2011

UCSF Student Poster Examples

Perfusion and Diffusion-Weighted Imaging are Predictive of Clinical Outcomes of Primary CNS Lymphoma

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Introduction

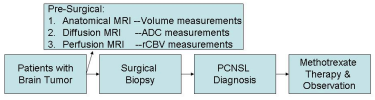
- Primary central nervous system lymphoma (PCNSL) is an aggressive malignant, extra-nodal non-Hodgkin's lymphoma with poor prognosis.
- The mortality of PCNSL patients receiving standard high-dose methotrexate treatment approaches 50% within two years of treatment.
- More aggressive forms of treatment involve whole brain irradiation, however this approach is known to have many deleterious effects.
- Identification of prognostic biomarkers of chemotherapeutic response would identify which patients are at risk of progression, shorter survival and should pursue more aggressive therapies earlier instead of awaiting 6-8 months to recognize failure of chemotherapy.
- At present, there are no established imaging biomarkers predictive of prognosis in PCNSL patients.
- We recently demonstrated that apparent diffusion coefficient (ADC) derived from diffusion-weighted MR imaging at initial diagnosis is highly predictive of overall survival.
- Previous studies have demonstrated that perfusion weighted MR imaging relative cerebral blood volume (rCBV), reflects patency of tumor vasculature. We surmise that this MRI variable could be a good biomarker for PCNSL response to methotrexate therapy.

Specific Aims

- The purpose of our current study was to test the hypothesis that relative cerebral blood volume (rCBV)-derived perfusion MRI reflects patency of tumor vasculature, which influences the delivery of chemotherapeutic agents and hence clinical outcome and survival in immunocompetent patients with PCNSL.
- We also aim to corroborate previous finding supporting ADC as a potential biomarker of survival in PCNSL patients.

Methods

- The study included 26 immunocompetent patients with previously untreated PCNSL who were treated uniformly with methotrexate-based chemotherapy.
- All 26 patients had high-grade B-cell lymphomas, based on surgical biopsy of contrast enhancing lesions on MRI (see flowchart).
- The preoperative MRI was used to measure tumor volume in anatomic MRI, make quantitative measurement of ADC and quantitative measurements of relative cerebral blood volume.
- Regions of interest were placed in all enhancing lesions, ADC and rCBV were measured within the areas of enhancement.



Methods (continued)

- Average and minimum lesion relative cerebral blood volume (rCBV) values of enhancing areas were normalized to a 50-mm² region of interest drawn around the contralateral normal-appearing white matter in the same trans-axial plane (rCBV, next column).
- Minimum ADC values were also measured within all the enhancing lesions. High and low ADC groups were stratified based on a previously published minimum ADC value of 384.
- High and low rCBV groups were stratified based on values determined receiver operator curve analysis.
- Three ADC-rCBV combined groups were formed, a high-high group consisting of patients that had intra-tumoral high ADC and high rCBV values, the low-low group consisting of patients that had low ADC and low rCBV intra-tumoral values and the mixed group which had mismatched measurements of either a low ADC and a high rCBV, or a high ADC and a low rCBV.
- The three groups formed were compared.

Statistical Analysis

- The Welch *t*-test assessed differences between the groups.
- Survival analysis at five years as well as multivariate Cox survival analysis was performed.
- Two-sided p-values were calculated for all test statistics and $P < 0.05$ was considered significant.
- Statistical analyses were performed using STATA Version 10 (College Station, TX).

Results

Survival Analysis Stratified by rCBV

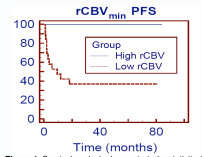


Figure 1. Survival analysis demonstrated a statistical difference (P=0.014) in progression free survival.

Survival Analysis Stratified by ADC

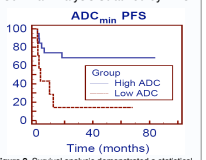


Figure 2. Survival analysis demonstrated a statistical difference (P=0.011) in progression free survival.

ADC vs rCBV Correlation

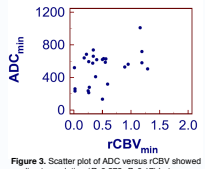
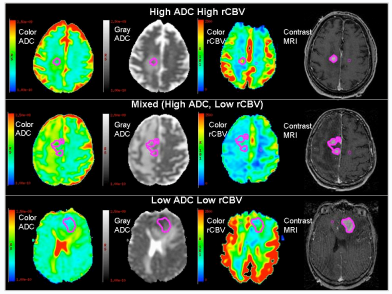


Figure 3. Scatter plot of ADC versus rCBV showed no direct correlation (R=0.272, P=0.17) between both measurements.

- No differences (P>0.05) in tumor burden or age was found between groups (data not shown).
- ADC stratification and rCBV stratifications provided different low and high patient cohorts.
- Combined survival groups (using ADC and rCBV stratifications), further stratified survival groups (Figure 4).
- Multivariate Cox survival analysis showed no other variables besides ADC and rCBV significantly affected survival (not shown).

Results (continued)

Combined ADC/rCBV Group Survival Analysis Images and Data



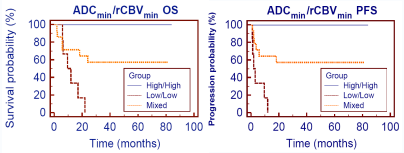


Figure 4. Representative patients from each combined group and survival analysis. Overall survival (OS) as well as progression free survival (PFS) was statistically different for all three groups. The lowADC-lowrCBV group, had very poor prognosis with 100% mortality within 2 yrs. The mixed group had intermediate survival (33.7 month mean survival); and the highADC-highrCBV group had the best clinical outcomes with 100% five year survival (mean survival 66.4 months).

Conclusion

- Our study suggests that rCBV derived from perfusion MRI predicts clinical outcomes (progression and survival) in patients with PCNSL undergoing methotrexate-based chemotherapy.
- We found that the lower the rCBV of the initial untreated tumor, the shorter the overall survival. We postulate that low intra-tumor rCBV suggests lower vascular density which may have impaired delivery of intravenous chemotherapy into tumors.
- Our study found ADC to be predictive of overall survival and postulate that low ADC reflects aggressive biology of PCNSL.
- We found that rCBV measurements were independent of ADC measurements. Our study suggests that the effects of these two variables are additive when used in combination to stratify patients. We surmise that these additive effects are due to the difference in physiology measured (cellularity in case of ADC, and vascularity in case of rCBV).

Acknowledgments

This project was supported by NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. Special thanks to PACCTR/CTSI at UCSF, Joel Palefsky, Peter Chin-Hong, Cecily Hunter, Ruby Singhrao and Marlene Berro.

Reduced Risk of Cerebral Palsy Among Asian Americans: A Population-based Study

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Introduction

- Cerebral palsy (CP) is a clinical syndrome of motor impairment due to a brain lesion occurring during the prenatal or perinatal period. The prevalence of CP is 2-3.6/1000 births[1,2,3].
- Although obstetric and perinatal technologies have improved, the incidence of CP has slightly increased over the last 40 years. The underlying cause of CP is often unknown and currently few preventative measures exist.
- Known risk factors for CP include preterm birth, low birth weight and gestational age, lack of prenatal care, male gender, chorioamnionitis, maternal age at extreme ends and low maternal educational attainment[4].
- CP rates vary significantly among different racial and ethnic groups. Compared to white infants, blacks demonstrate an increased risk of CP which is entirely explained by their increased risk of low birth weight babies[5]. In contrast, Asian American infants have a 20% reduced risk of CP than whites for unclear reasons[5].
- This study compares the prevalence of CP among different subgroups of Asian Americans, and seeks to determine whether differences in sociodemographic factors explain the reduced risk of CP seen among Asians.

Specific Aims

- Aim 1: Establish if all Asian subgroups based upon maternal ethnicity have a decreased risk of CP.
- Aim 2: Determine if differences in rates of birthweight, gestational age, infant sex, maternal age, education, and prenatal care explain the reduced risk of CP among Asians.

Methods

- We performed a retrospective cohort study of 6.2 million California births that were identified from the California Office of Statewide Health Planning and Development (OSHPD) hospital administrative database during the years 1991-2001.
- We identified all infants in this birth cohort who qualified for services from the California Department of Developmental Services for CP, and determined ethnicity from linked birth certificates.
- Asians were categorized into 6 groups: East Asians (Chinese, Japanese, and Koreans N=199 CP); Southeast Asians (Cambodian, Laotian, Thai, and Vietnamese N=137 CP); Pacific Islanders (Pacific Islanders, Guamanians, and Hawaiians N=20 CP); Indian (N=50 CP); Samoans (N=21 CP); Filipino (N=211 CP).
- Birth weight: <1500g very low birth weight (VLBW), 1500-2499g low birth weight (LBW), 2500-4499g normal birth weight (NBW), ≥ 4500g high birth weight (HBW)

Statistical Analysis

- For comparison of proportions, a chi-square test was used. Two-sided p-values were calculated for all test statistics and $p < 0.05$ was considered significant. Statistical analyses were performed using STATA Version 11.1 (College Station, TX).
- We compared CP rates among different Asian subgroups and then determined whether the lower CP risk among Asians persisted after adjusting for known demographic risk factors including birth weight, gestational age, infant sex, maternal age and education, and prenatal care using multivariate logistic regression.

Results

Figure 1: **Prevalence of CP among Asian and white infants born in California 1991-2001**

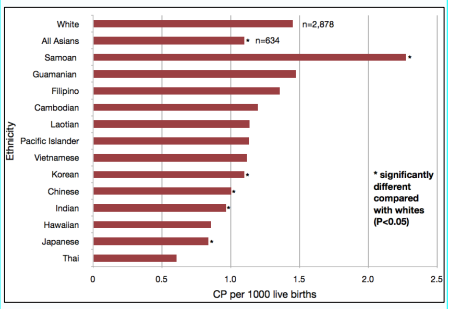

Table1: **Demographic risks for CP among 630,378 Asian births in California 1991-2001**

	n	%	per 1,000	RR	95% CI	P Value
Maternal age, years						
<18	12	1.9	1.2	1.2	0.7 -- 2.0	0.56
18-34	464	73	1.0	1.0	Ref	
≥ 35	158	25	1.3	1.3	1.1 -- 1.5	0.004
Maternal education, years						
Primary school or none (0-5)	32	5.1	1.3	1.4	1.0 -- 1.9	0.06
Secondary school (6-11)	71	11	1.3	1.3	1.0 -- 1.6	0.06
High school graduate (12)	146	23	1.1	1.1	0.9 -- 1.3	0.44
Some college (13-15)	173	27	1.3	1.3	1.0 -- 1.5	0.02
College graduate (≥16)	209	33	1.0	1.0	Ref	
Onset of prenatal care						
First trimester	533	84	1.1	1.0	Ref	
Second trimester	78	12	1.1	1.0	0.8 -- 1.2	0.75
Third trimester	16	2.5	1.1	1.0	0.6 -- 1.6	0.97
No prenatal care	7	1.1	2.2	2.0	0.9 -- 4.2	0.07
Birthweight, grams						
Very low (<1500)	122	18	17	22	18 -- 27	<0.001
Moderately low (1500-2499)	102	16	3.4	4.4	3.6 -- 5.4	<0.001
Normal (2500-4499)	415	65	0.8	1.0	Ref	
High (≥ 4500g)	5	0.8	0.9	1.1	0.8 -- 1.6	0.52
Gestational age, weeks						
<32	99	16	15	18	15 -- 23	<0.001
32-36	90	15	2.0	2.5	2.0 -- 3.1	<0.001
≥ 37	413	69	0.8	1.0	Ref	
Infant sex: male	**390**	**62**	**1.3**	**1.5**	**1.3 -- 1.7**	**<0.001**

Table 2: **Demographics of Asian infants born without CP in California 1991-2001**

	Maternal years of age		Maternal education years				No prenatal care	Birthweight			Male
Maternal ethnicity	<18	>34	0-5	6 - 11	12	13-15	(%)	HBW	LBW	VLBW	(%)
White	2.3	18	0.3	9.8	31	31	0.8	14	4.0	1.1	51
East Asian	0.3	25	1.2	6.7	19	52	0.2	6.5	4.2	0.8	52
Filipino	1.8	21	0.4	6.3	21	36	0.6	6.2	6.3	1.4	52
South East Asian	2.9	17	14	19.3	31	16	0.5	4.0	5.6	1.2	51
Indian	0.2	10	1.0	6.6	17	51	0.3	4.6	7.2	1.4	52
Pacific Islander	3.1	13	1.2	14	45	14	2.3	15	5.0	1.4	51
Samoan	3.0	9.3	1.1	16	59	4	3.8	21	3.5	1.3	52

Red indicates significant difference from whites (P<0.05); all numbers refer to percentages (%)

Results (continued)

Table 3: **Multivariate risk factors CP**

	Asians (n = 638 CP)		
Demographic Risks	**OR**	**95% CI**	
Ethnicity			
White	1.00	Ref	
Indian	0.55	0.39 --	0.78
Pacific Islander	0.59	0.34 --	1.01
East Asian	0.73	0.62 --	0.86
South East Asian	0.74	0.60 --	0.92
Filipino	0.87	0.74 --	1.04
Samoan	2.15	1.24 --	3.72
Maternal age, years			
<18	0.89	0.67 --	1.20
18-34	1.00	Ref	
≥ 35	1.32	1.20 --	1.46
Maternal education, years			
Primary school or none (0-5)	1.54	1.05 --	2.27
Secondary school (6-11)	1.30	1.12 --	1.52
High school graduate (12)	1.25	1.11 --	1.39
Some college (13-15)	1.05	0.94 --	1.17
College graduate (≥16)	1.00	Ref	
No prenatal care	0.70	0.44 --	1.12
Birth weight category			
Very low (<1500)	24	20 --	29
Moderately low (1500-2499)	5.41	4.79 --	6.12
Normal (2500-4499)	1.00	Ref	
High (≥ 4500g)	0.83	0.61 --	1.14
Male sex	1.41	1.29 --	1.52

*Logistic regression model includes all the variables above

Table 4: **Birth asphyxia among Asian subgroups**

	Birth asphyxia among controls		Birth asphyxia among CP cases		Risk of CP among births with no birth asphyxia		
Maternal ethnicity	%	*P values	%	*P values	RR	95% CI	
White	2.2	Ref	13	Ref	1.00	Ref	
Indian	1.9	0.72	11	0.001	0.62	0.45 -	0.86
East Asian	1.6	0.18	16	<0.001	0.65	0.55 -	0.77
Pacific Islander	2.5	0.78	15	0.01	0.70	0.42 -	1.17
South East Asian	1.8	0.47	8.8	<0.001	0.83	0.68 -	1.00
Filipino	1.9	0.59	11	<0.001	0.92	0.78 -	1.08
Samoan	6.4	0.049	14	0.29	1.95	1.12 -	3.38

*P values refer to comparison between Asian subgroup and whites.

Conclusion

- Demographic risk factors for CP among Asians include maternal age >35 years, lower maternal educational attainment, birthweight <2500g, gestational age < 37 weeks, and male sex.
- After adjusting for sociodemographic factors, Indians, East Asians, and Southeast Asians continue to demonstrate a significantly decreased risk of CP, while Samoans have a significantly increased risk compared with whites.
- Future analyses will consider parental ethnic discordance, maternal delivery complications, and congenital anomalies to investigate why most Asian American populations have a decreased risk of CP, while Samoans exhibit an increased risk of CP.

References

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Acknowledgements

This project was funded by the Cerebral Palsy International Research Foundation, by the National Institutes of Health Grant **R03-HD050575**, and is supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129** Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Incidence of and Factors associated with Benign Prostate Glands at Surgical Margins of Radical Prostatectomy Specimens

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Introduction

- Nearly 220,000 men diagnosed with prostate cancer (CaP) annually

  Radical prostatectomy, Open (ORP) or Robotic (RALRP), is the most common treatment for localized prostate cancer
- Benign glands (BGM) are benign epithelial cells which secrete prostate-specific antigen (PSA)
- Benign glands may also be present at the surgical margin. It is unknown if benign glands are generating PSA at levels sufficient to falsely categorize patients as having BCR

Objectives

- To determine the incidence of BGM
- To characterize the association between BGM and surgical technique
- To characterize the association between benign glands at the surgical margins and risk of biochemical recurrence

Methods

Pathology Review

- Identified RP specimens from men with clinical stage T1 or T2 prostate cancer who underwent RP after January 2004
- Single blinded uropathologist re-reviewed slides of prostatic apex and base
- Specimens scored based upon:
- Presence and extent of BGM
- Gleason patterns of tumor at the margins
- Presence of skeletal muscle at the apex
- BGM and/or tumor within the skeletal muscle
- Presence of detrusor muscle at the base

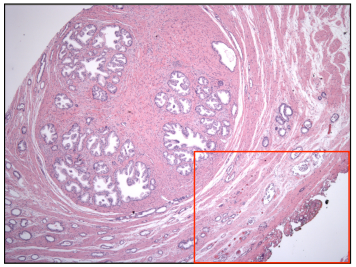
Statistics

- Dichotomous outcome: presence of BGM by surgical approach
- Multivariable logistic regression analyses to determine associations between patient or disease characteristics and presence of BGM
- Cox proportional hazards regression to determine factors independently associated with BCR free survival

Results

- 936 RP specimens were reviewed, 432 were managed by ORP and 504 by RALRP
- Benign glands were found in 274 (29%) cases: 36% at the apex, 50% at the base and 14% at both
- RALRP resulted in 3-fold greater odds of benign glands at the margin (p<0.01) including significantly greater BGM extent at the base (p<0.01), compared to ORP

Histology slide of RP surgical specimen showing presence of benign prostatic glands at the surgical margin



Clinical, pathologic and demographic characteristics of patients undergoing radical prostatectomy

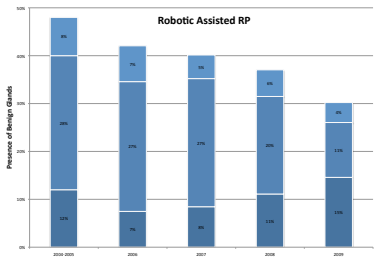
Patient Characteristics		*n = 936*
Year of Surgery, Median (Range)		2006 (2004-2010)
Age (years), Mean (SD)		59 (7)
Caucasian, Number (Percent)		830 (89)
PSA (ng/mL), Median (IQR)		5.6 (4.4-7.7)
Clinical Stage T1, Number (Percent)		419 (45)
Prostate volume (cc), Median (IQR)		29 (23-39)
Biopsy Gleason Grade, Number (Percent)	2-6	491 (53)
	7	306 (33)
	8-10	130 (14)
% Cores positive, Median (IQR)		43 (21-67)
Surgical approach, Number (Percent)	RALRP	504 (54)
Nerve Sparing, Number (Percent)	None	17 (2)
	Unilateral	74 (8)
	Bilateral	836 (90)
Pathologic Gleason Grade, Number (Percent)	2-6	318 (34)
	7 (3+4)	424 (45)
	7 (4+3)	149 (16)
	8-10	45 (5)
Pathologic Stage, Number (percent)	T2	743 (79)
	T3a	150 (16)
	T3b	35 (4)
Tumor volume (cc), Median (IQR)		1.3 (0.5-2.8)
Positive margins, Number (percent)		120 (13)

SD Standard Deviation; IQR Interquartile Range

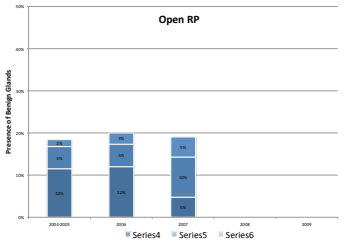
Multivariable logistic regression analysis of benign glands at the surgical margin

Patient Characteristics	OR	95% CI	p value
Age (per decade inc)	0.8	0.6-1.0	0.05
Caucasian (vs other)	1.6	0.9-2.9	0.09
PSA (per ng/ml inc)	1.0	1.0-1.0	0.9
Clinical T-Stage T1 (vs T2/T3)	0.9	0.6-1.2	0.4
Biopsy Gleason Grade	0.9	0.6-1.4	1.0
% Cores positive (cent, per 10% inc)	0.9	0.9-1.0	0.07
Prostate volume (per 10cc inc)	1.1	1.0-1.2	0.1
RALRP (vs ORP)	2.9	2.1-4.2	<.01

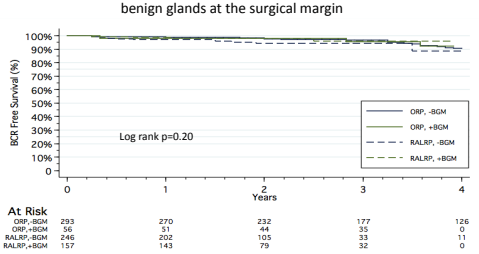
Proportion of cases with benign glands at the margin over time, stratified by type of surgery



Proportion of cases with benign glands at the margin over time, stratified by surgical approach



Biochemical Recurrence-free survival stratified by surgical approach and benign glands at the surgical margin



Conclusion

- Patients undergoing RALRP were more likely to have benign glands at the surgical margin, with greater extent at the base
- Presence of benign glands was not an independent risk factor for biochemical recurrence of prostate cancer

Including unpublished Food & Drug Administration (FDA) trial data changes the results of published meta-analyses

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Introduction

- Statistically significant results in support of a drug's efficacy are more likely to be fully reported than non-significant results.
- Reporting bias has been demonstrated for entire trials[1] as well as specific outcomes within published trial reports[2,3].
- Meta-analyses combine the results of several trials, increasing the power and precision of effect estimates; by synthesizing the available evidence, meta-analyses become an important tool for medical decision making.
- Results of meta-analyses may be biased by under-reporting of non-significant or negative results with regards to a drug's efficacy.
- Public availability of Food and Drug Administration (FDA) reviews of drug trials make them a good source of unpublished trial data for inclusion into meta-analyses.

Objectives

To determine the effect of including unpublished FDA trial data in published meta-analyses

Methods

- **Sample:** We studied 24 New Molecular Entities (NME) approved by the FDA between 2001-2002 with previously identified unpublished outcome data[2].
- **Search:** We performed a systematic search of PubMed, Embase, and the Cochrane Library in November 2010 to identify relevant meta-analyses for each of the study drugs.
- **Selection Criteria:** Two authors independently screened search results based on pre-specified selection criteria to identify all eligible meta-analyses for each drug and selected one for re-analysis.

Inclusion Criteria

- English Language
- Same comparator as FDA
- Contains relevant outcome(s)
- Diagnosis consistent with FDA approved indication
- Search performed beyond FDA approval date

Exclusion Criteria

- Clinical guidelines
- Conference proceedings
- Non-standard meta-analytic methods

- **Data Extraction:** Two authors independently extracted data from both the meta-analyses and the FDA reviews. All decisions regarding data extraction and analyses were concordant with the methods of the published meta-analysis.

Statistical Analysis

- We calculated summary statistics using RevMan 5.1.

Unpublished FDA data included in meta-analysis?

NO → Add → Recalculate
YES → Remove → Recalculate

- Each meta-analysis was re-analyzed using the same methods as in the published meta-analysis with regards to:
  - statistical method (Peto, Mantel-Haenszel),
  - analysis model (fixed vs. random effects),
  - effect measure (relative risk, odds ratio, mean difference)

Study Drugs (n = 24 drugs)

Neurologic:
- almotriptan (Axert)
- eletriptan (Relpax)
- frovatriptan (Frova)
- sodium oxybate (Xyrem)
- galantamine (Reminyl)

Psychiatric:
- aripiprazole (Abilify)
- ziprasidone (Geodon)
- atomoxetine (Strattera)

Ophthalmologic:
- travoprost (travatan)
- bimatoprost (Lumigan)

Allergy/Asthma/ID:
- desloratadine (Clarinex)
- formoterol (Foradil)
- tenofovir (Viread)

Cardiac:
- olmesartan (Benicar)
- eplerenone (Inspra)
- ezetimibe (Zetia)
- nesiritide (Natrecor)

Antibiotics:
- ertapenem (Invanz)
- cefditoren (Spectracef)

Oncologic:
- fulvestrant (Faslodex)

Dermatologic:
- pimecrolimus (Elidel)

Reproductive:
- Ortho Evra

Radiologic:
- perflutren (Definity)

Urologic:
- dutasteride (Avodart)

Black text used for included drugs
Red text used for excluded drugs

Results

Figure 1. Meta-analyses

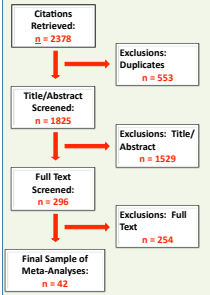
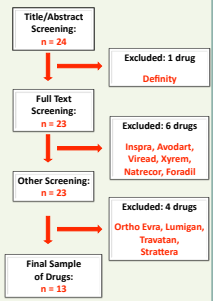


Figure 2. Drugs



Reasons for Exclusions (Full Text only):

Wrong outcome:	n = 33
Wrong comparator:	n = 35
Non RevMan Method:	n = 16
Not a meta-analysis:	n = 119
Other:	n = 51

Number of meta-analyses/drug:
Range: 1 – 8
Median: 2

Results (continued)

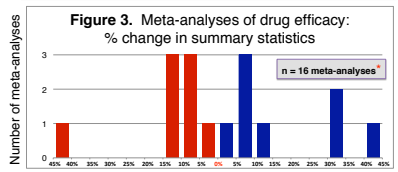
Table 1a. Efficacy Outcomes

Drugs/Outcomes	Proportion of unpublished FDA data in meta-analysis (%)	Effect Estimate w/o unpublished FDA data (95% CI)	Effect Estimate with unpublished FDA data (95% CI)	Change in Estimate (%)	Effect of including unpublished data
Almotriptan (Axert)					
1. Headache relief at 2h	11%	RR 1.6[1.07, 2.48]	RR 1.69[1.26, 2.27]	3.7%	more benefit
2. Pain free response at 2h	11%	RR 2.9[1.5,6, 5.12]	RR 2.8[0.1.97, 3.99]	-4.4%	less benefit
Eletriptan (Relpax)					
3. Pain Relief at 1/2 h	51%	RR 1.17[0.29, 4.80]	RR 1.2[4[0.65, 2.53]	6.0%	more benefit
4. Pain Relief at 1 h	22%	RR 2.5[1.95, 3.31]	RR 2.2[2.1.65, 2.90]	-12.2%	less benefit
5. Pain Relief at 2 h	18%	RR 2.42[1.97, 2.98]	RR 2.27[1.89, 2.73]	-6.2%	less benefit
6. Pain Free at 1 h	26%	RR 7.94[2.88, 21.87]	RR 6.75[2.65, 16.98]	-41.0%	less benefit
7. Pain Free at 2 h	17%	RR 6.83[3.05, 7.64]	RR 6.49[3.00, 6.71]	-7.0%	less benefit
8. Recurrence at 24 h	22%	RR 0.73[0.62, 0.85]	RR 0.84[0.58, 0.76]	-6.9%	more benefit
Pimecrolimus (Elidel)					
9. IGA Score (0 - 1) at 1 wk	55%	RR 2.09[1.06, 3.76]	RR 2.81[1.61, 4.90]	41.0%	more benefit
10. IGA Score (0 - 1) at 2 wks	55%	RR 1.58[1.00, 2.52]	RR 2.1[1.44, 3.09]	33.5%	more benefit
11. IGA Score (0 - 1) at 3 wks	52%	RR 2.6[1.70, 3.97]	RR 2.96[2.08, 4.21]	13.9%	more benefit
12. IGA Score (0 - 1) at 4 wks	55%	RR 1.42[1.00, 2.03]	RR 1.8[1.45, 2.50]	31.7%	more benefit
13. IGA Score (0 - 1) at 6 wks	68%	RR 2.29[1.43, 3.66]	RR 2.04[1.51, 2.76]	-11.0%	less benefit
14. Withdrawals: Any reason	23%	RR 0.38[0.22, 0.63]	RR 0.40[0.27, 0.58]	5.3%	less benefit
15. Withdrawals: lack of efficacy	24%	RR 0.22[0.10, 0.51]	RR 0.23[0.11, 0.41]	-8.7%	more benefit
Ziprasidone (Geodon)					
16. Withdrawal: Lack of Efficacy	47%	RR 0.59[0.40, 0.87]	RR 0.67[0.52, 0.87]	13.6%	less benefit

Table 1b. Safety Outcomes

Pimecrolimus (Elidel)					
17. Any Adverse Events	48%	RR 0.85[0.71, 1.03]	RR 0.92[0.82, 1.02]	8.2%	more harm
18. Withdrawals: adverse events	39%	RR 0.34[0.12, 0.95]	RR 0.43[0.19, 0.97]	26.5%	more harm

Figure 3. Meta-analyses of drug efficacy: % change in summary statistics



* Summary statistics did not change in statistical significance

Conclusion

- This preliminary analysis suggests that the inclusion of unpublished FDA trial data in meta-analyses affects their results.
- The magnitude and direction of the change in results varies with drugs.
- May have important implications for the risk/benefit ratio of a drug.
- **Limitations:** Small sample of drugs after exclusions, Quality of unpublished FDA trials not assessed, FDA reviews did not always provide sufficient information for re-analysis.
- **Recommendations:** We recommend that meta-analyses of drugs include a search of the FDA database.
- **Future Research:** Future research is need to determine how the risk/benefit ratio of a drug is affected by these findings.

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1. Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. *The New England Journal of Medicine*. 2008 Jan;358(3):252-260.
2. Rising K, Bacchetti P, Bero L. Reporting bias in drug trials submitted to the Food and Drug Administration: A review of publication and presentation. *PLoS Med*. 2008 Nov;5(10):e217. doi:10.1371/journal.pmed.0050217
3. Chan AW, Hrobjartsson A, Haahr MT, Gotzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials. *JAMA*. 2004 May; 290(20):2457-2465.

Acknowledgments

Many thanks to:
The Nordic Cochrane Center, Joel Palefsky, Peter Chin-Hong, Cecily Hunter, Erika Campbell, Yuliya Blyakherova, and Marlene Berro.
This work was supported by a grant from the Doris Duke Charitable Foundation to the University of California, San Francisco to fund Clinical Research Fellow Beth Hart.

Quality of Life in Pediatric Patients Who Underwent Colectomy for Ulcerative Colitis

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Research supported by NIDDK

CTSI

BACKGROUND

- Ulcerative colitis (UC) in children can have a negative impact on quality of life (QOL).
- Prior studies in adults suggest that colectomy leads to improved QOL.

AIM

To determine QOL in pediatric patients who underwent colectomy for UC.

METHODS

Subjects: 16 patients with colectomy for UC before 20 years of age between 1980 and 2005.

- 6 Male; 13 Caucasian, 3 African-American.
- 9/16 developed pouchitis.

Patients completed the validated Inflammatory Bowel Disease Questionnaire (IBDQ-32) developed by McMaster University by telephone interview.

IBDQ-32: Consisted of 4 systems:

- Bowel System: frequent stools, loose stools and abdominal pain.
- Emotional Health: irritability, anger and depression.
- Systemic System: fatigue, difficulty sleeping and maintaining weight.
- Social Function: attending social engagements, work or school.
- Each question was scaled from 1 (all the time) to 7 (none of the time); possible scores were 32 to 224, higher scores indicating better QOL.

Data Analysis
Median, Interquartile Range (IQR); Mann Whitney U Rank Sum Test, p≤0.05 = significant.

RESULTS

Table 1: Patient Characteristics

	Median (IQR)
Age at Diagnosis (yrs)	**11 (8-14)**
≤12 (n)	9
13+ (n)	7
Age at Colectomy (yrs)	**13 (10-16)**
≤12 (n)	6
13+ (n)	10
Age at Survey	**19 (17-25)**
≤19 (n)	8
20+ (n)	8
Time Post-Colectomy (yrs)	**6 (4-9)**
≤19 (n)	14
20+ (n)	2

Table 2: QOL by Systems

	Median (IQR)
Bowel System	6 (4-7)
Emotional Health	5 (4-7)
Systemic System	5 (3-5)
Social Function	7 (4-7)
Overall QOL	5 (4-7)

Figure 1: QOL by Age at Colectomy

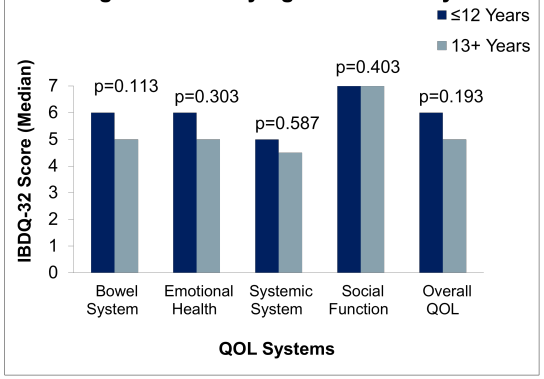
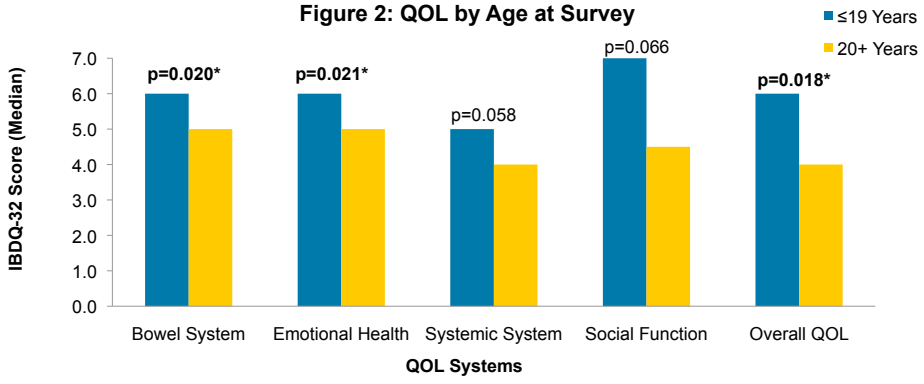


Table 3: Episodes of Pouchitis by QOL Scores

QOL Total Scores	Pouchitis (n=9)	Episodes (Range)
≤100	2	16-30
101-199	2	0-2
≥200	5	0-3

Figure 2: QOL by Age at Survey



RESULTS

- 6/16 patients (37.5%) had scores of 7 (maximum) across all social function questions, which was not found for any other system.
- QOL were similar for patients with pouchitis vs. no pouchitis (p>0.05).

CONCLUSIONS

- Children ≤12 years at colectomy tended to have higher QOL (Figure 1).
- Patients with greatest number of episodes of pouchitis had poor QOL measures (Table 3).
- Patients ≤19 years at the time of survey showed higher QOL in all categories, significance achieved in bowel systems, emotional health, and overall QOL (Figure 2).
- Our results suggest excellent outcome in QOL of pediatric patients with ulcerative colitis after colectomy. Further larger studies are needed.

ACKNOWLEDGEMENTS

Support in part by NIH grants DK060617 (DD, MBH) and DK08085 (JMW)

Pilot Project: Development of a Simple Electronic Reminder AdherenceSystem (SEARS) for Highly Active Antiretroviral Therapy

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DORIS DUKE CHARITABLE FOUNDATION

Introduction

- HAART success depends on patients being adherent to their antiretroviral regiment
- 95% adherence is the goal for treatment of HIV+ patients
- Recent trial of prophylactic antiretroviral therapy confirmed the importance of adherence with the best results (73% reduction in risk) in the group with greater than 90% adherence
- Significant resources are used to increase adherence within the HIV community
- Electronic reminder systems, using email or cell phone text messages, are not widely offered to HIV patients as part of an adherence strategy
- Cell phone deployment in the United States has greater than a 90% penetration rate
- Computers are available within HIV clinics with the necessary software (e.g. Microsoft Office™) to host an electronic reminder system.

Specific Aims

- Create a Simple Electronic Adherence Reminder System (SEARS) that is both low cost and robust
- Recruit patients to use SEARS and evaluate patient satisfaction, self-reported adherence data, and clinical data for design of future studies and enhancements to the system

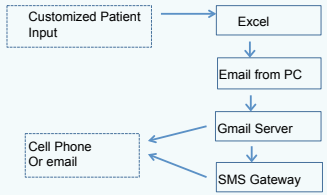
Methods

Inclusion:

- Over 18
- Initiated HAART
- Able to receive text or email messages
- English speaker

All participants were recruited at the UCSF Men's and Women's HIV clinic.

SEARS Overview



Methods (continued)

- The length of the study was 12 weeks
- Surveys were conducted at entry and exit including self-reported adherence using a visual analog scale (VAS)
- Viral loads and CD4 counts were collected at start and end of study

Statistical Analysis

Descriptive statistics were used for all data and paired t-tests were used for the self-reported adherence and clinical lab values.

Results

Table 1: Baseline Characteristics of SEARS Pilot study (N=17)

Age	45 range 22-56
Gender	
Male	24%
Female	65%
Transgender	12%
Number of Daily HIV Medications	3 range 1-5
Technology Use	
Daily E-mail	41%
Daily Text Message'	47%
Daily Electronic Communication (any type)	59%
Considered Electronic Communication Important	71%

Figure 1: Changes in Self-Reported Adherence Measures (N=12)

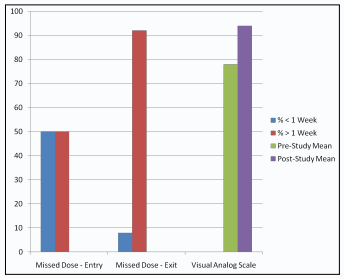


Table 2: Changes in Self-Reported Adherence Measures (N=12)

Result	Pre-Study Mean (SD)	Post-Study Mean (SD)	Change	P-Value
VAS	78 (26)	94 (6.8)	+ 15.4	0.08
< 1 week	6 (50%)	1 (8%)	+ 42%	NA
> 1 week	6 (50%)	11 (92%)		

Results (continued)

Figure 2: Change in CD4 Count (N=13)

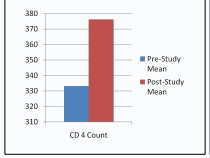


Figure 3: Viral Load (N=13)

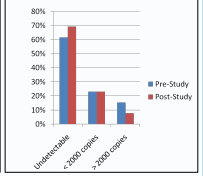
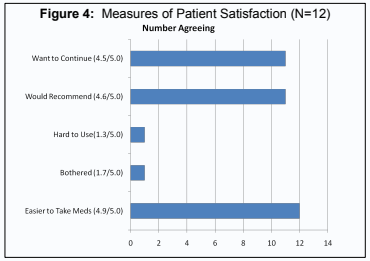


Table 3: Clinical Lab Values (N=13)

Result	Pre-Study Mean (SD)	Post-Study Mean (SD)	Change	P-Value
CD3 Count	333 (254)	376 (307)	+ 42	0.33
Viral Load				NA
Undetectable	8 (62%)	9 (69%)	+1 (7%)	
< 2000 copies	3 (23%)	3 (23%)	--- (0%)	
>2000 copies	2 (15%)	1 (8%)	-1 (7%)	

Figure 4: Measures of Patient Satisfaction (N=12)



Conclusion

- A low cost (zero incremental cost) system can be developed to send custom (time of day, text, and frequency) reminders to patients.
- Patient satisfaction with SEARS was high. Study participants were generally favorably disposed to the system and thought it was easy to use.
- There was a trend towards better adherence although the study was not powered for this outcome.

Acknowledgments

This project was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129 and NIMH Grant** 5K23MH087218-02. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH and NIMH.

Syntactic Deficits and Their Anatomical Correlates in Primary Progressive Aphasia: Insights from the Goodglass Story Completion Task

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[2]Department of Speech, Language and Hearing Sciences, [3]Department of Neurology, University of Arizona

Introduction

- Primary progressive aphasia (PPA) is a dementia syndrome whose most prominent clinical feature is difficulty with language for two years. The three variants of PPA have distinct speech-language characteristics and are associated with atrophy in various areas of the brain.

Table 1. The Three Variants of Primary Progressive Aphasia

	Speech-language core characteristics	Speech-language associated characteristics	For imaging-supported diagnosis (MRI, SPECT, or PET)
Non-fluent variant (NFV)	*One of the following must be present:* 1) agrammatic production 2) effortful, halting speech with speech sound errors, including distortions, deletions, insertions, substitutions, transpositions (consistent with apraxia of speech)	*Two of the following must be present:* 1) impaired syntactic comprehension 2) spared single-word comprehension 3) spared object knowledge	left posterior fronto-insular involvement
Semantic variant (SV)	*Both of the following must be present:* 1) impaired confrontation naming 2) impaired single word comprehension	*Three of the following must be present:* 1) poor object knowledge 2) surface dyslexia/dysgraphia 3) spared repetition 4) spared grammar and motor speech	anterior temporal lobe involvement
Logopenic variant (LV)	*Both of the following must be present:* 1) impaired word retrieval in spontaneous speech and confrontation naming 2) impaired repetition of sentences and phrases	*Three of the following must be present:* 1) phonological errors in speech 2) spared single-word comprehension and object knowledge 3) spared motor speech 4) absence of agrammatism	left posterior perisylvian or parietal involvement

- However, the simplification of NFV as the "non-fluent" form of PPA does not allow for exploration of the features that contribute to fluency, such as speech rate, phrase length, articulatory agility, complexity of sentences and syntactic structure.
- Past studies using picture description tasks have attempted to identify the specific syntactic deficits involved in NFV. However, the unstructured nature of these tasks makes it difficult to obtain data on the variety and complexity of syntactic structures that may be intact or damaged.
- Compared to the unstructured responses from picture description tasks, The Goodglass Story Completion Test provides constrained parameters in which to study a greater range of syntactic structures.

Specific Aims

- This study aims to further characterize syntactic deficits in the three variants (NFV, SV, LV) of primary progressive aphasia.
- We hypothesized that patients with NFV would perform poorly on the Goodglass Story Completion Test, a test of syntax, compared to other patient groups and controls.
- We also hypothesized that deficits would correlate with left inferior frontal cortex atrophy.

Methods

- Patients with the three variants of PPA, behavioral variant FTD (bvFTD), and mixed neurodegenerative diseases were recruited through the UCSF Memory and Aging Center. We recruited a total of 46 patients as well as 12 healthy individuals to serve as controls.
- We used the Goodglass Sentence Completion Test to examine a variety of common English syntactic constructions. Fourteen different constructions were prompted, each with two variations, for a total of 28 items.

Table 2. Sample Scenarios from the Goodglass Story Completion Test

Structure	Scenario	Sample Response
Imperative intransitive	My friend comes in. I want him to sit down. So I say to him… What?	Sit down.
Declarative transitive +s	Dogs always chase cats. A dog is in the street. A cat comes along. What happens?	The dog chases the cat.
Comparative	Mrs. Jones tried to open the jar. She wasn't strong enough. So she called her husband and he did it on the first try. How come?	He was stronger.

- Patients' responses were recorded on a Sony camcorder and digitized with VirtualDub. All responses were then transcribed.
- The responses were coded using several criteria:
  - The type of phrase attempted
  - Whether the target structure was attempted
  - Whether the target structure was correct
  - Presence of syntactic errors, semantic errors, distortions, phonological paraphasias

Statistical Analysis

- We used multivariate analysis to study the numbers and types of errors produced in relation to the subjects' diagnoses.
- Since attempts at three of the syntactic constructions were consistently difficult to elicit across the groups, we chose not to include these constructions in the final analysis.
- Structural MRI images (1.5T/3T/4T) were acquired for each patient and voxel-based morphometry (VBM) was performed with SPM8 to correlate areas of atrophy with performance on the Goodglass task.

Results

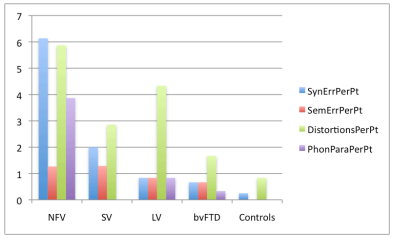
- Patients attempted the intended structure 62.6% of the time. This did not differ significantly across patient groups ($F(3,34) = 0.52$, $p = 0.6718$).
- Across groups, 91.2% of these attempted intended structures were syntactically correct (though they may have contained semantic and/or phonological errors).
- Although they attempted a similar number of structures compared to other patient groups and controls, NFV patients performed worse (74.0%) than the other four groups; this difference was highly significant ($F(4,41)=5.94$, $p = 0.0007$).
- NFV patients had a significantly higher rate of syntactic errors in their responses, regardless of whether they attempted the target structure ($F(4,41)=13.71$, $p<0.0001$).

Table 3. Attempted Items and Correct Items by Patient Group

	NFV	SV	LV	bvFTD	Controls
Avg Number of Attempted Items	12.60	11.71	12.83	14.33	17.50
Avg Percent of Attempted Items	0.57	0.53	0.58	0.65	0.80
Avg Number of Correct Items	9.33	10.57	12.17	13.83	17.42
Avg Percent of Correct Items	0.74	0.90	0.95	0.97	1.00

- NFV patients also had significantly higher rates of distortions ($F(4,41) = 3.6$, $p = 0.013226$) and phonological paraphasias ($F(4,41) = 2.68$, $p = 0.045$) in their responses. In addition, they often provided simplified or agrammatic responses lacking auxiliary verbs, articles, or prepositions, or with incorrect verb forms.
- In terms of specific syntactic structures, NFV patients made errors in even simple and moderately difficult constructs (imperative intransitive/transitive, declarative intransitive/transitive/ditransitive) while other patient groups continued to perform flawlessly. The performance of the NFV patients decreased as complexity increased.

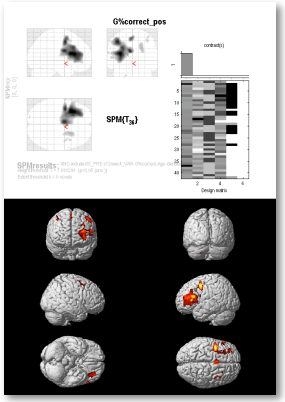
Figure 1. Types and Numbers of Errors by Patient Group



Results (continued)

- We used VBM to correlate syntactic accuracy with grey matter volumes across the whole brain. At a threshold of $p < 0.05$, uncorrected, the largest cluster was in the left inferior frontal gyrus (Broca's area).

Figure 2. VBM – Syntactic Accuracy



Conclusions

- This study used the Goodglass Story Completion Test to probe for the range of syntactic structures that are intact or impaired in a population of patients with PPA.
- The percentage of times that patients attempted the intended structures was roughly equal **across** all groups, suggesting that the structure or mode of administration of the Goodglass test did not create an advantage for any one group over another.
- Compared to controls and patients with other variants of PPA, patients with NFV had a lower percentage of attempted intended structures that were syntactically correct. Their performance decreased as the complexity of the structures increased.
- When considering all responses that contained a verb phrase, regardless of whether the response was the intended structure, the NFV patients also performed worse than the other groups. Patients with NFV also had a higher number of distortions and phonological paraphasias in their responses.
- On VBM, impaired performance on the Goodglass correlated with atrophy in the left inferior frontal cortex, which supports a role for this area in syntactic production.

Acknowledgments

This project was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129**. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

We thank all of the patients, caregivers and volunteers for their participation in our research.

Sensitivity and Specificity of Tests for Trachoma in the Absence of a Gold Standard

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[1]Department of Ophthalmology and F. I. Proctor Foundation, [2]Department of Epidemiology and Biostatistics University of California, San Francisco; [3]Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine; [4]Orbis International, Addis Ababa, Ethiopia

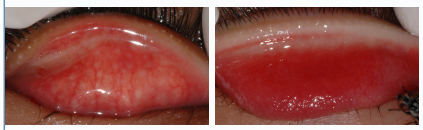
Purpose

- To estimate the sensitivity and specificity of commonly used tests for trachoma
- To develop a method for predicting the PCR prevalence of ocular chlamydia in a village using only clinical exam data

Background

- There is no gold standard for the diagnosis of trachoma [1]
- The WHO simplified grading criteria contains grades of follicular trachoma (TF) or intense trachomatous inflammation (TI)
- DNA-based PCR has been used in research protocols, and is sometimes assumed to be a gold standard for trachoma [2]
- Latent class analysis (LCA) allows characterization of tests without prior assumptions of test performance [3]
- Current WHO treatment protocols use only TF village prevalence [4]

TF **TI**



Examples of follicular trachoma (TF, left) and intense trachomatous inflammation (TI, right). TF is the presence of five or more follicles, at least 0.5mm in diameter, in the upper tarsal plate. TI is inflammatory thickening of the tarsal conjunctiva that obscures at least 50% of the normal vessels

Methods

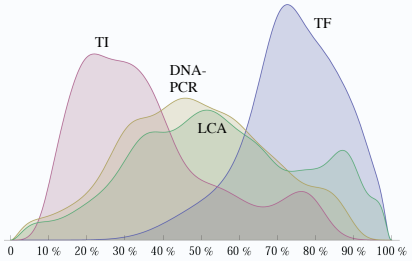
- Clinical exam (TF/TI) and DNA-PCR were obtained in a large clinical trial in Ethiopia in 2003
- We constructed a clustered LCA model which accounted for village clustering present in our data
- The clustered LCA model allowed us to estimate sensitivity and specificity of TF, TI, and DNA-PCR in comparison with a latent gold standard.
- The latent gold standard is a composite of all available data
- We constructed linear models of TF, TI, and their interaction predicting village PCR prevalence
- We selected the optimum linear model based on the Akaike Information Criterion

Results

Table 1. Sensitivity and Specificity versus a Latent Class Gold Standard

Test	Sensitivity (95% CI)	Specificity (95%CI)
TF	87.3% (83.3 – 90.1%)	36.6% (23.6 – 40.3%)
TI	53.6% (46.1 – 88.0%)	88.3% (83.3 – 92.0%)
DNA-PCR	87.5% (79.7 – 97.2%)	100% (69.3 – 100%)

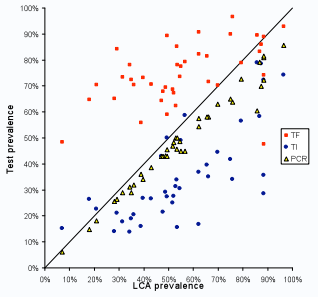
Figure 1. Village prevalence rates by test



Density plots of village prevalence (x-axis) by each diagnostic criteria.

Figure 2. Prevalence of TF, TI, and PCR at given values of the Latent Gold Standard

Latent class prevalence in each village is along the x- axis, test prevalence is along the Y axis. The diagonal line represents a perfect test; above the line is overestimation of true prevalence and below is underestimation



Results (continued)

Latent Class Analysis (LCA)

- TF was quite sensitive (87.3%) but lacked specificity (36.6%) and tended to overestimate disease prevalence (Figure 2, red)
- TI had moderate sensitivity (53.6%) and good specificity (88.3%) and tended to underestimate disease prevalence (figure 2, blue)
- PCR was the most sensitive (87.5%) and most specific (100%) and slightly underestimated disease prevalence (Figure 2, yellow)

Linear model

$$PCR = 0.374(TF) + 0.573(TI)$$

- Preferred model for estimating PCR prevalence contains TF and TI terms
- TI term has larger coefficient than TF

Conclusion

Latent Class Analysis (LCA):

- LCA allowed estimates of sensitivity and specificity
- PCR outperformed the clinical tests
- TI, which currently has no role in WHO treatment protocols, was far more specific than TF
- Our estimates assume conditional independence of tests, which may have biased our estimates

Linear model:

- Our linear regression model suggests that TF and of TI each contribute to the estimation of trachoma prevalence

Caveat

- Both the LCA and linear regression models are based on data from, and may only apply to, high prevalence areas

Acknowledgments

This work was supported by a grant from the Doris Duke Charitable Foundation to UCSF to fund Clinical Research Fellow Craig See.

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Epidermal growth factor module-containing mucin-like receptors (EMR) 2 and 3 confer an invasive phenotype in glioblastoma multiforme and are associated with poor overall survival

Martin J. Rutkowski, Michael E. Sughrue, Ari J. Kane, Joseph M. Kim, Orin Bloch, Andrew T. Parsa

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Introduction

- Glioblastoma multiforme (GBM) is a primary intraaxial brain tumor with high morbidity and mortality
- Its highly aggressive biology renders it a highly proliferative and invasive cancer
- Patterns of GBM invasion and dissemination have been characterized and correlate with overall survival
- Despite aggressive multimodality treatment strategies including surgical resection, radiation, and chemotherapy, GBM recurrence and invasion are common and deadly events
- Epidermal growth factor module-containing mucin-like receptors (EMR) 2 and 3 are proteins that have been previously studied for their ability to mediate invasion and migration of leukocytes
- Based on an analysis of publicly available microarray data accessible through the Cancer Genome Atlas, a government run database, we found a positive correlation between EMR2 and EMR3 RNA expression levels and overall survival

Specific Aims

We investigated the association between EMR2 and EMR3 expression and overall survival in GBM, hypothesizing that:

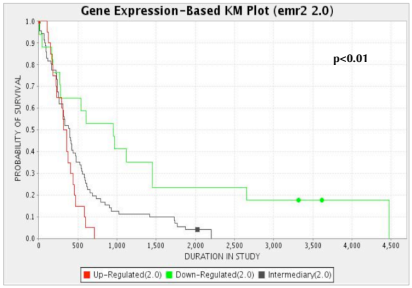
1. EMR2 and EMR3 are variably expressed on primary GBM tissues and GBM cell lines at both RNA and protein levels
2. EMR2 and EMR3 facilitate invasion and migration of GBM cells

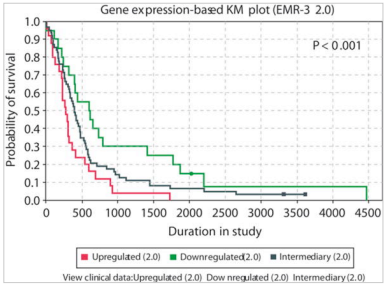
Methods

- Kaplan-Meier analysis of microarray data from the Cancer Genome Atlas was used to establish an association between EMR2 and EMR3 RNA levels and overall survival for GBM patients
- RT-PCR, immunohistochemistry (IHC), and western blotting were used to establish RNA and protein levels for primary GBM tissues and 4 different GBM cell lines
- Small interference RNA (siRNA) was utilized to knockdown EMR2 and EMR3 protein levels prior to functional experiments
- The matrigel transwell invasion assay was utilized to determine the invasive capability of EMR2 and EMR3 knockdown GBM cells compared to those transfected with a negative, non-targeting control
- The ATPlite chemiluminescent proliferation assay was used to determine whether EMR2 and EMR3 knockdown GBM cells grow differently than those transfected with a negative, non-targeting control

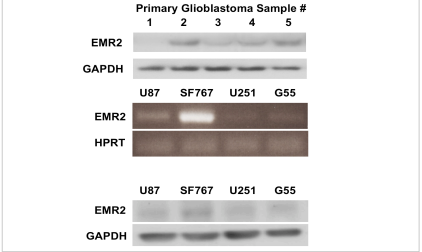
Results

1. EMR2 and EMR3 expression are positively associated with overall survival in GBM patients



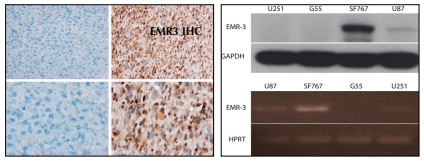


2. EMR2 is expressed at RNA and proteins levels in GBM

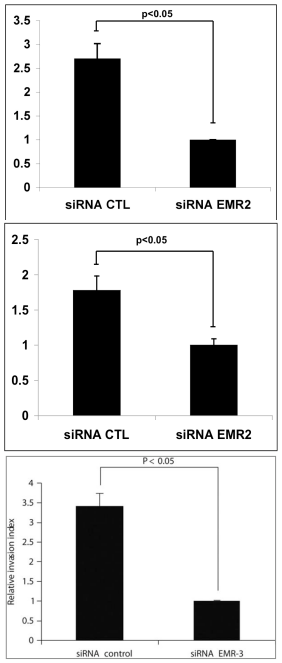


Results (continued)

3. EMR3 is expressed at RNA and proteins levels in GBM

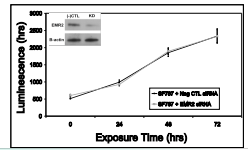


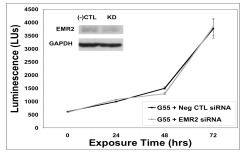
4. EMR2 and EMR3 knockdown decrease the invasive capability of GBM cells

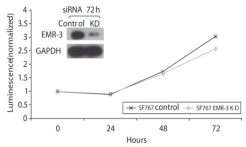


Results (continued)

5. EMR2 and EMR3 knockdown have no effect on proliferation of GBM cells







Conclusions

- EMR2 and EMR2 are variably expressed on primary GBM and GBM cell lines
- Their levels are associated with overall survival in GBM patients
- They facilitate invasion, but not proliferation, of GBM cell lines
- This phenomenon may be partly responsible for the poor overall survival seen among patients whose tumors express higher levels of EMR2 and EMR3

Acknowledgments

This project was supported by NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Many thanks to: The Doris Duke Clinical Foundation, Joel Palefsky, M.D., Peter Chin-Hong, M.D., Cecily Hunter, and Courtney Crane, Ph.D.

Long-term Effects of Initiation of Hormonal Contraception on Condom Use in a Cohort of Young Women

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[1]University of California, San Francisco School of Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, [2]Bixby Center for Global Reproductive Health

Objectives

- In the decade between 1996 and 2006, pregnancy rates among 15-19 year olds decreased nearly 33%, yet as of 2001, an estimated 82% of pregnancies in this age group remain unintended.
- Among adolescents and young adults, this amounts to more than 1.7 million unintended pregnancies yearly.
- At the same time, 15-24 year olds make up only 25% of the sexually active population, yet experience >50% of all new sexually transmitted infections (STIs) each year.
- Dual method use (hormonal methods, IUDs and implants plus condoms) has been promoted as an ideal way to mitigate the burden of both unintended pregnancy and STIs in teens and young adults, however, most recent national estimates indicate that only 8.3% of female teens are using dual methods.

Sexually Active Population

15-24 year olds

All others

Number of Sexually Transmitted Infections Yearly

The goal of this study is to:

- Describe the trends in condom use among women initiating hormonal contraception over time.
- Assess the predictors of dual method use in this group.

Methods

- **Design:** Prospective cohort study
- **Subjects:** 1,387 women aged 15-24 years initiating oral contraceptive pills (OCPs), the transdermal patch (Ortho Evra™), vaginal ring (NuvaRing™) or depo-medroxyprogesterone (DMPA) at public family planning clinics in Northern California. Eligibility criteria included being 15-24 years old, not married, able to read English or Spanish, not pregnant (self-report) or desiring pregnancy within the next year, and able to provide written informed consent and comply with study procedures. Women could not have previously used the method they were initiating at their baseline visit.

- **Study measures:** Research staff collected data on sociodemographics, reproductive/sexual history and attitudes towards condom use from enrolled participants via self-administered electronic questionnaires at baseline and 3, 6, and 12 months. Analysis was limited to the subset of women who had sex in the last 30 days. Condom use was dichotomized (≥80% versus <80% in the last 30 days) and comparisons between consistent and inconsistent condom users at baseline were made using chi-square statistics. The primary outcome measure was dual method use at one year.
- **Data analysis:** Logistic regression was used to analyze both bivariate and multivariable models. Independent variables considered included those found to be associated with dual method use in prior research, potential confounders, variables informed by the Health Belief Model (HBM)[1] and the Theory of Planned Behavior (TPB)[2].

1) HBM: states that individuals weigh the costs and benefits of a health-related behavior before attempting behavior change
2) TPB: takes into account subjective norms around the behavior based on attitudes of individuals close to the person

Results

Who is a consistent condom user?

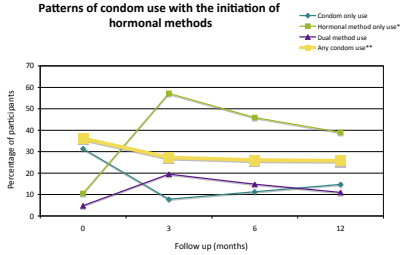
Table 1: Baseline characteristics of participants by condom use status

	Total	Consistent condom user		p-value
		Yes	No	
	N (%)	N (%)	N (%)	
	1,194	432	762	
Sociodemographics:				
Age (years) (N=1194)				<0.001*
15-17	413 (34.6)	170 (39.4)	243 (31.9)	
18-19	391 (32.8)	146 (33.8)	245 (32.2)	
20-24	390 (32.7)	116 (26.9)	274 (36.0)	
Race/Ethnicity (N=1194)				0.09
White	133 (11.1)	59 (13.7)	74 (9.7)	
Latina	320 (26.8)	105 (24.3)	215 (28.2)	
African American/Black	407 (34.1)	150 (34.7)	257 (33.7)	
Asian/Pacific Islander	141 (11.8)	43 (10.0)	98 (12.9)	
Multiracial/Other	193 (16.2)	75 (17.4)	118 (15.5)	
School and employment status (N=1194)				0.09
In school or employed (full or part time)	996 (83.4)	371 (85.9)	625 (82.0)	
Not working or in school	198 (16.6)	61 (14.1)	137 (18.0)	
Clinic site (N=1194)				0.77
Oakland	361 (30.2)	125 (28.9)	236 (31.0)	
Hayward	312 (26.1)	120 (27.8)	192 (25.2)	
Vallejo	139 (11.6)	49 (11.3)	90 (11.8)	
Richmond	382 (32.0)	138 (31.9)	244 (32.0)	
Low income neighborhood (N=1171)	655 (55.9)	244 (58.1)	411 (54.7)	0.27
Reproductive history				
Baseline method initiated (N=1194)				0.01
Pill	366 (30.7)	158 (36.6)	208 (27.3)	
Patch	339 (28.4)	112 (25.9)	227 (29.8)	
Ring	232 (19.4)	74 (17.1)	158 (20.7)	
DMPA	257 (21.5)	88 (20.4)	169 (22.2)	
Prior pregnancy (N=1194)	586 (49.1)	165 (38.2)	421 (55.2)	<0.001
Prior sexually transmitted infection (STI) (N=1165)	255 (21.8)	83 (19.7)	172 (23.0)	0.19
Perceived STI risk in next 3 months with main partner (N=1194)				0.73
Not at all/a little likely/somewhat	875 (73.3)	314 (72.7)	561 (73.6)	
Very likely	319 (26.7)	118 (27.3)	201 (26.4)	
Partner concurrency (sex with man other than main partner) (N=1194)	170 (14.2)	47 (10.9)	123 (16.1)	0.01
Length of sexual relationship (months) (N=1194)				<0.001*
0-6	518 (43.4)	228 (52.8)	290 (38.1)	
7-12	140 (11.7)	41 (9.5)	99 (13.0)	
>12	352 (29.5)	97 (22.5)	255 (33.5)	
No sex yet	184 (15.4)	66 (15.3)	118 (15.5)	
Attitudes towards condom use				
Main partner views of condoms (N=1008)				<0.001*
Very important	307 (30.5)	204 (56.0)	103 (16.0)	
Somewhat important	327 (32.4)	115 (31.6)	212 (32.9)	
Not at all important	321 (31.8)	43 (11.8)	278 (43.2)	
Don't know	53 (5.3)	2 (0.5)	51 (7.9)	
Believes should always use condoms, even if on birth control (N=1187)				0.0014*
Strongly agree	419 (35.3)	185 (43.1)	234 (30.9)	
Agree	417 (35.1)	132 (30.8)	285 (37.6)	
Neither	212 (17.9)	70 (16.3)	142 (18.7)	
Disagree	119 (10.0)	33 (7.7)	86 (11.3)	
Strongly disagree	20 (1.7)	9 (2.1)	11 (1.5)	

*p. is for the chi-square statistic for test of trend of the odds, all others are based on chi-square statistic

- Of the 1,387 women in the cohort, 1,194 women were eligible for analysis.
- The cohort was racially/ethnically diverse with 61% describing themselves as either Latina or African American. Nearly two-thirds lived in a low-income neighborhood and 67% were adolescents.
- At baseline, 36.2% of women were consistent condom users and 4.7% were dual method users.
- Consistent condom users at baseline were more likely to have had a prior pregnancy, been in a relationship of shorter duration, and have main partner with positive views of condoms (Table 1).

Patterns of condom use with the initiation of hormonal methods



Results (continued)

There is a trade-off, but is there also a trade-back?

- After initiation of a hormonal method, condom use dropped to 27%, but remained relatively unchanged thereafter.
- Dual method use increased to a peak of 19% at 3 months but decreased over time, largely due to discontinuation of hormonal methods with less than half of participants reporting use at 1 year.
- Women who were only using a hormonal method at 3 months, with subsequent discontinuation of that method, were more likely to adopt condoms than use no method at all at 12 months (54% vs. 37%, p=0.001).

It's all about the partner

Table 2: Predictors of dual method use at 12 months

	Unadjusted OR (95% CI)			Adjusted OR (95% CI)		
Variable	**N=1018**		**p-value**	**N=1012**		**p-value**
Baseline condom use						
<80% of time	1 (reference)			1 (reference)		
≥80% of time	2.4	(1.6 - 3.6)	<0.001	2.0	(1.3 - 3.1)	<0.01
Prior sexually transmitted infection	1.4	(0.9 - 2.0)	0.12	1.6	(1.0 - 2.6)	0.07
Perceived STI risk in next 3 months						
Not at all/a little/somewhat likely	1 (reference)			1 (reference)		
Very likely	0.9	(0.6 - 1.4)	0.64	0.5	(0.3 - 1.0)	0.05
Partner concurrency (other than main)	0.8	(0.4 - 1.4)	0.40	0.7	(0.4 - 1.4)	0.34
Main partner's views of condoms						
Not at all important	1 (reference)			1 (reference)		
Somewhat important	1.7	(0.9 - 3.2)	0.13	1.5	(0.8 - 3.0)	0.23
Very important	3.5	(1.9 - 6.3)	<0.001	2.8	(1.4 - 5.6)	<0.01
Don't know	2.5	(1.3 - 4.8)	0.01	3.0	(1.3 – 6.6)	<0.01

Adjusted for age, race/ethnicity, clinic site, woman's belief in the importance of dual method use.

- Women who were consistent condom users at baseline had nearly twice the odds of being a dual method user at 12 months compared to inconsistent condom users (adjusted odds ratio (AOR)=2.0, 95% CI: 1.3-3.1, p<0.01).
- Women who believed their main partner thought condoms were "very important" or did not know their partner's opinion, regardless of perceived STI risk or the participant's own views of condoms, had higher odds of dual method use at 12 months (AOR=2.8, 95% CI: 1.4-5.6, p<0.01 and AOR=3.0 95% CI: 1.3-6.6, p<0.01 respectively).

Conclusion

- Initiation of hormonal contraception negatively impacts condom use, however, the trade-off between hormonal contraception and condom use is dynamic.
- Many women appear to resume condom use as they discontinue their hormonal method.
- Given the impact of initiation of a method, as well as the significant role of the partner in condom use in this population, providers should emphasize the importance of continued condom use among women initiating hormonal contraception.

Acknowledgments

This project was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129** and by the **National Institute of Child Health and Human Development Grant R01 HD045480**. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Many thanks to: the Pathways to Careers in Clinical and Translational Research (PACCTR) Program, Dr. Peter Chin-Hong, Dr. Joel Palefsky, Cecily Hunter, Ruby Singharo, Marlene Berro, and faculty and colleagues in the Advanced Training in Clinical Research (ATCR) Program at UCSF.

With Pills, Patches, Rings and Shots: Who Still Uses Condoms?

Rachel L. Goldstein[1], Ushma D. Upadhyay PhD, MPH[1,2], Beth A. Brown MA, MPA[1,2], Tina R. Raine MD, MPH[1,2]

[1]University of California, San Francisco School of Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences
[2]Bixby Center for Global Reproductive Health

Introduction

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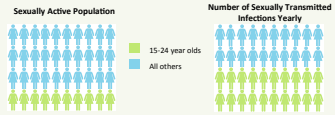

Specific Aims

- Describe the trends in condom use in women initiating hormonal contraception over time.
- Assess the predictors of dual method use in this group.

Methods

- **Design:** prospective cohort study
- **Subjects**: 1,387 women aged 15-24 years initiating oral contraceptive pills (OCPs), the transdermal patch (Ortho Evra™), vaginal ring (NuvaRing™) or depo-medroxyprogesterone (DMPA) at public family planning clinics in Northern California.

- **Study measures:** Research staff collected data on sociodemographics, reproductive/sexual history and attitudes towards condom use from enrolled participants via self-administered electronic questionnaires at baseline and 3, 6, and 12 months. Analysis was limited to the subset of women who had sex in the last 30 days. Condom use was dichotomized (≥80% versus <80% in the last 30 days) and comparisons between consistent and inconsistent condom users at baseline were made using chi-square statistics. The primary outcome measure was dual method use at one year.

Statistical Analysis

Logistic regression was used to analyze both bivariate and multivariable models. Independent variables considered included those found to be associated with dual method use in prior research, potential confounders, variables informed by the Health Belief Model (HBM)[1] and the Theory of Planned Behavior (TPB)[2].

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Results

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Table 1: Baseline characteristics of participants by condom use status

	Total	Consistent condom user Yes	Consistent condom user No	p-value
	N (%) 1,194	N (%) 432	N (%) 762	
Sociodemographics:				
Age (years) (N=1194)				<0.001*
15-17	413 (34.6)	170 (39.4)	243 (31.9)	
18-19	391 (32.8)	146 (33.8)	245 (32.2)	
20-24	390 (32.7)	116 (26.9)	274 (36.0)	
Race/Ethnicity (N=1194)				0.09
White	133 (11.1)	59 (13.7)	74 (9.7)	
Latina	320 (26.8)	105 (24.3)	215 (28.2)	
African American/Black	407 (34.1)	150 (34.7)	257 (33.7)	
Asian/Pacific Islander	141 (11.8)	43 (10.0)	98 (12.9)	
Multiracial/Other	193 (16.2)	75 (17.4)	118 (15.5)	
School and employment status (N=1194)				0.09
In school or employed (full or part time)	996 (83.4)	371 (85.9)	625 (82.0)	
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Clinic site (N=1194)				0.77
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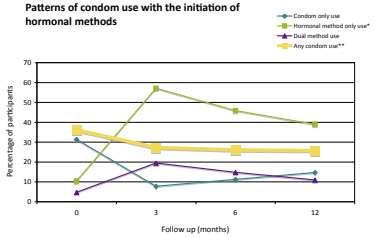
DMPA	257 (21.5)	88 (20.4)	169 (22.2)	
Prior pregnancy (N=1194)	586 (49.1)	165 (38.2)	421 (55.2)	<0.001
Prior sexually transmitted infection (STI) (N=1169)	255 (21.8)	83 (19.7)	172 (23.0)	0.19
Perceived STI risk in next 3 months with main partner (N=1194)				0.73
Not at all/a little likely/somewhat	875 (73.3)	314 (72.7)	561 (73.6)	
Very likely	319 (26.7)	118 (27.3)	201 (26.4)	
Partner concurrency (sex with man other than main partner) (N=1194)	170 (14.2)	47 (10.9)	123 (16.1)	0.01
Length of sexual relationship (months) (N=1194)				<0.001*
0-6	518 (43.4)	228 (52.8)	290 (38.1)	
7-12	140 (11.7)	41 (9.5)	99 (13.0)	
>12	352 (29.5)	97 (22.5)	255 (33.5)	
No sex yet	184 (15.4)	66 (15.3)	118 (15.5)	
Attitudes towards condom use				
Main partner views of condoms (N=1008)				<0.001*
Very important	307 (30.5)	204 (56.0)	103 (16.0)	
Somewhat important	327 (32.4)	115 (31.6)	212 (32.9)	
Not at all important	321 (31.8)	43 (11.8)	278 (43.2)	
Don't know	53 (5.3)	2 (0.5)	51 (7.9)	
Believes should always use condoms, even if on birth control (N=1187)				0.0014*
Strongly agree	419 (35.3)	185 (43.1)	234 (30.9)	
Agree	417 (35.1)	132 (30.8)	285 (37.6)	
Neither	212 (17.9)	70 (16.3)	142 (18.7)	
Disagree	119 (10.0)	33 (7.7)	86 (11.3)	
Strongly disagree	20 (1.7)	9 (2.1)	11 (1.5)	

*p is for the chi-square statistic for test of trend of the odds, all others are based on chi-square statistic

- Of the 1,387 women in the cohort, 1,194 women were eligible for analysis.
- The cohort was racially/ethnically diverse with 61% describing themselves as either Latina or African American. Nearly two-thirds lived in a low-income neighborhood and 67% were adolescents.
- At baseline, 36.2% of women were consistent condom users and 4.7% were dual method users.
- Consistent condom users at baseline were more likely to have had a prior pregnancy, been in a relationship of shorter duration, and have main partner with positive views of condoms (Table 1).

Patterns of condom use with the initiation of hormonal methods



Results (continued)

There is a trade-off, but is there also a trade-back?

- After initiation of a hormonal method, condom use dropped to 27%, but remained relatively unchanged thereafter.
- Dual method use increased to a peak of 19% at 3 months but decreased over time, largely due to discontinuation of hormonal methods with less than half of participants reporting use at 1 year.
- Women who were only using a hormonal method at 3 months, with subsequent discontinuation of that method, were more likely to adopt condoms than use no method at all at 12 months (54% vs. 37%, p=0.001).

It's all about the partner

Table 2: Predictors of dual method use at 12 months

	Unadjusted OR (95% CI)			Adjusted OR (95% CI)		
Variable	N=1018		p-value	N=1012		p-value
Baseline condom use						
<80% of time	1 (reference)			1 (reference)		
≥80% of time	2.4	(1.6 - 3.6)	<0.001	2.0	(1.3 - 3.1)	<0.01
Prior sexually transmitted infection	1.4	(0.9 - 2.0)	0.12	1.6	(1.0 - 2.6)	0.07
Perceived STI risk in next 3 months						
Not at all/a little/somewhat likely	1 (reference)			1 (reference)		
Very likely	0.9	(0.6 - 1.4)	0.64	0.5	(0.3 - 1.0)	0.05
Partner concurrency (other than main)	0.8	(0.4 - 1.4)	0.40	0.7	(0.4 - 1.4)	0.34
Main partner's views of condoms						
Not at all important	1 (reference)			1 (reference)		
Somewhat important	1.7	(0.9 - 3.2)	0.13	1.5	(0.8 - 3.0)	0.23
Very important	3.5	(1.9 - 6.3)	<0.001	2.8	(1.4 - 5.6)	<0.01
Don't know	2.5	(1.3 - 4.8)	0.01	3.0	(1.3 – 6.6)	<0.01

Adjusted for age, race/ethnicity, clinic site, woman's belief in the importance of dual method use.

- Women who were consistent condom users at baseline had nearly twice the odds of being a dual method user at 12 months compared to inconsistent condom users (adjusted odds ratio (AOR)=2.0, 95% CI: 1.3-3.1, p<0.01).
- Women who believed their main partner thought condoms were "very important" or did not know their partner's opinion, regardless of perceived STI risk or the participant's own views of condoms, had higher odds of dual method use at 12 months (AOR=2.8, 95% CI: 1.4-5.6, p<0.01 and AOR=3.0 95% CI: 1.3-6.6, p<0.01 respectively).

Conclusion

- Initiation of hormonal contraception negatively impacts condom use, however, the trade-off between hormonal contraception and condom use is dynamic.
- Many women appear to resume condom use as they discontinue their hormonal method.
- Given the impact of initiation of a method, as well as the significant role of the partner in condom use in this population, providers should emphasize the importance of continued condom use among women initiating hormonal contraception.

Acknowledgments

This project was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129** and by the **National Institute of Child Health and Human Development Grant R01 HD045480**. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Many thanks to: the Pathways to Careers in Clinical and Translational Research (PACCTR) Program, Dr. Peter Chin-Hong, Dr. Joel Palefsky, Cecily Hunter, Ruby Singharo, Marlene Berro, and faculty and colleagues in the Advanced Training in Clinical Research (ATCR) Program at UCSF.

Medical Student Perceptions of Anesthesiology

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ABSTRACT

Perceptions of another's field of practice can significantly impact interprofessional collaborations[1]. These perceptions can be influenced by a variety of sources. We asked medical students to describe their preconceptions about anesthesiology prior to their clinical clerkship.

➢ ***We assessed the:***
1. ***Content and tone of student preconceptions about the field***
2. ***Impact of the source of the described preconceptions***

Understanding the impressions medical students have of anesthesiology may inform educators on how to best structure clinical clerkships or shadowing opportunities.

BACKGROUND

- Harboring negative views of respective professional roles is a significant barrier to interprofessional teamwork[1].
- Student perceptions of specialties can form early in training, and may be difficult to extinguish if unchallenged[2].
- Clinical clerkships allow medical students to learn about different specialties under direct mentorship concentrated and provide the most concentrated environments for perceptions to evolve[3-4].

- Anesthesiology clerkships are typically voluntary following completion of third year rotations.
- The role of the anesthesiologist may be experienced peripherally as students rotate through core rotations, such as surgery, ob/gyn, and internal medicine.

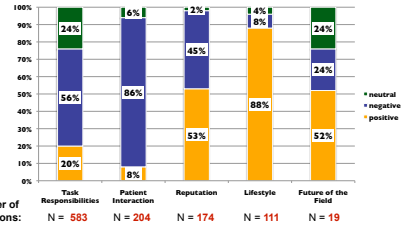
METHODS

- UCSF medical students described one preconceived notion about anesthesiology prior to their anesthesiology clerkship.
- Responses were collected from **1,091 students** from **2003 – 2010**
- Students specified the source of the preconceptions starting in 2009.
- Key themes were initially identified using a general inductive approach.
- Two reviewers independently assigned a theme and tone (**positive, negative,** or **neutral**) to each preconception.
- Discrepancies in assignment were discussed and reconciled.

RESULTS

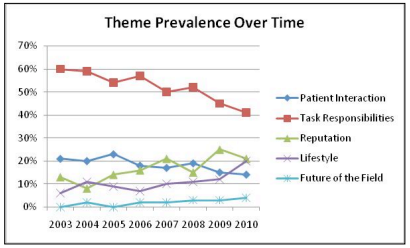
- **Five main themes** emerged: Task Responsibilities, Patient Interaction, Reputation, Lifestyle, and Future of the Field
- **Tone** was negative for the majority of entries (55%); distribution varied by theme [Fig. 1]

Figure 1: Tone Distribution of Preconception Themes



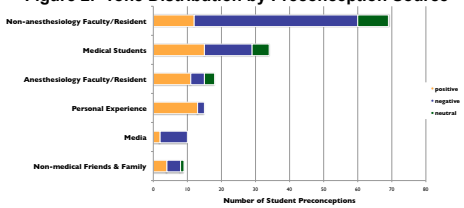
Total Number of Preconceptions: N = 583 | N = 204 | N = 174 | N = 111 | N = 19

- **Trends over time**: Preconceptions about Task Responsibilities and Patient Interaction are declining as students focus more on Lifestyle, Reputation, and the Future of the Field



- 155 medical students noted the **source of their preconception** [Fig. 2]
- Faculty outside of the field prominently influenced student preconceptions, usually in a negative fashion
- Students typically interacted with these faculty during clinical rotations in surgery and ob/gyn

Figure 2: Tone Distribution by Preconception Source



RESULTS (continued)

- ***Task Responsibilities***: Students felt anesthesiologists were confined to the operating room and were often unclear about their role following intubation. Multiple students minimized the skill required to manage patients intra-operatively, referring to it as "free time" used to "surf the web".
- ***Patient Interaction***: Many doubted the ability of anesthesiologists to overcome the challenge of establishing rapport with patients during the fast-pace of the pre-operative time period. Concerns were expressed about limited opportunities for longitudinal patient care.
- ***Reputation***: Anesthesiologists were praised for their "laid-back" demeanor and enthusiasm for teaching. "Tense relationships" with surgeons and susceptibility to drug abuse were also frequently mentioned.
- ***Lifestyle***: Flexible hours, lucrative salaries, and enviable work-life balance were repeatedly emphasized as perks of a career in anesthesiology.
- ***Future of the Field***: Increased residency competitiveness was highlighted in addition to curiosity about the impact of growing numbers of certified registered nurse anesthesists (CRNAs) on future job opportunities.

DISCUSSION

Student preconceptions of anesthesiology are largely negative.
Heavily concentrated in prevalent themes regarding work responsibilities and patient contact.

Preconception source may play a pivotal role.
Direct interaction with anesthesiology faculty led to more positive preconceptions. Preconceptions influenced by non-anesthesiology faculty were typically negative. Increased opportunities to interact with anesthesiology faculty early in training may allow students to perceive the specialty more positively overall.

Preconception themes change over time.
Increased focus on lifestyle and reputation may indicate changing motivations and values among new student generations.

FUTURE STEPS

Curricular interventions may help neutralize negative perceptions:

- Targeted shadowing, preferably early, dispels inaccurate student perceptions[3-5]
- Increase opportunities for students to interact directly with anesthesiology faculty
- Encourage anesthesiology faculty participation in preclinical lectures and training
- Consider incorporating an anesthesiology clerkship into clinical requirements
- Increase exposure to sub-specialties of anesthesiology outside of the operating room

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Telemedicine Screening for Cytomegalovirus Retinitis Among HIV Patients in a Primary Care Setting in Thailand

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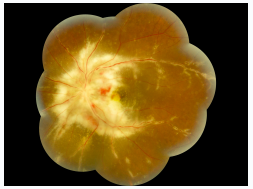
Introduction

- CMV retinitis (CMVR) is the most common cause of blindness in HIV/AIDS patients.
- Anti-retroviral use has decreased CMVR prevalence in Western countries, but it remains high in Southeast Asia.
- 200,000 patients are at risk for CMVR in Thailand, but there are no large-scale screening programs for HIV-infected patients.
- We propose a new screening method using telemedicine in contrast to the gold standard ophthalmologist-led indirect ophthalmoscope examination.
- Our previous research at a tertiary care center in Chiang Mai, Thailand, demonstrated a sensitivity and specificity of 90% for remote screening of CMVR.



CMV in left optic disc and along the vessels

- We now aim to test the efficacy of telemedicine screening and to determine the prevalence of CMVR in a non-ophthalmological primary care setting.

Specific Aims

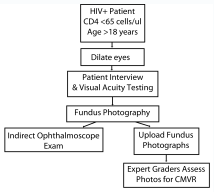
1) The prevalence of CMV retinitis in patients with a CD4 count <65 cells/ul in a primary care setting.
2) The risk factors for presence of CMV retinitis, with presence of CMV retinitis as the outcome, and various demographic and medical information as predictors.
3) The sensitivity and the specificity for diagnosing CMV retinitis remotely in a primary care setting (Nakornping Hospital, Chiang Mai,Thailand).

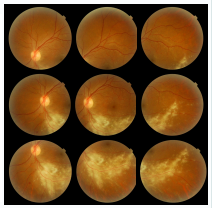
Methods

- 42 consecutive patients at Nakornping Hospital's HIV Clinic in Chiang Mai, Thailand were enrolled
- Inclusion criteria: CD4 count <65 cells/ul, age >18
- Exclusion criteria: Patients who cannot have their eyes dilated, who cannot sit comfortably during photography, who are pregnant
- Patients are followed at 3 month intervals until they develop CMVR or until their CD4 exceeds 100 cells/ul

Methods (continued)

Methods Flowchart





Nine fields of fundus taken by trained photographer

Statistical Analysis

- Specific Aim 1: We will calculate the prevalence as the proportion of participants who have at least one eye affected with CMVR with exact 95% confidence intervals
- Specific Aim 2: We will calculate the risk factors for CMVR development with logistic regression.
- Specific Aim 3: We will compute both sensitivity and specificity to determine the accuracy of remote grading for CMV retinitis diagnosis with 95% confidence intervals with indirect ophthalmoscopy as the gold standard.

Results and Anticipated Results

- Study still in process of enrollment
- Remote grading of fundus photographs has yet to be completed
- Anticipated sensitivity and specificity of remote CMVR diagnosis is 90% for both, based on pilot study at a tertiary care center

Patient Baseline Characteristics

Characteristics	N = 42	95 % CI
Mean Age	38.2 years	35.2-41.2
Sex	63.4% Male	48.0-79%
Median CD4	21 cells/ul IQR: 15-36	22.0-33.6
On ART	75.6%	61.9-89.3%
Prior OI	43.9%	28.9-61.1%
Prior STD	42.8%	28.0-59.8%

Results (continued)

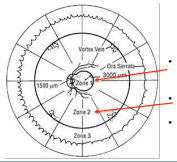
Ophthalmological Exam

	Eyes N = 84 95% CI	Patients N = 42 95% CI
Visual Acuity ≤ 20/60	7.1% (1.5-12.8%)	17.5% (5.2-29.8%)
Visual Symptoms	28.6% (18.7-38.4%)	41.5% (25.7-57.2%)
CMVR	10.7%* (4.0-17.4%)	16.7%* (0.2-19.2%)

*Period prevalence from June 18 2010 to March 9, 2011

CMV Characteristics

Characteristics	N = 9
Active	88.9% (8 eyes)
Zone 1 & 2	55.5% (5 eyes)
Zone 3	44.4% (4 eyes)
Lesion size <10%	66.7% (6 eyes)
Visual Acuity 20/20	44.4% (5 eyes)



Zones in CMV Retinitis

- Zone 1 covers the optic nerve and area surrounding the fovea
- Zone 2 extends from Zone 1 to equator of the eye.
- The fundus camera covers all of zone 1 and some of zone 2

Conclusion

- We found a lower prevalence of CMVR in a primary setting than previously reported in a tertiary care setting (33% of HIV/AIDS patients with CD4 <50) in Chiang Mai, Thailand.
- Telemedicine screening for CMVR can be performed effectively among HIV patients in a primary care setting and may prove to be helpful in locations with limited access to ophthalmologists.
- Early screening of CMVR has the potential to prevent blindness in HIV/AIDS patients.

Acknowledgments

This work was supported by a grant from the Doris Duke Charitable Foundation to University of California, San Francisco to fund Clinical Research Fellow Jenny Chen.

This publication was supported by Doris Duke Charitable Foundation. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of DDCF.

Clinical and Translational Science Institute / CTSI

Peripheral Nerve Repair with Aligned Nanofiber Scaffolds

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Introduction

- The treatment of patients with nerve injuries is a major challenge.
- Complete nerve transections are generally treated with end-to-end suture of the nerve stumps. However, if an entire segment of nerve is damaged, the resulting nerve gap must be bridged in order for nerve regeneration to occur.
- The gold standard for gap repair is to use nerve autograft to bridge the distance, but this carries substantial donor site morbidity.
- Artificial tubular nerve conduits are a promising alternative but outcomes remain inferior to autograft.
- The goal of this project is to test a new poly-lactide-caprolactone (PLCL) aligned nanofiber nerve conduit (NanoNerve, Berkeley, CA) in a rat model of segmental nerve injury. Our hypothesis is that PLCL conduit is equivalent to nerve autograft in the repair of a 1 cm sciatic nerve defect in the rat model.

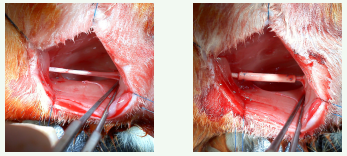
Specific Aim

- *In vivo* testing of aligned PLCL nanofiber scaffolds in a rat sciatic nerve model of segmental nerve injury in comparison to nerve autograft (gold standard) using sciatic nerve electrophysiology, muscle weight and force, pinprick sensation, and nerve histology as measurements of the success of nerve regeneration.

Methods

- Twenty female Lewis rats were randomly assigned to receive nerve autograft or PLCL conduit (1.1 mm inner diameter, 200 um thickness, 12 mm length) (n = 10 per group).
- In all rats, a 10 mm segment of the right sciatic nerve was removed. For autograft, this segment was reversed and sutured back in place. For conduit, the gap was bridged with PLCL conduit.

Figure 1. *Exposure of sciatic nerve in Lewis rat and repair with PLCL conduit.*



- Post-operatively, rats were tested weekly for 12 weeks for return of pinprick sensation in the hindpaw.
- The 12-week neuromuscular endpoints were:
  - Nerve conduction velocity;
  - Gastrocnemius compound muscle action potential amplitude;
  - Isometric tetanic force of gastrocnemius muscle; and
  - Wet muscle mass of gastrocnemius muscle.
- Nerve histology endpoints at 12 weeks included axon number and diameter at the mid-graft and distal sciatic nerve stump.

Statistical Analysis

- Student's *t*-test was used for comparison of continuous variables. Two-sided p-values were calculated for all test statistics and $p < 0.05$ was considered significant.

Results

- All rats recovered well from surgery and gained weight.
- **Sensory Endpoints**: By 12 weeks, both groups had regained half of baseline pinprick sensory function (measured as number of paw withdrawals to 12 consecutive pinpricks) in operated hindlimb.

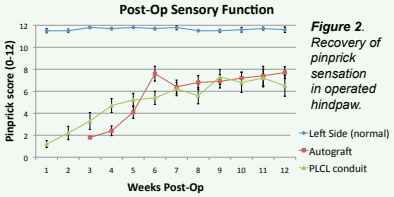
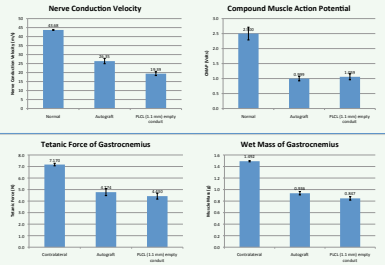


Figure 2. *Recovery of pinprick sensation in operated hindpaw.*

- **Neuromuscular Endpoints**: Nerve conduction velocity was slower in the conduit group (p=0.001) compared to nerve autograft. However, the amplitude of the compound muscle action potential measured in the gastrocnemius muscle and the maximum isometric tetanic force of the gastrocnemius muscle was equivalent between groups, as was the wet mass of the gastrocnemius muscle.

Figure 3. *Neuromuscular function endpoints at 12-weeks post-op after autograft or PLCL conduit repair.*

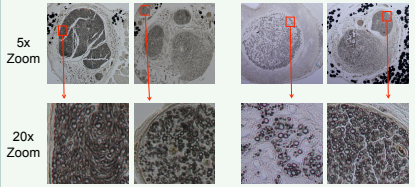


Note: Normal data were collected from age-matched un-operated rats; Contralateral data were collected from unoperated left hindlimbs. Error bars denote SEM.

Results (continued)

- **Nerve Histology Endpoints**: Analysis of axons in the midgraft and distal sciatic nerve in both groups showed a greater number of regenerating axons in the autograft group (midgraft 4572 vs. 7476 axons, p<0.001; distal nerve 4169 vs. 5775 axons, p=0.017). However, there was no statistically significant difference in the mean axon diameter (midgraft 4.00 vs. 4.11 um; distal nerve 3.61 vs. 3.77 um).

Figure 4. *Cross sections of autograft nerve and PLCL conduit at 12 weeks post-op. Sections were treated with 2% osmium tetroxide to stain myelin black. Whole nerve/conduit is shown at 5x and individual axons are shown at 20x zoom.*



Conclusion

- In a rat model of a 1 cm sciatic nerve defect, we demonstrated that nerve repair using aligned nanofiber PLCL conduits is equivalent to nerve autograft in several measures of sensory and motor function recovery, although nerve conduction velocity and the number of regenerating axons remain lower with conduit than autograft.
- Future directions include delivery of neurotrophic growth factors on the surface of the conduit or within a hydrogel matrix placed inside of the conduit to further improve nerve regeneration, as well as testing of the conduit for repair of longer nerve gaps in larger animal models prior to human clinical studies.

Acknowledgments

This publication was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129**. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Funding for this research project came from **Department of Defense Grant Number W81XWH-05-2-0094**.

Pregnant Women's Perceptions and Experiences of HIV Stigma in Rural Kenya

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University of California, San Francisco

Introduction

- 33 million people around the world are living with HIV/AIDS, 22 million in sub-Saharan Africa. In this region, women make up 60% of people living with HIV/AIDS (PLHA).
- Antiretroviral therapy helps people live longer and healthier lives, and significantly reduces the risk of mother-to-child transmission.
- However, HIV-related stigma is still a problem. PLHA have experienced emotional, physical, and structural abuse. Stigma can be a barrier for HIV testing and treatment.
- Women may be disproportionately affected by stigma because of their social status. Women who fear stigma may chose not to access important health care services, and pregnant women may not access perinatal care.

Objective

To examine sociodemographic predictors of anticipated, perceived, and experienced stigma among pregnant women attending antenatal care clinics in rural Kenya.

This information can help health care workers identify women who are most at risk of experiencing stigma, and provide more appropriate counseling and services. Ultimately, this may improve testing and treatment, and the health of women and their children.

Methods

- This is a secondary analysis of a prospective cohort study, "The Effects of HIV/AIDS Stigma on Use of Services by Pregnant Women in Kenya," conducted in the context of the UCSF/Kenya Medical Research Institute Family AIDS Care and Education Services (FACES) project.
- 1,777 women who did not know their HIV status were interviewed.
- Women who tested HIV-positive, and a random sample of those who tested negative or refused testing, were selected for follow-up: 432 had a postpartum interview (157 HIV+, 168 HIV-, 107 status unknown).
- HIV knowledge: 10 questions (eg. "Do you think a healthy-looking person can be infected with HIV, the disease that causes AIDS?" "Can the HIV virus be transmitted from mother to child during delivery?")
- Anticipated stigma: the anticipation that one will experience stigma if one tests HIV-positive and one's HIV-positive status is disclosed to others.
- Perceived stigma: how often various stigmatizing events happened to the woman in the past three months because of her HIV-positive status (eg. "Someone insulted me," "I felt completely worthless").

Statistical Analysis

- Variables were selected for the multivariable model based on significance in bivariate analyses (ps.05), potential confounders, and factors that were *a priori* considered to be important, based on the literature.
- Analysis of anticipated and perceived stigma included all of the women interviewed at baseline (n=1,777). Analysis of experienced stigma included only HIV-positive women interviewed at postpartum (n=157).

Results

Characteristics of Study Participants (n=1,777)

Age, years, mean ± SD		23.6 ± 5.4 (range: 18-49)
Level of education completed		
	Primary	82.5%
	Secondary+	17.5%
Literacy	Read easily	43%
	Read with difficulty	41%
	Do not read at all	16%
Marital Status	Single (never married)	8.4%
	Married	87.5%
	Separated or Divorced	1.1%
	Widowed	3.0%
Husband has other wives (yes)		24.7%
Work	Housework	22.6%
	Other	77.4%
Ownership of Household goods		
	Electricity	3.6%
	Radio	74.9%
	Television	10.5%
	Landline telephone	1.3%
	Mobile phone	47.2%
	Refrigerator	.96%
Mean pregnancies, including current		3.2 ± 2.0 (range: 1-16)
Mean live births		2.2 ± 2.0 (range: 0-15)
Anticipated any stigma		28.4%
	From partner	35.3%
	From family	35.0%
	From community/others	59.1%
Mean Community stigma score (range: 0-3)		.84 ± .38
	Negative Attitudes	.78 ± .46
	Perceived Discrimination	.88 ± .43
HIV Knowledge (mean percent correct)		82.6%
HIV Status	HIV-positive	257 (14.5%)
	HIV-negative	1,204 (67.8%)
	Refused HIV Testing	99 (5.6%)
	Testing Service Not Available	203 (11.4%)
	Missing Result in Med Record	14 (0.8%)

Results (continued)

Anticipated Stigma

- Women with significantly greater adjusted odds of anticipating stigma were 25+ years old (AOR=1.35, p=.046), could read only with difficulty (AOR=1.43, p=.007), and had husbands who had other wives (AOR=1.42, p=.006).
- Those who had lower adjusted odds had more education (AOR=.59, p=.006) and more HIV knowledge (AOR=.92, p=.003; .58, p=.015).

Negative Attitudes

- Women whose husbands had other wives had significantly higher adjusted negative attitudes scores (beta=.07; p=.018).
- Those who had lower scores worked inside the home (beta= -.07, p=.029), and had more HIV knowledge (beta= -.10, p=.003).

Perceived Discrimination

- Women's perceptions of discrimination against PLHA were lower among those worked inside the home (beta = -.11, p <.0001) and those with better HIV knowledge (beta = -.15, p <.0001).
- Perceptions of discrimination were higher among those who lived in households that had electricity (beta = .23, p<.0001).

Experienced Stigma

- Among the 157 HIV+ women who had a postpartum interview, those who did not know whether their partner had been tested for HIV had 4.1 greater adjusted odds of experiencing any stigma than women who knew that their partner had been tested (p=.039).

Conclusions

- Levels of HIV-related stigma vary widely in this population. Education, literacy, and HIV knowledge were important predictors of anticipated stigma, negative attitudes, and perceived discrimination.
- HIV-positive women who did not know whether their partner had been tested for HIV were more likely to experience stigma than women who did know whether their partner had been tested.
- Women whose husbands have other wives were more likely to anticipate stigma, but were also more likely to have negative attitudes toward people living with HIV/AIDS. The role of such relationships warrants further research, including examination of marriage order.
- Future research in this area should examine more closely the impact of differential power relationships within a society on HIV-related stigma.

Acknowledgments

This project was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129**. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Many thanks to the Pathways to Careers in Clinical and Translational Research (PACCTR) program, Joel Palefsky, Peter Chin-Hong, Cecily Hunter, Ruby Singhrao, Marlene Berro, the Advanced Training in Clinical Research (ATCR) program, and Erik Carter and Rachel Goldstein.

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Examining Health Equity through a Race Theory Lens

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Background

In the United States, "health disparities" discourse evolved around racial/ethnic concerns. In contrast, European nations employ the term "health equity", emphasizing socioeconomic status.

Research Question

As health equity gains prominence in the U.S., how does this framing clarify or obscure the role of race in health disparities?

Critical Theories of Race

- Race is a fundamental axis of social relations that cannot be reduced under class, culture, or biology[1]
- Race, class, and gender are interlocking and mutually constituted systems of power[2]
- Disrupting racialization processes is a form of resistance[3]

[1]Racial Formation Theory; [2]Intersectionality; [3]Postcolonial Theory

Methodology

Critical Discourse Analysis

- Qualitative study of the social construction of knowledge and practice through discourse
- Emphasis on power, ideology, inequity, & social change

Analytic Process

- *Thematic coding*: Iterative process identifying themes in the data
- *Thematic focus*: Identify abstract (general) and particular (concrete) examples of discursive themes
  - "Abstractions" refer to high level concepts (e.g., socioeconomic status) that generalize phenomena
  - "Particulars" refer to concrete elements of phenomena

  Both can act as discursive devices to obscure or illuminate power relations (via mechanisms, actors, responsibility) and/or provide pragmatic and strategic ways of discussing issues

Data Sources

- Health equity reports & communications guides (n=8)
- Key informant interviews (n=12)

Findings

I. Politics of Racial Discourse

Different approaches to addressing racial concerns within health equity discourse:

'Race is a dominant, though implicit, theme in the conservative framing that progressives must address...If progressives remain silent about race, they not only concede the race frame to the right: They concede all of the issues that conservatives successfully racialize.' DOC-G

"I was in a room recently with another researcher who feels that you need to call things by their right name and that you need to use the "R" word as in racism. It's like you sell out if you don't use it…I think that's not wise…Politics at one level is the art of the possible and you have to work within the system we have. And within [that] system…we need to keep our eyes on the prize, the big picture, but we need to be smart about how we get there." INT-14

Findings (continued)

II. Constructing Racial Disparities & Equity

	Theme	Abstract*	Particular*
1	History	Data presented as time trends, "ahistorical"	History contextualized and linked to past\current health disparities
2	Agency & Responsibility	Actors, accountability, and\or responsibility not noted; passive tense	Actors & roles in reproducing/ interrupting health equity identified
3	Privilege	Focus on disadvantage rather than privilege	Privilege discussed in relation to disadvantage
4	Fundamental Causes	Macro social processes presented as decontextualized variables (e.g., race, class)	Macro social factors articulated as processes (e.g., racism, classism)
5	Social Determinants	Generic (e.g., social and economic factors)	Detailed; population sensitive (e.g., criminal justice, workforce diversity)
6	Intersections	Race and class categorized as independent & additive	Race and class categorized as complex, interactive & mutually constructed
7	Community Participations	Generalized stakeholder category	Communities defined & actively pursued; support mechanisms & decision-making power explicit

Theme 1: History

Abstract: It just *is*

'Residential segregation into affluent, middle income and poor communities contributes to the reasons why where we live can have a significant influence on how long we can expect to live.' DOC-B

Particular: Historicize racism

"But what was missing from the equity frame...is an explicit understanding of history and redistribution…You can't help people understand it if you don't understand the history that helped create these problems." INT-07

'Blacks, American Indians, Hispanic Americans, Pacific Islanders and some Asian-American groups are disproportionately represented among the more socioeconomically disadvantaged groups in the U.S. This reflects a long history of racial inequality in which race or ethnic origin was legally used to exclude individuals from employment, educational opportunities and property ownership…the legacy of segregation, together with subtle institutional forms of racial bias that limit economic and social opportunities, continues to shape living and working conditions for many people of color.' DOC-D

Theme 2: Agency & Responsibility

Abstract: It just *is*

'African Americans and Hispanics/Latinos were more likely to be unemployed compared to their White counterparts…' DOC-C

Particular: Inequities are socially created

'[A] government agency decides that low-income housing must be built, which will house low-income African Americans and Latinos. It fails to look for locations near jobs and important infrastructure, like working schools, decent public transportation and other services… The public housing residents are left isolated, in under-funded schools, with no transportation to job centers.' DOC-A

Theme 3: Privilege

Abstract: Problem of disadvantaged

'Most health disparities affect groups marginalized because of socioeconomic status, race/ethnicity...' DOC-C

Particular: Problem of relationality between groups

'Structural racism…is the normalization and legitimization of an array of dynamics–historical, cultural, institutional, and interpersonal–that routinely advantage whites while producing cumulative and chronic adverse outcomes for people of color. Structural racism lies beneath social and economic inequities that are at the root of the vast majority of health disparities.' DOC-F

Findings (continued)

Theme 4: Fundamental Causes

Abstract: A variable

'Most health disparities affect groups marginalized because of socioeconomic status, race/ethnicity...' DOC-C

Particular: A process

'Health disparities are not about race or ethnicity in a cultural or biological sense; rather, they result from racism and its social and institutional manifestations.' DOC-F

Theme 5: Social Determinants

Abstract: General

'Social, economic, and environmental conditions' DOC-C

Particular: Specific, population sensitive

'Criminal and juvenile justice, workforce and economic development, family support and child welfare, education, housing' DOC-E

Theme 6: Intersections

Abstract: Race + class, additive

'[M]ajor differences exist …particularly for communities of color and people living in poverty' DOC-E

Particular: Race x class, complex intersection

"[I]t doesn't just so happen that people of color are over represented in poverty, that's because of …racism." INT-08

Theme 7: Community Participation

Abstract: Generic stakeholder

'[T]his new relationship requires an ability to work with a broad sector of the community on a wide range of issues.' DOC-B

Particular

'Groups that are the most affected by inequities must have a voice in identifying policies that will make a difference as well as in holding government accountable for implementing these policies.' DOC-A

Conclusion

- Abstractions and particulars shape discourse in specific ways
- Use of such discursive devices should reflect conscious considerations regarding audiences and consequences
- Attention to and integration of racial concerns within health equity discourse can interrupt the reproduction of inequities

Acknowledgments

Thanks to the many individuals and organizations who contributed to this research

This project was supported by **NIH/NCRR/OD UCSF-CTSI Grant Number TL1 RR024129**. Its contents are solely the responsibility of the author and do not necessarily represent the official views of the NIH. Other funding includes Meyer-White Memorial Scholarship, Philip R. Lee Fellowship, School of Nursing Andrews Scholarship, and Graduate Research Award.

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