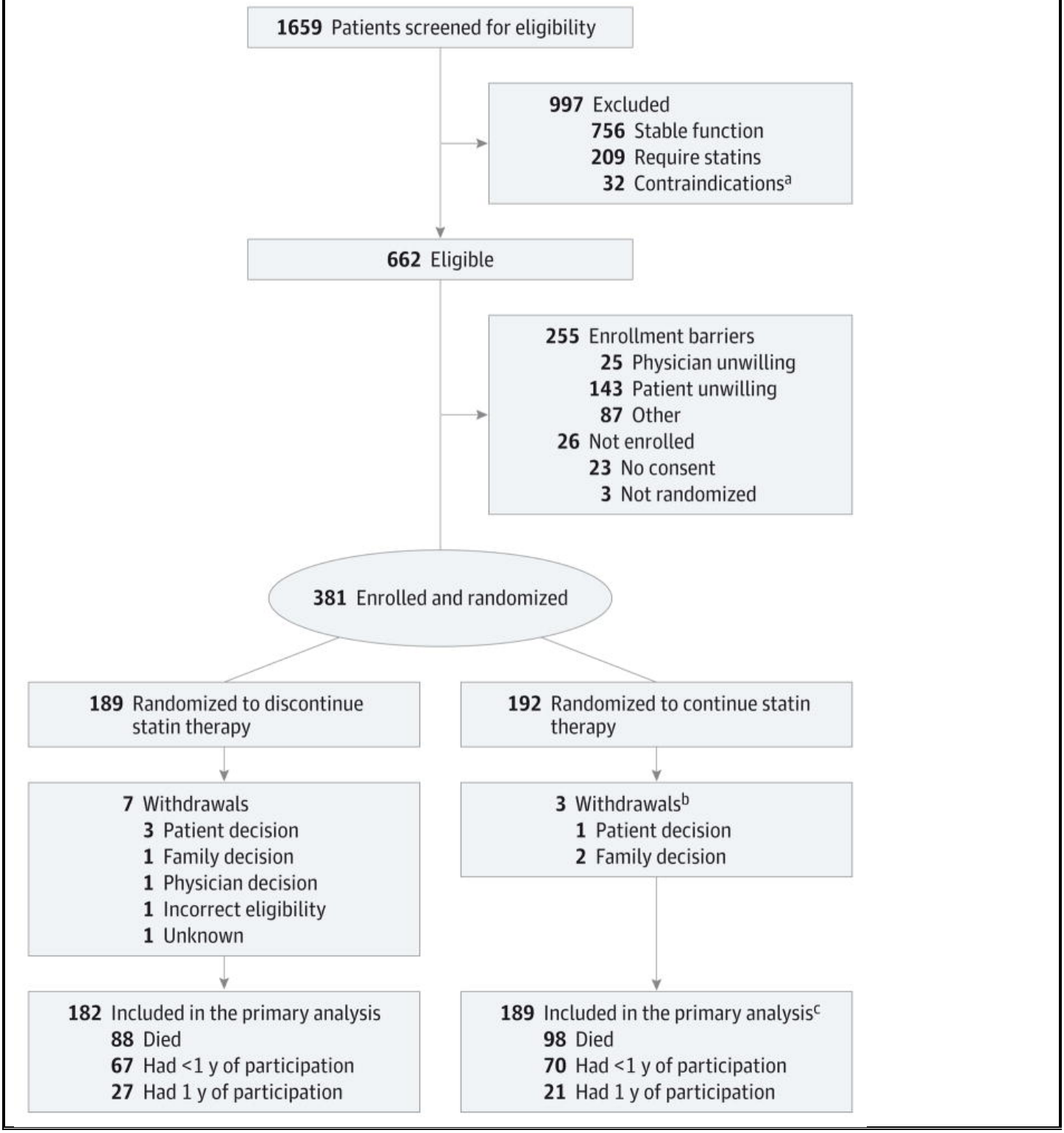
The intervention group discontinued their statins. The control group continued on statins until those medications could no longer be administered or the participant's primary treating physician/primary care provider judged the statin to be unsafe. Adherence was carefully monitored. Extensive communication with treating physicians/primary care providers was part of the recruitment procedures; the treating/primary care provider was required to agree to eligibility; each participant's treating physician/primary care provider was thus fully knowledgeable about the study by the time the participant is randomized.

MEASURES:

- **Participant demographics (age, gender, ethnicity, education). Source – medical records or patient/family caregiver/proxy**
- **Primary diagnosis (date, ICD-9 code). Source – medical records**
- **Co-morbid illnesses and Charlson Comorbidity Index score. Source – medical records and patient/caregiver/proxy.**
- **Smoking history in pack years and current smoking status. Source – patient/caregiver/proxy**

- **Most recent laboratory studies (hemoglobin, creatinine, lipid panel, LFTs, and CK, with dates and reference ranges). Source – medical records reviewed for the past 6 months with preference for test performed within 4 weeks prior to randomization**
- **Statin name, dose, frequency, number of years, indication. Source – medical record**
- **Cognition (SPMSQ). Source – patient**
- **Insurance status using Agency for Healthcare Research and Quality (AHRQ) categorization. Source – administrative records**
- **Potential concerns related to medication discontinuation (study specific questionnaire). Source - patient**
- **The primary endpoint for this study was the proportion of deaths within 60 days. The secondary endpoints included two additional safety endpoints: overall survival and time-to-first CV important event (where events consisted of hospital or ED admission for a reason related to CVD, invasive CV procedure or diagnosis with a new CV event).**
- **Quality of Life was measured with the McGill QOL questionnaire using the single item overall QOL score, and the physical symptom, psychological symptom, existential well-being and support subscales.**
- **Symptoms were measured using the Edmonton Symptom Assessment Scale (ESAS). The nine standard items (pain, fatigue, nausea, depression, anxiousness, drowsiness, appetite, well-being, and breathing) were supplemented with four additional items covering symptoms related to statin use: muscle-related pain, weakness, headaches, and fever.**
- **Performance status was measured using the Australia-Modified Karnofsky Performance Status (AKPS) scale.**
- **Polypharmacy was measured as the number of medications (excluding statins) that were 1) regularly scheduled medications, 2) PRN medications taken greater than 50% of days, and 3) PRN medications taken less than 50% of days in the prior week.**
- **Satisfaction with care was quantified through the use of a question determining the likelihood of recommending your current health care to others, measured on a five point scale (1 = very unlikely to 5 = very likely).**
- **Health resource utilization including hospitalizations, emergency department presentations, cardiovascular procedures, new cardiovascular events, venous thromboembolism, and pneumonia. Source – patient/caregiver/proxy report**
- **Adherence to intervention. Source – patient/caregiver/proxy**
- **Enrollment in hospice and/or palliative care (yes/no)**

SUBJECT FLOW (CONSORT):



STUDY CALENDAR:

Study Calendar

To minimize participant burden, study measurements will be efficiently collected. Independent variables will be measured at baseline only, and variables potentially impacted by the intervention will be measured at baseline, weeks 2 and 4, and every 4 weeks thereafter until death or 6 months (Week 24). The exceptions are survival, health resource utilization (HRU), and performance status, which will be monitored weekly in Weeks 1-4, every other week from Week 4 until death or 6 months (Week 24) and then monthly until death or 1 year (Week 52).

Data collected	Baseline (Day 0 – 2) (in person)	Weekly, weeks 1-4; Even weeks, weeks 5-24 or death (by telephone)	Even weeks , week 2-4; Every 4 weeks, weeks 5-24 or death (by telephone)	Monthly, weeks 25-52 or death (by telephone)
Demographics	X			
Primary diagnosis	X			
Comorbid illness	X			
Smoking history	X			
Recent labs	X			
Information on statin taken	X			
Potential concerns related to medication discontinuation	X			
Insurance status	X			
SPMSQ	X			
AKPS[1]	X	X		X
Survival[1]		X		X
Enrolled in hospice (y/n)	X		X	
Receiving palliative care (y/n)	X		X	
MQOLQ	X		X	
ESAS	X		X	
Likelihood to recommend	X		X	
Adherence to study intervention	X		X	
Non-statin medications	X		X	
Health resource utilization (hospital admissions, emergency department visits, invasive procedures for new cardiovascular events, venous thromboembolism[1]		X		X

[1]monitored weekly for Weeks 1-4, every other week for Weeks 6-24, (i.e., 6 months). After 6 months, survival , AKPS and health resource utilization will be monitored until death or 1 year (Week 52) via monthly phone calls made by the Clinical Research Coordinator.

[2]Costs will be calculated from medication (including statin) and health resource utilization information using standardized reimbursement rates.

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BASELINE CHARACTERISTICS (TABLE 1)

		Continue	Discontinue	Total
Total	N	**191**	**189**	**380**
Female	N	79	91	170
Hispanic	N	10	6	16
White	N	161	153	314
Black	N	22	32	54
Non Hispanic White	N	157	149	306
Age Mean (SD)		73.5 (11.5)	74.8 (11.7)	74.1 (11.6)
Grade School	N	5	6	11
Some HS	N	19	21	40
HS Graduate	N	40	37	77
Training After HS	N	21	19	40
Some College	N	34	44	78
College Graduate	N	42	37	79
Graduate School	N	27	24	51
Medicare	N	139	140	279
Medicaid	N	16	18	34
Private	N	20	23	43
Other Insurance	N	13	8	21
COPD	N	20	27	47
Congestive Heart Failure	N	14	18	32
Dementia	N	14	14	28
Renal Disease	N	8	8	16
Malignant Lymphoma	N	4	6	10
Malignant Tumor (w/o Mets)	N	29	15	44
Malignant Tumor (w/ Mets)	N	72	69	141
Other Primary Dx	N	25	28	53
Cognitively Impaired		32	51	83

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PCRC STANDARDIZED DATA ELEMENTS

Please see the separate information sheet "DISC Standardized Data Elements" for the exact wording and format of the data elements.

DATA ELEMENT	Collected?	Var Name(s)	Data source (e.g. self-report, EHR) or reason not applicable
1. Site ID (if multi-site)	☒	Site	CRC
2. Who is the research participant? (e.g., patient, caregiver, etc.)	☐		Only patients participated
3. Sex	☒	sex	EHR
4. Ethnicity	☒	ethnicity	Self-reported
5. Race	☒	race	Self-reported
6. Age in years	☒	eligAge	EHR
7. Current Marital Status	☐		Not collected
8. Primary life-limiting diagnosis/illness	☒	priDx	EHR
9. Performance status (AKPS)	☒	AKPS	CRC
10. Enrolled in Hospice	☒	hospice	Self-reported
a. If yes to hospice, where is hospice care provided?	☐		Not collected
11. Receiving Palliative Care (PC)?	☒	palCare	Self-reported
a. If yes to receiving PC, where is PC provided?	☐		Not collected
12. Source of Death information	☒	fuWho	CRC
13. Location of Death	☐		Not collected
14. Enrolled in Hospice at time of death?	☐		Not collected
15. Receiving PC at time of death?	☐		Not collected

Cells in blue only need to be collected for patient research participants. Cells in orange should be collected regardless of participant type.

PCRC OUTCOME INSTRUMENTS

CONTENT *(e.g., PS)*	ABBREV *(e.g., AKPS)*	INSTRUMENT NAME *(e.g., Australian Modified Karnofsky Performance Status)*
Performance Status	AKPS	Australia-modified Karnofsky Performance Status scale
Health-related Quality of Life	MQOLQ	McGill Quality of Life Questionnaire
Symptoms	ESAS	Edmonton Symptom Assessment Scale (ESAS)