Using [marketing] research to address the challenges of research recruitment and retention

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What's the problem?

- Not as many PTs enroll or remain in research as we think could, or should
- We only diagnose and treat AD because there is a dyad of patient and caregiver-knowledgeable informant-decision maker
- Dyad's are interdependent
- Choices and options should reflect this interdependence

How to improve recruitment and retention

- Methods to identify barriers
  - face to face interviews
  - focus groups
  - freelisting
- Methods to measure the value of changing the barriers
  - conjoint analysis
  - quality improvement
  - randomized and controlled trial

Methods to identify barriers to recruitment and retention

- Freelisting
  - quantitative anthropology method
  - identifies shared understandings
  - participants list out all the words that describe a category
    - What words come to mind when you think of Alzheimers Disease? Just list them out and I'll write them down.
  - shared understanding means the most frequent or salient words

Feelisting

- Present CGs a description of a 12 month AD RCT
- Ask them to freelist
  - Reasons to join
  - Reasons not to join
  - Harms and burdens to PT / to CG
  - Benefits to PT / CG

The harms and burdens of an AD clinical trial

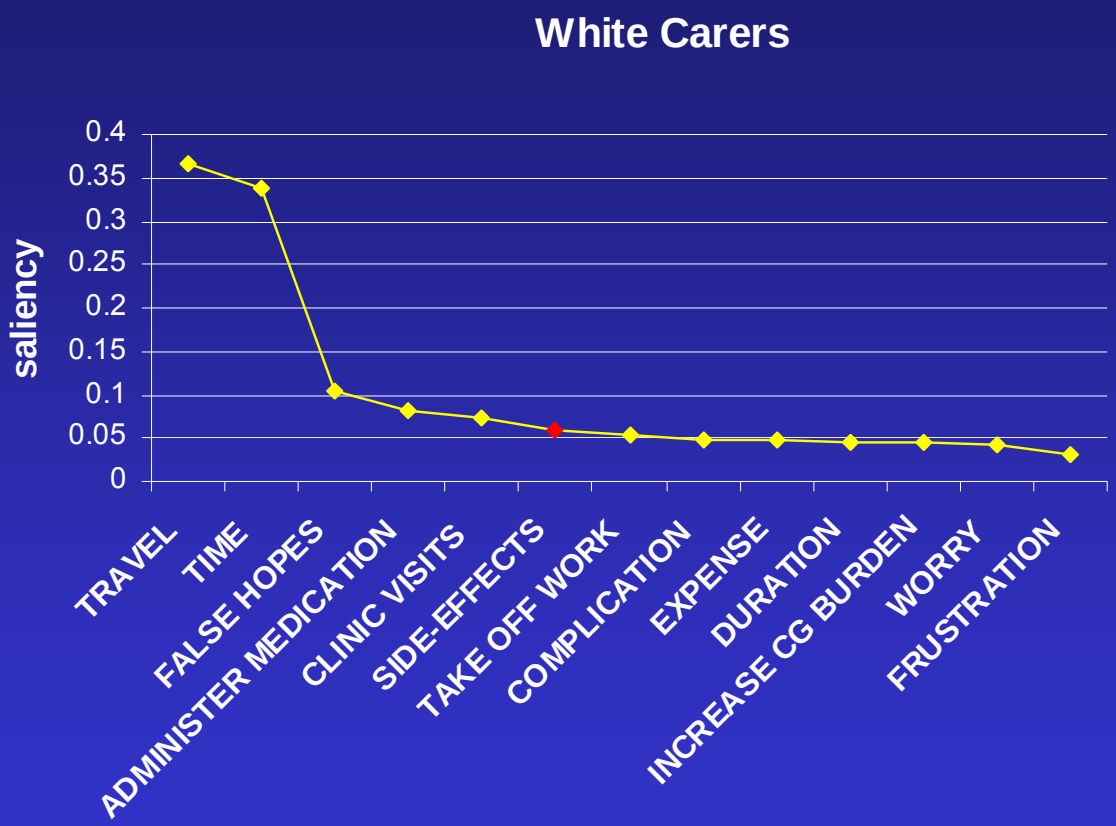
Harms or burdens of the study to a patient with Alzheimer's Disease		
	No harm **Condition worsens** **Don't know** Side-effects **Fear**	Side-effects **Travel** **Time** **Take pills**
Harms or burdens of the study to a family carer		
	No harms **Side-effects** **Don't know** Time	**Travel** Time **False hopes** **Administer medication**

[a] Lists were gathered after participants reviewed a description of an AD randomized and controlled trial. The words in each group are ordered from the most to least salient after selection based on inspection of elbow plots of the saliency scores.

[b] Bolded words denote responses that were salient only in that group of individuals.

Harms and burdens to a CG of an AD clinical trial

F	ITEM	Smith's
2	TRAVEL	0.366
1	TIME	0.339
3	FALSE HOPES	0.105
5	ADMINISTER MEDICATION	0.082
6	CLINIC VISITS	0.072
4	SIDE-EFFECTS	0.059
9	TAKE OFF WORK	0.053
10	COMPLICATION	0.048
8	EXPENSE	0.047
11	DURATION	0.046
7	INCREASE CG BURDEN	0.044
12	WORRY	0.042
13	FRUSTRATION	0.031



Designing a better clinical trial – results of freelisting exercise

What do caregivers see as the *actionable reasons* not to participate in an AD clinical trial?

To patient

- Placebo
- Side effects
- Travel
- Time

To caregiver

- Time
- Travel
- Side effects to patient

Designing a better clinical trial

- Freelisting suggests barriers to recruitment and retention in an AD clinical trial
  - How can we test the value of addressing these barriers?
  - Can we compensate for bad things (such as risk) with convenience features?
- Quicker recruitment and better retention make our research dollar go farther
- We want a better experience for AD research participants

How to redesign them…

- The location of study visits
- Transportation
- Potential risk
- Chance of receiving the experimental treatment

Conjoint analysis

- A method from market research called "conjoint analysis" developed originally at Penn's Wharton School
  - Conjoint = "CONsidered JOINTly"
  - Used by Marriott Courtyard, Easypass, BIGPharma, etc.
- Caregivers rate different scenarios on how likely they would be to participate in a specific AD clinical trial
- From these ratings, we compute the value or "utility" of the alternatives for each caregiver

How to redesign them…

- The location of study visits
  - All ten visits at Penn
  - Initial and final at Penn, eight intermediate at home
- Transportation
  - A transportation (car) service is provided
  - Caregiver is responsible
- Potential risk
  - Basic risk level
  - Basic, plus small risk of heart inflammation
- Chance of receiving the experimental treatment
  - 50-50
  - 67-33

Attribute

Levels of the attribute

Conjoint analysis

- Description of Phase III trial of Alzprotex being done at Penn
  - NIH funded RCT
  - Testing safety, tolerability, and effectiveness
- CGs of community dwelling AD patients with very mild to severe AD (Penn ADCC cohort)
- Key point understanding assessment
  - Purpose, procedures, risks, and benefits
- Willingness to Participate (WTP)

1	.	.	4	.	.	7
Definitely would not participate			Might or might not participate			Definitely would participate

The conjoint sorting task

Research questions

- Is WTP sensitive to reducing the hassles of participation?
  - Have much more WTP as we add features?
- Are medical risks of research overwhelming?
- Does decreasing the hassles of travel increase WTP among sicker patients? "Sicker" CGs? People who live far away?

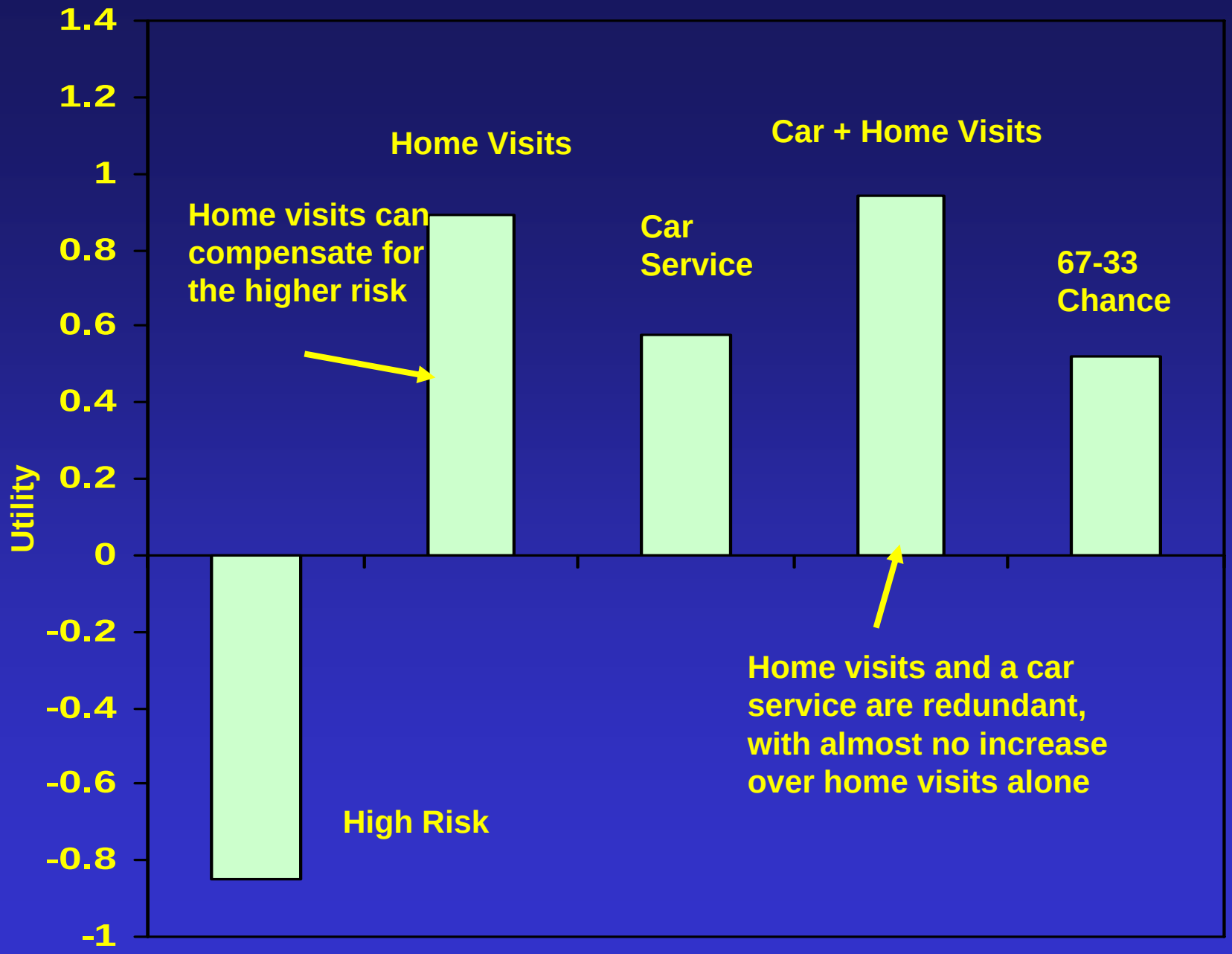
Caregiver Demographics (N=108)

Sex	Female	69%
	Male	31%
Race	Caucasian	77%
	African-American	19%
Ethnicity	Non-Hispanic	96%
	Hispanic	4%
Age (yrs)	Caregiver	63.0±14.5 (32 to 87)
	Patient	78.0± 8.2 (45 to 93)
Relationship to patient	Spouse	52%
Education (yrs)		15.7±2.9 (9 to 24)

Caregiver Travel Distances

	Mean ± SD (range)
Total *Estimated* Travel Time to UPenn MDC (minutes):	53 ± 35 (10 to 180) minutes
Total *Calculated* Travel Time to UPenn MDC (minutes):*	35 ± 27 (4 to 179) minutes

*calculated using Mapquest


1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
Utility
Home Visits
Car + Home Visits
Home visits can compensate for the higher risk
Car Service
67-33 Chance
Home visits and a car service are redundant, with almost no increase over home visits alone
High Risk

What combinations move choice?

- We can use a score of 5 or above on our 7 point scale as a proxy for being “willing to participate”

- Willingness to Participate (WTP)

1 . . 4 . . 7

Definitely would not participate

Might or might not participate

Definitely would participate

By offering home visits and a 67-33 chance, we double the predicted willingness to participate over baseline

Scenario	Predicted willingness to participate N(%)
Low risk, home visits, 67-33 chance ★	65 (60%)
Low risk, home visits	51 (47%)
High risk, home visits, 67-33 chance	45 (42%)
High risk, home visits	29 (27%)
High risk, 67-33 chance	27 (25%)
Low risk and no amenities	26 (24%)
High risk, car service	20 (19%)
High risk and no amenities (the usual AD RCT)	18 (17%)

Additional subjects gained by altering study design

Scenario	Subjects gained
Low risk, home visits, 67-33 chance*	47
Low risk, home visits	33
High risk, home visits, 67-33 chance*	27
High risk, home visits	11
High risk, 67-33 chance*	9
Low risk and no amenities	8
High risk, car service	2
High risk and no amenities (the usual AD RCT)	Baseline

Who finds travel important?

Characteristic of patient or caregiver	Association with overall value of travel reduction efforts*	p
Instrumental ADLs	0.41	<.001
Basic ADLs	0.38	<.001
CG health	0.15	.12
Subjective burden	0.09	.35
Behavior Severity score	0.24	.01
Behavior Distress score	0.23	.02

*Spearman rank order correlation with Σ(Uhome visits + Ucar service + Ucar*home)

Related research supports these results

- The “tailored design method” (Dillman, 2000) maximizes *survey response rate* by
  - creating respondent trust and relationship
  - increasing perceptions of reward
  - reducing the costs of participation

Next steps

- Try these methods out
  - at other sites (a test of the value of the site)
  - examine other research decisions
  - examine other ways to frame and present research
- Try these changes out in a real RCT

Reasons to / not to participate in an AD clinical trial

	Latino Carer	Non-Latino Carer
Reasons why a person with Alzheimer's Disease would want to participate in study		
	Patient improvement **Learn about disease** Improve memory	Patient improvement **Carer** **Help others** **Help research** Improve memory
Reasons not to participate in the study		
	Patient unwilling **Fear** Time	**Placebo** **Side-effects** **Travel** Time **Go off Rx** **No answer** **Stage**

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But, at what cost?

Amenity	Estimated Additional Cost per respondent*
Car service for 10 visits	$1576
Car service for 2 visits plus 8 home visits	$843
8 home visits, no car service	$617
67-33 chance	~12% more sample

*These costs are specific to Penn, calculated on a per respondent basis

Cost estimates for subjects with WTP>=5

Scenario	Average calculated additional cost per subject
Low risk, home visits, 67-33 chance*	$1200
Low risk, home visits	$600
High risk, home visits, 67-33 chance*	$1200
High risk, home visits	$600
High risk, 67-33 chance*	$600
Low risk and no amenities	$0
High risk, car service	$1600
High risk and no amenities (the usual AD RCT)	Baseline

*67-33 chance adds 12% cost because the number of subjects increases 12%, or $600 (assuming a baseline of $5,000), to each subject.

What about the choice to enroll in an AD RCT?

- 21 month RCT comparing drug to placebo
  - 2% risk of heart inflammation
  - All 10 visits at university study site
  - Get to site as best as you can
  - 50-50 chance of the active treatment
- Who wants to be in this study?
  - About 1 in 100 patients enroll in RCTs

Is it worth it?

- Currently, the cost per participant is about $5000
- Adding 8 home visits increases our costs about 12%, and increases WTP by 60% (absolute increase of 10%)
- Using a 67-33 chance of active treatment adds about 12%, and increases WTP by 50% (absolute increase of 8%)

We may improve the representativeness of the sample

Characteristic of patient or caregiver	Association with overall value of travel reduction efforts*	p
Attitudes about research	-0.21	.03
Estimate of travel time	0.28	.003
Actual travel time	0.15	.13

*Spearman rank order correlation with Σ(Uhome visits + Ucar service + Ucar*home)

We may save time and money

- We may be able to screen half as many persons in order to obtain a respondent, saving time and staff costs
  - Currently, when we contact potential respondents, 26% agree to participate, and 22% do participate
- We may have a side effect of reducing dropout, improving statistical power and reducing bias
  - Among those who participate, 18% drop out before the last session

How to increase WTP in AD clinical trials

- A redesigned trial is a more attractive trial
  - Home visits and a better chance at drug may be sufficient – may even compensate for disutility of risk
  - Perhaps “low risk” as well
  - Probably don’t need a car service
- A redesigned trial will bring in sicker patients
  - increasing representativeness and scientific value
  - But not more “burdened” caregivers