REBUTTAL REPORT OF LINDA L. REMY, PhD

DATED OCTOBER 9, 2015

REBUTTING THE OPINION EXPRESSED BY

ELLEN T. CHANG, SC.D.

IN HER REPORT DATED SEPTEMBER 10, 2015

In the matter of

Whitlock, et al. v.

PepsiAmericas, et al.

(United States District Court for the

Northern District of California, Case

No. C-08-2742 SI)

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GLOSSARY OF ACRONYMS

AHRQ	Agency for Healthcare Research and Quality
BD	Breslow-Day
CCS	Clinical Classification Software developed by AHRQ
CDC	Centers for Disease Control
CDPH	California Department of Public Health
CHS	Center for Health Statistics
CI	Confidence interval
CMH	Cochran-Mantel-Haenzel
DOF	Department of Finance
DSMF	Death Statistical Master File
DX(N)	Diagnosis (Diagnoses) or number of secondary diagnoses
ED	Emergency Department
FCM	Family and Community Medicine
FHOP	Family Health Outcomes Project
GDM	Gestational diabetes mellitus
HCUP	Healthcare Cost and Utilization Project
IHPS	Institute for Health Policy Studies
LCL	Lower confidence limit
LOG	The LOG is a file SAS automatically produces when the analyst submits a program for execution. It is a record of the statements in the program and messages from SAS about their execution.
LOS	Length of stay in days
LST	The LST is a file SAS automatically produces to document output of procedures requested in a submitted program.
MCAH	Maternal, Child, and Adolescent Health
NP	Non-pregnant
OSHPD	Office of Statewide Health Planning and Development

PDD	Patient Discharge Data
PX(N)	Procedure(s) or number of secondary procedures
ROC	Residence in a Mendocino County community other than ZIP 95490
RR	Relative risk
SAS	Name of software that once stood for Statistical Analysis System
SSNC	Social Security Number, encrypted to protect confidentiality
UCL	Upper confidence limit
UCSF	University of California, San Francisco
ZIP-Code	Numeric code developed by the US Postal Service to facilitate mail delivery

LEGEND FOR FIGURES

Not significantly different (Willits vs ROC relative risk)

Significantly different

Significantly different, non-significant change

Significantly different, significant change

Not significantly different, significant change

OBJECTIVES

The document titled “Expert Report of Ellen T. Chang, Sc.D.”, filed 10-Sep-2015, makes assertions related to my longitudinal research on behalf of Willits residents. Plaintiff’s counsel asked me to respond on behalf of Plaintiff Danielle Smith. Specifically, I address comments related to the methodologies I have employed.

In this report, I continue to use hospital data released by the Office of Statewide Health Planning and Development (OSHPD), for the period 1983-2012, which includes the Social Security number (SSNC, encrypted to protect confidentiality) from 01-Jul-1990 forward. I define the reproductive population as age 15 to 44 for women born between 1950 and 1989 and infants born between 1983 and 2012. For the life course models, I define the reproductive cohort as people born between 1950 and 1989 followed from 01-Jul-1990 to 31-Dec-2012. The following references are to earlier reports I published in connection with the litigation [1-14], which by reference I incorporate into this report.

In addition to this report, I am providing all supporting documents to the defendant. SAS programs, logs, and listings are in the file PGMS.ZIP. Excel files are in XLS.ZIP. Results of literature searches are in ENDNOTE.ZIP. My report and updated resume are in WRITE.ZIP. I also incorporate by reference all documents of a similar nature submitted in earlier reports. Other than public health research-related books of a general nature, I do not have documents or materials relevant to this case in non-electronic media.

I conceived the study, prepared the datasets, did all data analysis, prepared figures and tables, and wrote this report. As before, a colleague provided statistical consultation and wrote all standard SAS production macros that I use regularly in my role as FHOP’s Research Director. As I examine additional materials and perform further analyses, I reserve the right to revise and supplement my opinions.

MAJOR CRITIQUES BY DEFENDANT EXPERTS

Statement

"The major critiques of Dr. Remy's study by Drs. Kelsh and Mandel remain valid. (p. 8-17)"

Response

I have rebutted these critiques numerous times in the past. Publication of my work in the prestigious peer-review journal Environmental Health [9] signifies that these methodologic critiques lack merit. I also note that Dr. Chang states that Drs. Kelsh and Mandel no longer work on this case or even at Experian, and I observe that this follows two significant critiques I filed with the court about the quality of their work [7,9].

Discussion

The team of experts Plaintiffs organized for this litigation reflect a broad background in training and experience. I am not responsible for any area other than reporting on health outcomes from a population viewpoint. Other areas are outside my scope of training and competence.

The ATSDR and Drs. Byers and O'Connor have been responsible for providing information to the Court about exposure to emissions from Remco.

I have made clear repeatedly that I am studying group outcomes. Dr. Byers is responsible for studying and reporting on individual outcomes.

I always have adjusted for what I view as the most important influences on health and hospitalization in Willits that could account for my findings, and I do so again in several later sections in this report.

I previously reported on whether health outcomes first occurred before or after patients started living in the County [9] and I return to this once more later in this report.

I am not responsible for identifying specific health conditions that Remco caused in individuals. Dr. Byers is responsible for identifying the scientific evidence to evaluate causation, including studies of specific health endpoints in both humans and animals.

My work combined with that of Drs. Byers and O'Connor clearly shows causation beyond a reasonable doubt.

Summary

I responded to some of Dr. Chang's critiques, which did not substantially modify results. The methodologic critiques of Drs. Kelsh, Mandel, and Chang lack merit.

THE ROLE OF TIME

Statement

"The time periods and generations defined by Dr. Remy are not meaningful with respect to potential exposures from the Remco facility. (P. 20)"

"Dr. Remy's results by time period are not consistent with a causal effect of emissions from the Remco facility. (P. 24)"

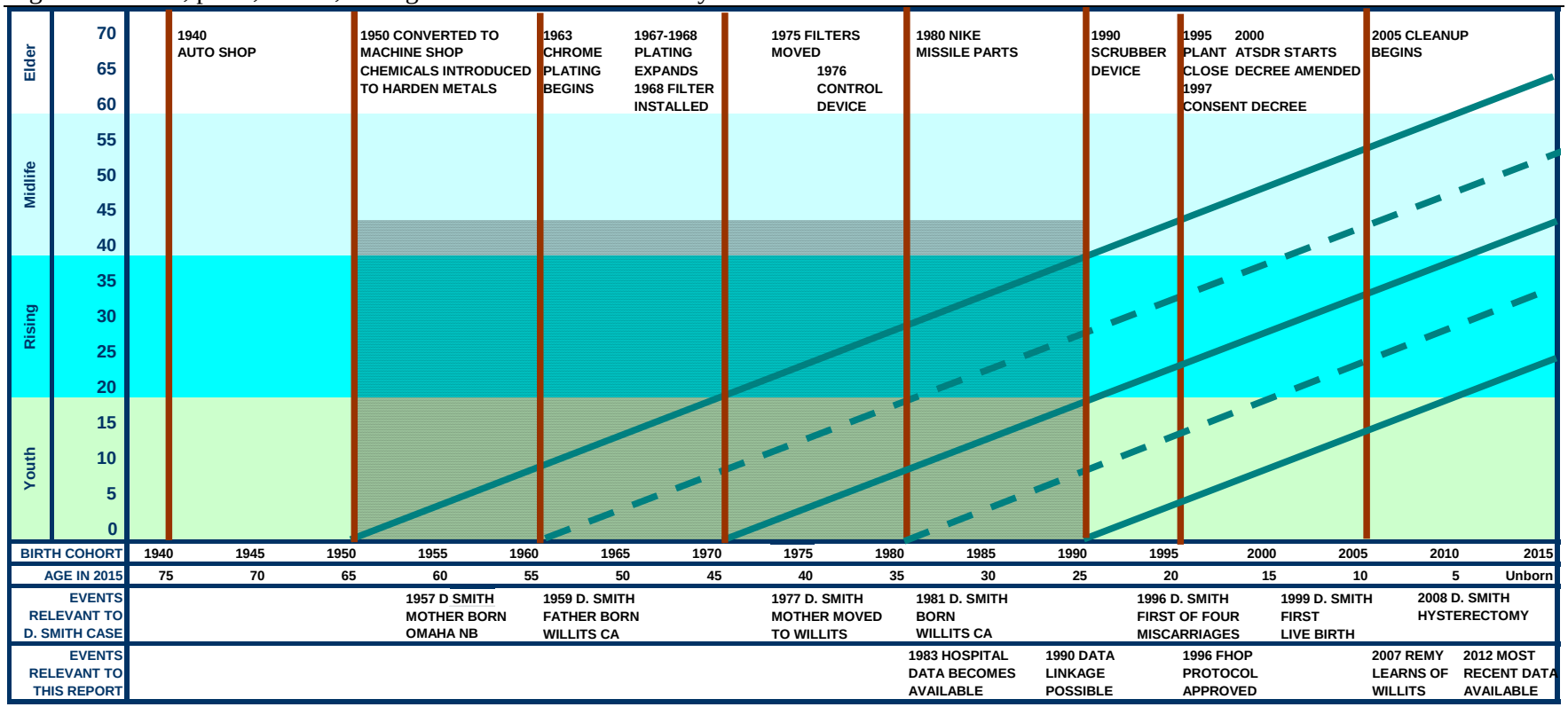
Response

I have been consistently cognizant of and respectful of the role time in this research. It drives my professional career and underlies every analysis I have done.

Discussion

Figure 1 again revisits the graph of time, place, events, and age location in Willits history. As Plaintiff's counsel seemed disturbed during my September 2015 deposition that red vertical lines were not nearer decade marks (my intent), I edited text to make this possible. I also appreciate that Dr. Chang identified certain dates in Remco history that I had not known. As stated before, my current interest focuses on the population born 1950-1989 (greyed) and infants born to them. It was not possible to study health outcomes occurring before 1983, as the data did not exist. It was not possible to do a life course model before 1990 because SSNC was not in the data.

Figure 1. Time, place, events, and age location in Willits history



Longitudinal research uses time to evaluate the population effect of major life events or changes in public policy, as here the decision to permit the Remco plant to operate in Willits, and tries to grasp the meaning and impact of those events. For the Willits research, I have been concerned primarily with two types of time measures. In Figure 1, red vertical lines indicate sequential periods, and green diagonal lines emphasizing the life course. I also have done analyses ignoring time, based solely on residence.

The number of years in sequential periods depends on the number of years available to study. Methodologically, sometimes we cannot use fewer years because we cannot estimate reliable rates. The DataBooks we prepare for the state test for 1-, 2-, and 3-year intervals. In addition, for Willits, I have tested 4-, 5-, 10-, 15- and 20-year intervals and I have submitted that work to the Court.

Intervals selected for a given analysis ultimately depend on the interplay between substantive issues and what the data tell us. For my July 2015 report to the Court, I used two 15-year intervals 1983-1997 and 1998-2015 roughly representing the period before and after Remco closed, and collapsed the adult decade cohorts into 20-year generations. I made these decisions for substantive reasons.

A study funded by the World Health Organization defines the preconception period as "a minimum of 1-2 years prior to the initiation of any unprotected sexual intercourse that could possibly result in a pregnancy. [15]" The preconception period is important for maternal and infant outcomes, as it sets the stage for the wellbeing of the mother and infant during pregnancy, birth, and the post-natal period.

Remco closed in December 1995. Figure 2 visualizes the two-year preconception period, 9-month pregnancy period, and one-year post-pregnancy outcomes period relative to closure and the Dec-1997 end-date I used. The latter date was the first full post-closure preconception period when Remco did not operate. As I showed in my July 2015 report to the

Court, this same period coincided with the major shift of the mother's generation to the daughter's generation for reproductive outcomes.

Figure 2. Preconception, pregnancy, and pregnancy outcome periods

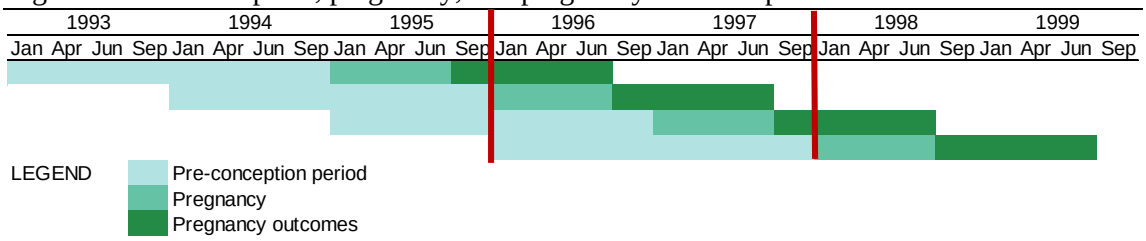
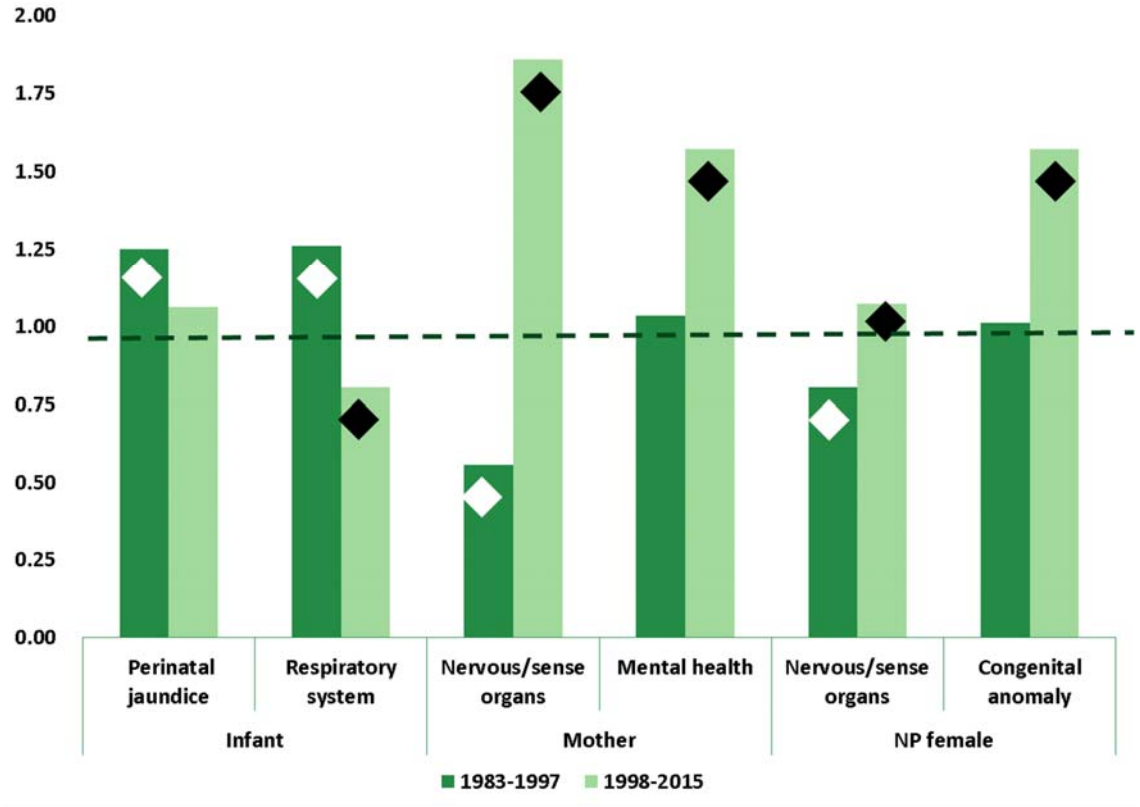


Figure 3 reflects both the conceptual and quantitative validation of this decision. The year 1997 coincided with major changes in conditions that are important indicators for maternal and infant health and for non-pregnant (NP) females, where measures for mothers and NP females reflect the underlying generational shift discussed in my July 2015 report.

Figure 3. Infant, maternal, and non-pregnant female outcomes by Remco closure



As in my earlier report, vertical bars show RR for each condition by period. The symbols are as follows:

( ) Difference is not statistically significant (P less than or equal to 0.05).

( ) In pre-closure period (1983-1997) geography (ROC, Willits) difference is significant. That is, Willits RR was statistically higher or lower than ROC.

( ) In pre-closure period geography is significant and time is significant in that RR changed from pre-closure.

( ) In pre-closure period geography is not significant but time is significant in that RR changed from pre-closure.

( ) In pre-closure period geography is significant but the between-period difference is not.

Summary

Time measures used for my July 2015 report are valid both conceptually and quantitatively.

CODING VARIABILITY

Statement

"Additionally, secondary discharge diagnoses often are not completely coded, and the completeness of coding varies by hospital and patient characteristics (Jencks et al. 1988, Iezzoni et al. 1992). Differential completeness of secondary discharge diagnosis codes would particularly affect some of the main perinatal conditions analyzed by Dr. Remy, such as low birth weight, hypoxia/asphyxia, and perinatal jaundice, which are more likely to be coded as secondary than primary hospital discharge diagnoses for newborns. Dr. Remy claims that "[c]oding variability equally affects both areas" in her study (Remy expert report, July 6, 2012, p.16), but she does not present any evidence to support this statement. Given that studies have demonstrated systematic differences in the coding of secondary discharge diagnoses among California

hospitals (Jencks et al. 1988, Iezzoni et al. 1992), equal variability in Willits and the rest of Mendocino County cannot reliably be assumed. Unequal variability leads to biased estimates of association. (P. 11)"

Response

I agree with Dr. Chang's statement that coding can be incomplete, that it varies by hospital and patient, and that there are systematic differences in the coding of secondary diagnoses (DX). However, I disagree with her assertion that hospital-level coding differences explain differences in health outcomes reported for Willits residents. Further, as I have stated in all previous reports, I search across ***ALL*** primary and secondary fields.

Nonetheless, to be responsive to Dr. Chang's statement that equal variability in Willits and ROC cannot reliably be assumed, I tested whether hospitals with 100 or more admissions of pregnant and NP females or infants, living in Willits or ROC, assigned equal numbers of diagnoses (DX) and procedures (PX). As Tables 1 and 2 show, in 34 comparisons, 5 returned a statistically higher number for females living in ROC, 7 returned a statistically higher number for females living in Willits, and 22 were not significantly different. In 12 comparisons of hospital-level infant coding (Table 3), 3 returned a statistically higher number of DX for ROC and 1 for Willits.

Coding variability indeed exists.

To the extent that illness severity can be measured by number of DX or PX versus the actual conditions coded in those fields, the clinical judgement of physicians treating non-pregnant (NP) females in the same hospitals tended to result in no overall significant differences between the groups. However, when women were pregnant, physicians in these same hospitals tended overall to code more PX for Willits women.

Among infants, physicians in these same hospitals tended overall to code more DX for Willits and more PX for ROC.

Given these findings, the data do not support Dr. Chang's hypothesis that hospital coding variability distorts the results I have reported over the years. Physicians in the same hospitals treating both ROC and Willits patients tended to record more DX and/or PX for pregnant Willits women and their infants.

Discussion

When FHOP makes the master files that are the source for my series of reports, we make two variables counting the number of secondary DX and E-codes (DXN) and secondary procedures (PXN) on the record. Readers of my SAS programs will see that I use these variables to search over the array of DX and PX to classify conditions.

In the program UPCODE.SAS, I selected discharge-level data from 1983 forward for pregnant and NP females born between 1950 and 1989, and infants age less than one year. I summarized these data by the hospital identifying code (OSHPDID) and place of residence (WILLITS), and selected all hospitals that admitted 100 or more from both Willits and ROC over the interval 1983 to 2012. I returned to the file and found all records for those admissions. Detailed results including graphs are in the file UPCODE.XLSX.

Ten hospitals admitted 100 or more women when NP, and five when pregnant. For each hospital, Tables 1 and 2 show the number of records, average, standard deviation, and maximum DXN and PXN for ROC and Willits, with T-tests and P-values for differences of means.

The top of each table shows the DXN and PXN grand mean without stratification by area, followed by the number of total records by area. Below that is the percent of total records used from hospitals with 100 or more patients from each area. When females were NP (Table 1), 10 hospitals accounted for 87% of ROC admissions and 89% of Willits admissions.

Ukiah Valley Medical Center at Hospital Drive admitted the greatest number of NP ROC females (N = 11,811) while Frank R. Howard Memorial Hospital admitted the greatest number of NP Willits females (N = 2,617). On average, Ukiah Valley recorded more DXN for ROC than Willits (ROC = 4.98 vs Willits = 3.98, T = 6.94, P = <0.001) and about the same number of PXN (ROC = 0.55 vs Willits = 0.59, T = -1.30, P = 0.1938). Observe the same general effect in Frank R. Howard Memorial Hospital for DXN and a greater number of PXN for ROC females.

Table 1. Hospitals admitting 100 or more women when not pregnant

		ROC				Willits				T-Test	
Hospital	Measure	N	Mean	Sdev	Max	N	Mean	Sdev	Max	T-Val	P-Val
Grand mean	Diagnoses	43,742	3.62	4.46	29						
	Procedures	43,742	0.65	1.47	20						
Discharges when County resident	Total	36,766				6,976					
	% gt 100	87				89					
Overall Mendocino resident	Diagnoses	31,973	3.64	4.55	29	6,184	3.72	4.57	29	-1.29	0.1957
	Procedures	31,973	0.57	1.33	20	6,184	0.58	1.38	20	-0.53	0.5959
230949 Frank R Howard Memorial Hospital	Diagnoses	1,653	5.01	5.38	29	2,617	4.48	5.09	29	3.24	***0.0012***
	Procedures	1,653	0.55	1.19	16	2,617	0.43	1.07	17	3.29	***0.0010***
231013 Mendocino Coast District Hospital	Diagnoses	6,618	2.54	3.25	27	317	1.24	1.93	10	11.3	***<.0001***
	Procedures	6,618	0.37	0.87	9	317	0.33	0.79	6	0.72	0.4702
231339 Ukiah Valley Medical Center/Dora Street	Diagnoses	4,428	0.66	1.04	6	705	0.75	1.08	6	-2.11	***0.0345***
	Procedures	4,428	0.17	0.62	8	705	0.15	0.59	6	0.95	0.3413
231396 Ukiah Valley Medical Center/Hospital Drive	Diagnoses	11,811	4.98	5.03	29	1,292	3.98	3.99	27	6.94	***<.0001***
	Procedures	11,811	0.55	1.17	20	1,292	0.59	1.13	17	-1.30	0.1938
234004 Mendocino Co Ment Hlth - Phf	Diagnoses	1,159	0.86	0.78	4	151	0.93	0.75	4	-1.06	0.2872
	Procedures	1,159	0.00			151	0.00				
281078 St. Helena Hospital	Diagnoses	926	6.48	5.27	27	213	4.99	4.79	23	3.80	***0.0002***
	Procedures	926	0.34	1.27	13	213	0.51	1.44	11	-1.60	0.1103
80929 California Pacific Med Ctr-Pacific Campus	Diagnoses	583	4.32	4.83	26	117	4.61	4.64	28	-0.58	0.5608
	Procedures	583	1.71	2.38	19	117	1.63	2.27	12	0.31	0.7565
381154 Ucsf Medical Center	Diagnoses	1,660	3.81	4.05	27	232	3.89	4.70	28	-0.23	0.8165
	Procedures	1,660	1.63	2.09	14	232	1.74	2.68	20	-0.63	0.5267
490919 Sutter Medical Center Of Santa Rosa	Diagnoses	1,160	3.54	4.43	28	190	4.17	4.65	26	-1.82	0.0685
	Procedures	1,160	1.17	2.06	20	190	1.45	2.40	13	-1.55	0.1230
491064 Santa Rosa Memorial Hospital-Montgomery	Diagnoses	1,975	4.78	5.45	29	350	5.10	5.32	26	-1.01	0.3103
	Procedures	1,975	1.21	2.18	20	350	1.47	2.30	17	-2.03	***0.0425***

Table 2. Hospitals admitting 100 or more women when pregnant

		ROC				Willits				T-Test	
Hospital	Measure	N	Mean	Sdev	Max	N	Mean	Sdev	Max	T-Val	P-Val
Grand mean	Diagnoses	35,707	2.33	2.04	26						
	Procedures	35,707	1.31	1.26	20						
Discharges when County resident	Total	30,352				5,355					
	% gt 100	91				91					
Overall Mendocino resident	Diagnoses	27,764	2.28	1.92	21	5,032	2.33	2.03	19	-1.79	0.0737
	Procedures	27,764	1.32	1.25	9	5,032	1.44	1.27	10	-6.29	***<.0001***
230949 Frank R Howard Memorial Hospital	Diagnoses	166	1.26	1.01	6	282	1.22	1.32	11	0.35	0.7240
	Procedures	166	0.14	0.42	2	282	0.21	0.56	4	-1.39	0.1650
231013 Mendocino Coast District Hospital	Diagnoses	6,756	1.71	1.80	12	532	1.03	1.29	9	11.4	***<.0001***
	Procedures	6,756	0.55	0.76	7	532	0.48	0.70	3	2.22	***0.0270***
231339 Ukiah Valley Medical Center/Dora Street	Diagnoses	3,679	1.47	1.04	6	665	1.56	1.13	6	-1.81	0.0713
	Procedures	3,679	1.33	1.25	7	665	1.57	1.27	5	-4.49	***<.0001***
231396 Ukiah Valley Medical Center/Hospital Drive	Diagnoses	16,211	2.70	2.02	21	3,431	2.78	2.15	19	-2.13	***0.0334***
	Procedures	16,211	1.68	1.27	9	3,431	1.69	1.25	10	-0.40	0.6907
490919 Sutter Medical Center Of Santa Rosa	Diagnoses	952	2.43	1.84	18	122	2.19	1.67	9	1.37	0.1708
	Procedures	952	0.81	1.02	7	122	0.77	1.08	4	0.39	0.6975

Table 3. Hospitals admitting 100 or more infants

		ROC				Willits				T-Test	
Hospital	Measure	N	Mean	Sdev	Max	N	Mean	Sdev	Max	T-Val	P-Val
Grand mean	Diagnoses	37,165	1.09	1.71	29						
	Procedures	37,165	0.15	0.88	20						
Discharges when County resident	Total	31,725				5,440					
	% gt 100	92				95					
Overall Mendocino resident	Diagnoses	29,249	1.03	1.63	24	5,143	1.11	1.60	24	-3.15	***0.0016***
	Procedures	29,249	0.12	0.79	20	5,143	0.10	0.66	18	2.03	***0.0428***
230949 Frank R Howard Memorial Hospital	Diagnoses	164	0.59	0.93	6	306	0.67	1.08	5	-0.86	0.3908
	Procedures	164	0.04	0.27	2	306	0.00	0.06	1	2.08	***0.0377***
231013 Mendocino Coast District Hospital	Diagnoses	6,855	0.51	0.89	7	487	0.44	0.84	5	1.71	0.0869
	Procedures	6,855	0.03	0.21	4	487	0.02	0.17	2	1.00	0.3156
231339 Ukiah Valley Med Ctr/Dora Street	Diagnoses	3,598	0.55	0.92	6	621	0.68	1.02	6	-2.97	***0.0030***
	Procedures	3,598	0.05	0.34	5	621	0.04	0.30	4	0.72	0.4697
231396 Ukiah Valley Medical Center/Hospital Drive	Diagnoses	16,497	1.13	1.41	13	3,416	1.16	1.39	11	-1.09	0.2759
	Procedures	16,497	0.03	0.24	6	3,416	0.03	0.24	7	0.32	0.7453
381154 Ucsf Medical Center	Diagnoses	1,047	4.41	4.05	24	148	4.31	4.23	24	0.29	0.7740
	Procedures	1,047	2.21	3.22	20	148	2.05	2.84	18	0.58	0.5589
490919 Sutter Medical Center Of Santa Rosa	Diagnoses	1,088	1.28	1.85	15	165	1.66	2.00	10	-2.46	***0.0138***
	Procedures	1,088	0.30	0.91	10	165	0.44	1.01	6	-1.85	0.0639

Summary

Overall, when not pregnant, average number of DX and PX were not significantly different by place of residence but were significantly different when pregnant.

To the extent that the <u>number</u> of DX and PX (rather than the <u>content</u> of the fields) reflects illness severity, the overall clinical judgement of treating physicians in the same

hospitals was that there were few differences when women were not pregnant. When they were pregnant, the judgement of physicians in those same hospitals was that Willits women and their infants required more detailed documentation.

Variability in hospital coding did not disadvantage ROC residents relative to Willits.

ADMISSIONS PRIOR TO MENDOCINO COUNTY

Statement

"Dr. Remy's data do not establish whether health outcomes in women first occurred before or after they started living in Willits. (Page 13)"

Response

Of females born between 1950 and 1989, 11% of discharges were before their first in the County. Summarized to the person level, 13% had at least one previous admission. Statistical tests for differences between Willits and ROC in average number of prior admissions and average number of prior pregnancies were non-significant.

As with coding variability discussed above, the data do not Dr. Chang's hypothesis that conditions are distributed dissimilarly among the groups. The number of prior admissions did not differ.

I reported similar conclusions to the court in an earlier report [9], and this issue again withstood inquiry. As in previous linked analyses, I removed prior records before summarizing to the person level for the NP female life course model (DXCHNP20).

However, the process of analysing prior admissions responsive to Dr. Chang identified that Willits females admitted to hospital in County had fewer pregnancy admissions than ROC females. I interpret this as another indicator of impaired fertility.

Discussion

For this response to Dr. Chang, I reclassified the person-level data into five groups: Only lived in Willits, only lived in ROC, lived in Willits before ROC, in ROC before Willits,

or combinations of both. I describe the restructuring and its impact on the linked analysis in a later section titled "Overestimation of hospitalization rates".

Responding to Dr. Chang's concerns about the impact of admissions before the County, I examined records for females with admissions ***only in Willits or only in ROC (97% of people)***. I evaluated each record as to whether it was before the first County admission (PRIOR). I further classified each record as to whether it was pregnancy-related (PREG) or other (i.e, medical), and if PREG, whether it occurred before (PREGPRIOR) or after (PREGMEND) the first County admission. I summarized these records to the person level, and then tested for differences. Results are in Table 3 below. Statistically significant differences are in ***bold and italics***.

Table 4. Average person-level admissions by generation and area Jul-1990-2012

Measure	Gen	ROC	Willits	T-Val	P-Val
Prior admission	1950	0.36	0.42	-1.45	0.1464
	1970	0.27	0.29	-0.66	0.5094
Prior pregnancy	1950	0.10	0.10	0.63	0.5271
	1970	0.16	0.19	-1.90	0.0569
Mend pregnancy	1950	0.65	***0.58***	2.85	***0.0044***
	1970	1.64	***1.47***	4.69	***<.0001***
Mend medical	1950	2.1	***1.8***	2.20	***0.0281***
	1970	0.8	0.8	0.45	0.6500

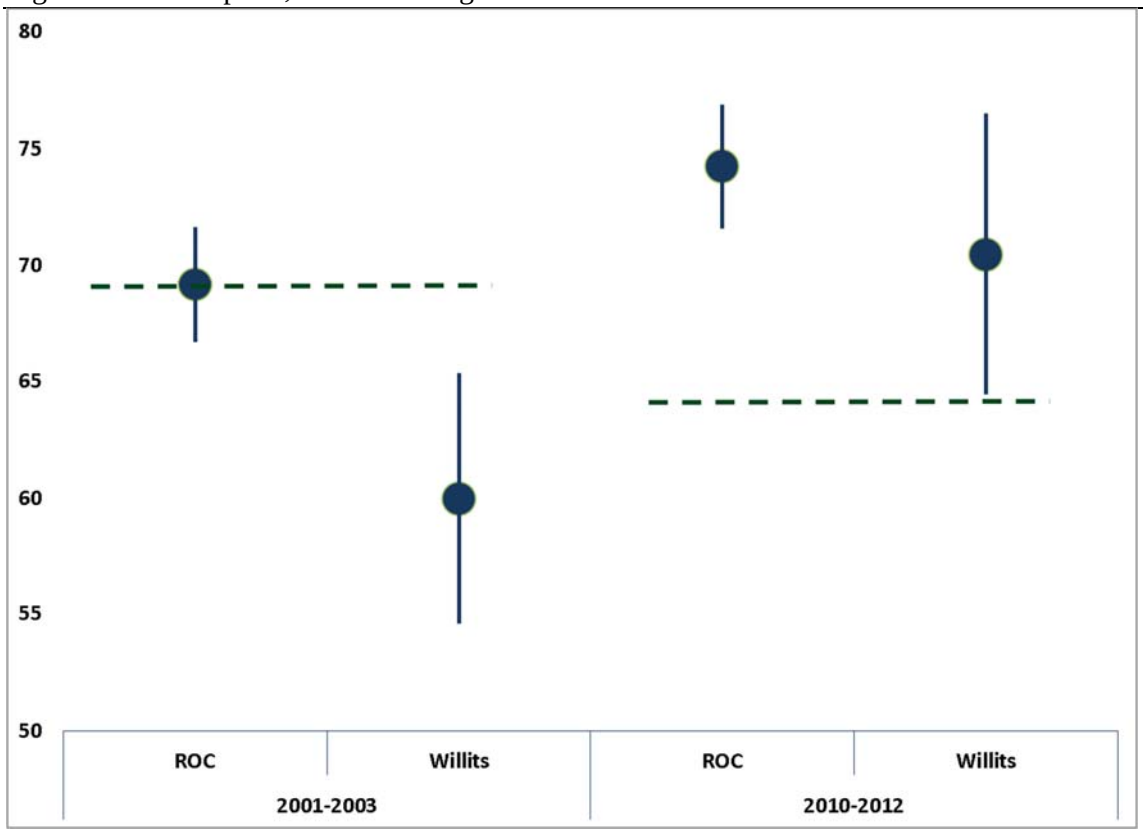
ROC and Willits women did not have a significantly different number of prior admissions or prior pregnancy admissions. The near-significant P-value for the younger generation of Willits females (0.0569) suggests they may have had more pregnancies before living in the town than women who moved to ROC. However, both generations of Willits females have significantly fewer pregnancy admissions after they arrive.

Additionally, the older generation of Willits women had fewer medical admissions ***after*** living in-county, while the younger generation had about the same number in-county. This again counters Dr. Chang's concerns about possible upcoding. Risk ratio differences are

not based on upcoding, but on differences in underlying health conditions precipitating admission. ***What matters are conditions that physicians record in the discharge abstracts.***

Focusing on reproduction, I reviewed the fertility DataBooks FHOP makes for the State. In DataBooks, we report differences in rates between the local area and State for the three-year start of period (SOP) and three-year end of period (EOP). Figure 4 compares fertility rates for the periods 2001-2003 and 2010-2012. The vertical bars show the CI, the round circle the rate, and the dashed line shows the State average.

Figure 4. Births per 1,000 females age 15 to 44 – 2001-2003 and 2010-2012



At SOP, the Willits CI shows that its' fertility rate was well below both ROC and State. At EOP, ROC rates increased slightly and Willits rates increased significantly, and both were higher than the State rate, which dropped over the interval.

Summary

For most young women, the birth of a child represents their first experience with a hospital. Women who lived elsewhere before moving to the County had no differences in number of prior admissions or pregnancy admissions. When living in Willits, both generations of women had fewer pregnancy admissions. This suggests problems conceiving or maintaining pregnancies, similar to Danielle Smith. Information from DataBooks prepared for the State suggests this may be abating.

Contrary to Dr. Chang's inference, no evidence suggests that pre-residence conditions contaminate results after people enter hospital as a County resident. Further, substantial evidence suggests that living in Willits reduced fertility.

These findings further strengthen my conclusion that Willits rates are not different because of the number of DX, but because of genuine differences in health conditions that precipitated admission.

DEMOGRAPHIC AND SOCIOECONOMIC DIFFERENCES

Statement

> "Dr. Remy overlooks demographic and socioeconomic differences between Willits and the rest of Mendocino County that could explain her findings. … Such differences could make residents of the rest of Mendocino County less likely to seek hospital care, on average, than residents of Willits, thereby biasing results toward higher hospitalization rates in Willits."
>
> (Pp. 32-37)

Response

In my 26-Aug-2015 deposition [14], I was asked, "But did you do any statistical analysis specifically to compare Willits versus the rest of the county or did you just eyeball it?" (P. 354). Before the deposition, I had looked at certain indicators and concluded that Willits and ROC were not significantly different. After the deposition, I revisited those

indicators and confirmed my impression. ***I was correct that differences between Willits and ROC were not statistically significant***. ***Both tend to be different from the State, and Willits is not importantly different from ROC.***

Discussion

Eliminating disparities is one of the four foundation public health measures. Healthy People 2020 defines a disparity as "a particular type of health difference that is closely linked with social, economic, and/or environmental disadvantage. Health disparities adversely affect groups of people who have systematically experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; ***gender; age; mental health***; cognitive, sensory, or physical disability; sexual orientation or gender identity; ***geographic location*** (LR emphasis added); or other characteristics historically linked to discrimination or exclusion," [16]. The CDC seldom tests for differences after stratification except when they are addressing disparities, for example, relationships between geographic (e.g., Willits vs. ROC) and environmental disparities (e.g., air quality) [17].

I have consistently stratified Willits analyses by the demographic characteristics sex, age (e.g., 15-44) or cohort (a direct conversion of age), and geography. Except for race/ethnicity, other demographic variables are not available in hospital files. Below the age of 65, we do use the fact of public payment for care as a proxy for income. However, I also said that I had looked at some demographic and socioeconomic indicators and concluded there were few important differences. Here I revisit them.

Race/ethnic disparities

Willits usually has too few cases of any ethnicity except White to calculate race/ethnic rates for any three-year period over the twelve-year interval used for DataBooks. Four relevant examples are infant low birth weight, preterm birth, gestational

diabetes during pregnancy, and mental health admissions of women or pregnant women age 15 to 44.

12% of pregnant Willits women identified themselves as Hispanic all-race, compared with 24% for ROC (CMH Chi-square = 405.9, P-value = <0.0001, OR = 0.43, LCL = 0.39, UCL = 0.47). In logistic regressions reported in another section of this response to Dr. Chang, among the set of variables I included White non-Hispanic and Hispanic all-race into the models, using stepwise selection. White non-Hispanic did not enter any model, and Hispanic all-race reduced risk of the adverse pregnancy outcomes studied.

Age

Dr. Chang incorrectly described my methods as not adjusting for the age of hospitalized patients, or of not adjusting for the age of the population in the community. In fact, the opposite is true.

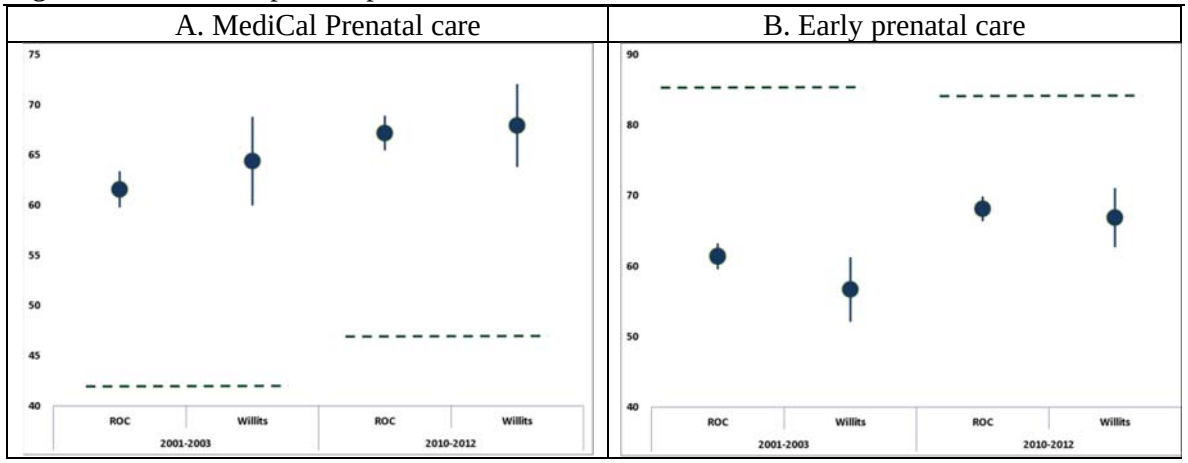
Period is a direct conversion of age [18]. In the pregnancy analysis DXCLM20, I converted age into the period when women were born and adjusted rates based on the number of live deliveries, the standard population denominator for pregnancy indicators. I similarly converted age into period born for the non-pregnant female life course model DXCLNP20, and used external Federal population denominators also with age converted into period.

Access Disparities

In DataBooks we make for the State, two from birth certificates are particularly sensitive access indicators for pregnant women: Medi-Cal as the payor for prenatal care, and early receipt of prenatal care. The first indicator generally reflects economic disparity, while the second generally reflects lack of access to providers early in pregnancy.

Figure 5 shows rates for the local area and State for the three-year SOP and three-year EOP. Rates for both indicators are significantly different from the State, not different from each other, and both have similar disparities.

Figure 5. Access disparities per 100 live births 2001-2012

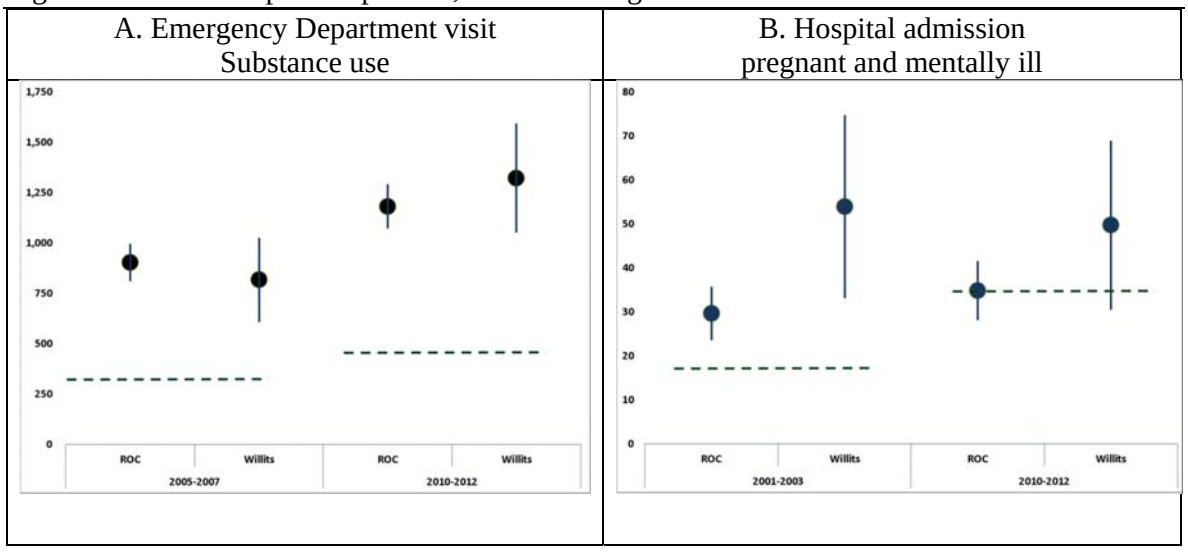


Health disparities

Figure 6 compares ROC and Willits for health disparities among females age 15 to 44. ED data did not exist before 2005. Adjusted for population, women age 15 to 44 living in Willits and ROC have significantly more ED visits for substance use than the state average, and the overlapping CI show these rates are not significantly different at either period.

Hospital admission with a mental health diagnosis while pregnant is another common reason for a non-delivery episode-of-care. Here, ROC and Willits are not significantly different from each other at either period, but the State rate rises so they no longer have higher rates than State at EOP.

Figure 6. Health disparities per 100,000 females age 15 to 44



In the DataBook addressing pregnancy complications, from which Figure 6B is taken, we also calculate substance use admissions while pregnant with much the same results. We had planned to do a parallel DataBook for ED visits. However, hospitals admit most pregnant women presenting in the ED for this and other high-risk conditions such as gestational diabetes mellitus (GDM) in pregnancy, and we did not have enough cases to make the pregnancy complications DataBook for ED visits. Most of these are admissions while pregnant that do not result in delivery. Neither Willits nor ROC women are significantly different from the state for GDM. In logistic regressions addressing pregnancy outcomes, described elsewhere, GDM and mental health were significant predictors of admissions that did not result in a delivery or terminated without a live birth.

Other demographic disparities

In my deposition, I alluded to examining education attainment (P. 357) and homes burning wood fuel (as an indicator of air quality) (P. 353). Patient education is not available in OSHPD data. Table 4 highlights those disparities. The Nation [19] and California [20] have higher proportions of college-educated workforces and much lower percent of homes burning wood fuel [21,22]. As I mentioned in my deposition, Willits homes used less wood fuel for home heating than the County (P. 355).

Table 5. College educated and wood fuel, US, California, County and Willits

Geography	College	WoodFuel
Nation	28.8	1.7
California	37.6	1.8
Mendocino	21.6	29.4
Willits	20.3	8.0

Summary

From the above, we can see that demographic and socioeconomic differences do not exist such that ROC residents would be less likely than Willits residents to seek hospital care. Both areas are disadvantaged, and differences do not bias toward higher

hospitalization rates in Willits. The data do not support Dr. Chang's hypothesis that differences in these indicators may underlie differences in admission rates.

HOSPITAL DATA TO STUDY PREGNANCY OUTCOMES

Statement

> "Dr. Remy states that hospitalizations during pregnancy for non-pregnancy-related conditions are a reason not to analyze birth outcomes using hospitalization data. Specifically, she states that "a lot of times a lot of women are admitted while they are pregnant not for the pregnancy, like they'll fall. Okay? … Or they'll – they'll have – you know, they'll be in a car crash or something; so they're pregnant when they're admitted but they're not there to deliver the baby. So when you're doing studies for pregnancy, which is a – ***they are really hard to do well*** (LR emphasis added)" (Remy deposition, November 9, 2010, pp.102-103)" (P. 30)

Response

I did ***NOT*** state that admissions for pregnancy-related conditions are a reason ***not*** to use hospital data to study pregnancy outcomes. I said that such studies are hard to do ***WELL***.

Further, Dr. Chang omits my statement on the immediate prior page (101) of my 09-Nov-2010 deposition [13], where I clearly am discussing a ***LINKED*** study of California maternal outcomes. I stated, "I actually worked on the first study where they tried to do a pregnancy outcome study for the State of California and we had so much trouble with the ***linkage*** (LR emphasis added) that … we all agreed that we couldn't release it."

I have not done a LINKED analysis of pregnancy and birth outcomes for Willits, and the pregnancy and birth outcome studies on which I worked were done very well.

Discussion

The purpose of the 1996 OSHPD study referenced in my 2010 deposition was to rank hospitals by pregnancy outcomes for the two-year period 01-Jul-1990 to 30-Jun-1992 [23].

At that time, 20% of pregnancy records lacked SSNC -- an important reason linked studies are harder to do for this population.

In 2008, I did another linked analysis of maternal morbidity and mortality, this time for the period 2001-2005 [24]. In the second study, funded by a consortium of Bay Area counties, SSNC availability had not changed: overall, 21% of pregnant women still did not have SSNC, and the rest of State had proportionately more discharges without SSNC than the Bay Area (respectively 22% and 19%). At that time, because we were not ranking hospitals, the funders agreed to let us develop methods to compensate for the absence of SSNC.

Now I turn to why I have not done a linked pregnancy analysis for Willits, and why it was possible to do a linked NP analysis. Table 5 summarizes the absence of SSNC at the discharge level for County residents admitted to hospital from Jul-1990 through 2012, stratified by age and sex, and pregnancy status among women. .

Table 6. Absence of SSNC by age, sex, and pregnancy (%) 1990-2012

			Age Group										
Sex	Pregnant	Area	15	20	25	30	35	40	45	50	55	60	Avg
Male		State	30	17	13	10	8	7	6	5	5	5	11
		ROC	18	9	6	5	3	3	2	2	4	3	5
		Willits	14	3	4	4	2	1	1	2	4	2	4
Female	No	State	26	12	10	8	6	5	5	4	5	5	9
		ROC	17	5	4	3	2	2	2	2	3	3	4
		Willits	11	4	1	1	1	1	1	1	4	6	3
	Yes	State	26	25	22	16	13	12					19
		ROC	16	17	16	13	12	10					14
		Willits	6	8	9	8	6	5					7

The absence of SSNC is more marked statewide than in the County for men, women, and pregnant women. Pregnant women generally have fewer SSNC than NP women. This is why it is why doing a linked analysis of pregnancy outcomes is challenging.

Another issue directly addresses why ROC residents have fewer SSNC than Willits residents. Specifically, OSHPD exempts hospitals from submitting the SSNC if it is not in the medical record [25], and some do not submit SSNC at all. This apparently includes Ukiah

Valley Hospital, Dora Street, with 8,107 female ROC admissions and 1,370 Willits admissions with zero (0) SSNC. See UPCODE.XLSX, sheet SSNC. This means that SSNC is not missing randomly. In reality, ROC residents may have about the same percent of SSNC as Willits residents. We simply are not able to identify their records for the person-level life course analysis.

Because differences based on residence are smaller for non-pregnant women (1% on average), I adjust for the absence of SSNC when I prepare to calculate population rates and related statistics for the life course models as in DXCHNP20 for non-pregnant females.

Summary

Dr. Chang's charge that I believe pregnancy outcome studies should not be done is false and completely without merit. I have done a number of such studies, and did all of them very well.

HOSPITAL ADMISSIONS WHILE PREGNANT

Statement

> "I … did not identify any published articles that used all non-delivery-related hospital admissions during pregnancy as an indicator of fetal viability risk." (P. 30)

Response

Hospital admissions while pregnant that do not result in a live birth is a valid indicator of pregnancy risk and fetal viability. It also can indicate the lack of access to preventive care for pregnant women.

Discussion

The variable NODELIV flags hospital admissions while pregnant that do not result in a live birth. One DataBook we produce for the State of California calculates rates for "Gestational diabetes mellitus during pregnancy (GDM)" by searching admissions while pregnant that do not result in a delivery. By definition, physicians diagnose GDM during

pregnancy and before delivery. In our 2008 study of maternal morbidity and mortality, we also used GDM, injury, and mental health as pregnancy risk indicators [24]. As to in-hospital terminations (pregnancies that do not end in a live birth), we noted, "Whether induced or spontaneous, most abortions occur outside of hospitals and women rarely enter a hospital for these except in a high risk situation (p 12)".

Summary

The variable "Hospital admissions while pregnant that do not result in a delivery" is a good indicator to monitor high-risk pregnancy outcomes.

ADJUSTMENT FOR CONFOUNDING

Statement

> "Dr. Remy's analysis does not adjust for confounding by important influences on health and hospitalization that could account for her findings. (P. 10)"

Response

Basic public health monitoring methods typically do not **adjust** for potentially confounding factors. They ***stratify*** by those factors. No Healthy People 2020 DataBook that I produce for the State of California as Research Director of FHOP ***adjusts*** for confounding.

As the CDC does, we ***select*** by group (e.g., infants or women between the ages of 15 and 44), then ***stratify*** by race/ethnicity to calculate rates over intervals of equal length. Using small number rules developed by FHOP and approved by the California Department of Public Health [26], we calculate rates and associated statistics where a given group in a given local area has enough cases over the number of years we are studying. Unlike the CDC, FHOP tests rates and trends for statistical significance, to answer the question as to whether the jurisdiction is moving toward, moving away from, or making no progress to meet the national objective.

Other methods also test hypotheses. For example, when I stratify data into two fifteen-year periods or two twenty-year generations, my work on Willits is a retrospective public health surveillance study, defined as ***a systematic collection, analysis, and interpretation of data essential to plan, implement, and <u>evaluate</u>*** (LR added emphasis) public health practice. It falls within the discipline of social epidemiology because it seeks to understand environmentally caused illness arising from public policy [45], specifically to permit building Remco in Willits. These are valid methods to test hypotheses about the impact of Remco on the health of Willits residents.

Multivariate logistic regression is another method used to "adjust for confounding". Responsive to Dr. Chang, I developed logistic models for two maternal outcomes: (1) hospital admissions that did not result in a live birth; and (2) in-hospital pregnancy terminations that do not end in a live birth (miscarriage, abortion, still-born infants). ***Willits remains statistically significant in both models with no meaningful change in the odds ratios or confidence intervals.***

Discussion

After my August deposition, I reviewed the code to calculate the two indicators in question. I found I had omitted certain DX codes for fetal loss (FETLOS) as well as another group of related codes (OTHTERMDX). I also printed and reviewed various data inconsistencies and reclassified indicators based on the review. Given these changes responsive to the deposition, I re-ran the residence (DXRESPG), closure (DXCLMYRC15), and generation (DXCLM20) pregnancy models. Note that these are NOT LINKED models, and reflect women who live in the areas. ***From the linked analysis, 97% of women lived only in one area. Thus, movement from area to area is minor***.

In these programs, I also added variables that I had calculated earlier but had not reported including race/ethnicity, injury, and sub-groups used to make the higher-level variables TERMDX and TERMPX.

Responsive to Dr. Chang's report, I then developed two logistic regression models focusing on maternal pregnancy outcomes. The objective was to test whether Willits remained statistically significant after adjusting for potential confounders. In these models, I included the following sets of dichotomous variables:

- **Time**: mother born before 1970 (COH20D), delivery between 1983-1997 (YRC15D), and an interaction variable (MOMPRE)
- **Mother's race/ethnicity**: White Non-Hispanic, Hispanic all-race
- **Access to care**: public payment for care (Medi-Cal, uninsured) (PAYPUB), emergency room admission (SRCER), and admitted out-of-county (OOC). FHOP uses these standard access variables in outcome studies, for example, our studies on maternal morbidity and mortality [24] and mental health in the reproductive age population [27].
- **CCS body system conditions**: mental health (which includes substance use) (DXCH05), and injury, which combines injury diagnoses and E-codes (INJDX) (used for FHOP's mental health and injury DataBooks.
- **CCS Pregnancy conditions**: hemorrhage in pregnancy (DXCL182), early labor (DXCL184), diabetes mellitus in pregnancy (DXCL186), fetal distress (DXCL190), and fetal anomaly (FETANOM)
- **Exposure**: Resident of ROC or Willits (WILLITS)

The models included all variables in the time set because of the interaction variable (MOMPRE), and permitted stepwise selection of the others. Tables 7 and 8 show that SAS entered Willits into each model. ***That is, Willits remained statistically significant after controlling for other clinically meaningful variables.*** The odds ratios in the adjusted models

were slightly higher than in the unadjusted models, but not significantly different (1.14 versus 1.13 in the model predicting admission without live birth, and 1.36 versus 1.32 in the model predicting termination.). The C-statistics (respectively 0.823 and 0.798) indicate that the predictive accuracy of these logistic regression models is good.

Greyed sections highlight that multivariate regression models did not importantly affect the odds ratios and confidence intervals. ***In other words, living in Willits while pregnant adds to our understanding of the risk of these adverse maternal outcomes. The measure is not confounded with other variables.***

Table 7. Logistic model to predict admitted to hospital with no live birth (C = 0.823)

Variable			Pregnant, admitted, no live birth						
Group	Name	Label	Est	Std Err	Chi-Sq	P-Val	OR	LCL	UCL
	Intercept		-2.50	0.07	1,136	<.0001			
Time	COH20D	Born 1950-1969	-0.2	0.075	5.7	0.0167	0.84	0.72	0.97
	YRC15D	Pregnant 1983-1997	0.15	0.07	3.8	0.0518	1.16	1.00	1.34
	MOMPRE	B. 1950-1969, Preg. 1983-1997	0.33	0.09	12.7	0.0004	1.39	1.16	1.67
Race/ethnicity	RACEDOF1	White non-Hispanic							
	RACEDOF3	Hispanic all-race	-0.29	0.05	37.8	<.0001	0.75	0.68	0.82
Access	PAYPUB	Public insurance or uninsured	2.38	0.05	2,297	<.0001	10.8	9.8	11.9
	OOC	Out-of-County	0.15	0.04	15.6	<.0001	1.16	1.08	1.25
	SRCER	ER Admission	0.36	0.05	50.5	<.0001	1.43	1.30	1.58
CCS Body	DXCH05	Mental Health	0.63	0.07	71.3	<.0001	1.87	1.62	2.16
System	INJDX	Injury	0.89	0.09	102.9	<.0001	2.43	2.05	2.89
Pregnancy	DXCL182	Hemorrhage in pregnancy	0.67	0.09	51.4	<.0001	1.95	1.63	2.35
Conditions	DXCL184	Early labor	2.28	0.04	2,933	<.0001	9.78	9.00	10.62
	DXCL186	Diabetes mellitus in pregnancy							
	DXCL190	Fetal distress	-2.59	0.11	567.7	<.0001	0.08	0.06	0.09
	FETANOM	Fetal anomaly							
Exposure	WILLITS	Willits resident	0.13	0.05	7.0	0.0080	1.14	1.03	1.25
	SAS program	Model							
	DXCRESPG	Resident			9.6	0.0020	1.13	1.05	1.22

Table 8. Logistic model to predict in-hospital pregnancy termination (C = 0.798)

Variable			In-hospital pregnancy termination						
Group	Name	Label	Est	Std Err	Chi-Sq	P-Val	OR	LCL	UCL
	Intercept		-3.56	0.12	912	<.0001			
Time	COH20D	Born 1950-1969	-0.7	0.123	29.7	<.0001	0.51	0.40	0.65
	YRC15D	Pregnant 1983-1997	-0.04	0.12	0.1	0.7097	0.96	0.76	1.21
	MOMPRE	B. 1950-1969, Preg. 1983-1997	0.29	0.17	2.9	0.0866	1.34	0.96	1.87
Race/ethnicity	RACEDOF1	White non-Hispanic							
	RACEDOF3	Hispanic all-race	-0.20	0.09	5.1	0.0237	0.82	0.69	0.97
Access	PAYPUB	Public insurance or uninsured							
	OOC	Out-of-County	2.20	0.07	947	<.0001	8.99	7.81	10.34
	SRCER	ER Admission	0.46	0.09	25.7	<.0001	1.59	1.33	1.90
CCS Body System	DXCH05	Mental Health	0.36	0.13	7.3	0.0068	1.43	1.10	1.85
	INJDX	Injury	0.78	0.14	32.5	<.0001	2.17	1.66	2.84
Pregnancy Conditions	DXCL182	Hemorrhage in pregnancy							
	DXCL184	Early labor	-1.4	0.16	76.4	<.0001	0.25	0.18	0.34
	DXCL186	Diabetes mellitus in pregnancy	-0.69	0.21	10.4	0.0013	0.50	0.33	0.76
	DXCL190	Fetal distress	-2.48	0.17	218	<.0001	0.08	0.06	0.12
	FETANOM	Fetal anomaly	1.55	0.09	270	<.0001	4.69	3.90	5.64
Exposure	WILLITS	Willits resident	0.31	0.08	13.7	0.0002	1.36	1.15	1.60
	SAS program	Model							
	DXCRESPG	Resident			13.4	0.0003	1.32	1.14	1.54

Summary

Multivariate models add to our understanding of underlying factors when pregnant women enter the hospital without delivery. The models help us grasp that these admissions truly reflect high-risk situations that put the pregnancy at risk. Among those predictors, ***the fact of living in Willits remains a highly significant independent risk factor that is unchanged in multivariate models.***

OVERESTIMATION OF HOSPITALIZATION RATES

Statement

"Dr. Remy's analytic method is prone to overestimation of hospitalization rates, especially among Willits residents (Pp. 26-29)"

Response

Dr. Chang's statement applies only to the linked life course model, and specific to this litigation, DXCLNP20. The criticism consisted of several topics, each of which I address below: symmetrical handling of persons who moved between ROC and Willits, the use of

population denominators that did not include persons who left the area, and possible effects of persons leaving Willits more than ROC.

To be responsive to Dr. Chang, I slightly modified the method to assign people to place of residence and recalculated rates. Specifically, if people ever lived in both ROC and Willits, I assigned discharges to both places. When assigned to Willits, I used all discharges after first in Willits, and when assigned to ROC I assigned all discharges after first in ROC. Focusing on the life course model for non-pregnant females born between 1950 and 1989, this modification slightly reduces estimates as Dr. Chang suggested.

This modification does not eliminate statistically significant disparities for any important indicator.

Discussion

I first modified the program CONP.SAS to clarify geographic origin. I previously classified discharges found for plaintiffs ((CASE) included for the paper Dr. Byers and I are preparing) as both MENDO and WILLITS. Now I classify CASE, MENDO, and WILLITS without dependence. This removed 64 discharge records from assignment to MENDO and WILLITS. I also removed records with length of stay (LOS) greater than or equal to 365 days, which I previously did in the program BIGP.SAS.

When I plan to do a life course analysis, as here for non-pregnant females born between 1950 and 1989, the second program PERSON identifies potential candidates for further search. I modified this program to count the number of records and first and last date in MENDO, WILLITS, and ROC. Overall, 97% of people were in one area only. Thus, right from the top, one can see that the impact of living in multiple locations is trivial.

Table 9 (from PERSON.XLSX) displays the number of people admitted only from one place and those with admissions first in place 1 then in place2 (ROC to Willits or Willits to ROC). Although number of people moving between communities is approximately even,

note that only 1.4% of ROC residents moved to Willits, while 7.3% of Willits residents moved intracounty to another location. Over the interval Jul-1990-2012, only 172 people (not shown, 0.4%) were admitted in both places with cross-linked periods, that is, moving from place1 to place2 to place1.

Table 9. People admitted in one place or going between places – Jul-1990-2012

	One Plc	P1>P2	Total	% Tot
ROC	31,730	429	32,159	1.4
Willits	5,755	418	6,173	7.3

This supports my early conclusion regarding population stability as well as Census data that Willits residents are more likely to move intra-county. From the Census, I earlier showed that residential stability in the County had been in the top 10% of the State from 1970 through 2000 [4]. In 2000, Willits' stability was slightly higher than ROC, with 85% of Willits residents reporting they lived in the same county 10 years earlier, compared to 82% for the County and Willits residents were more likely to move intra-county.

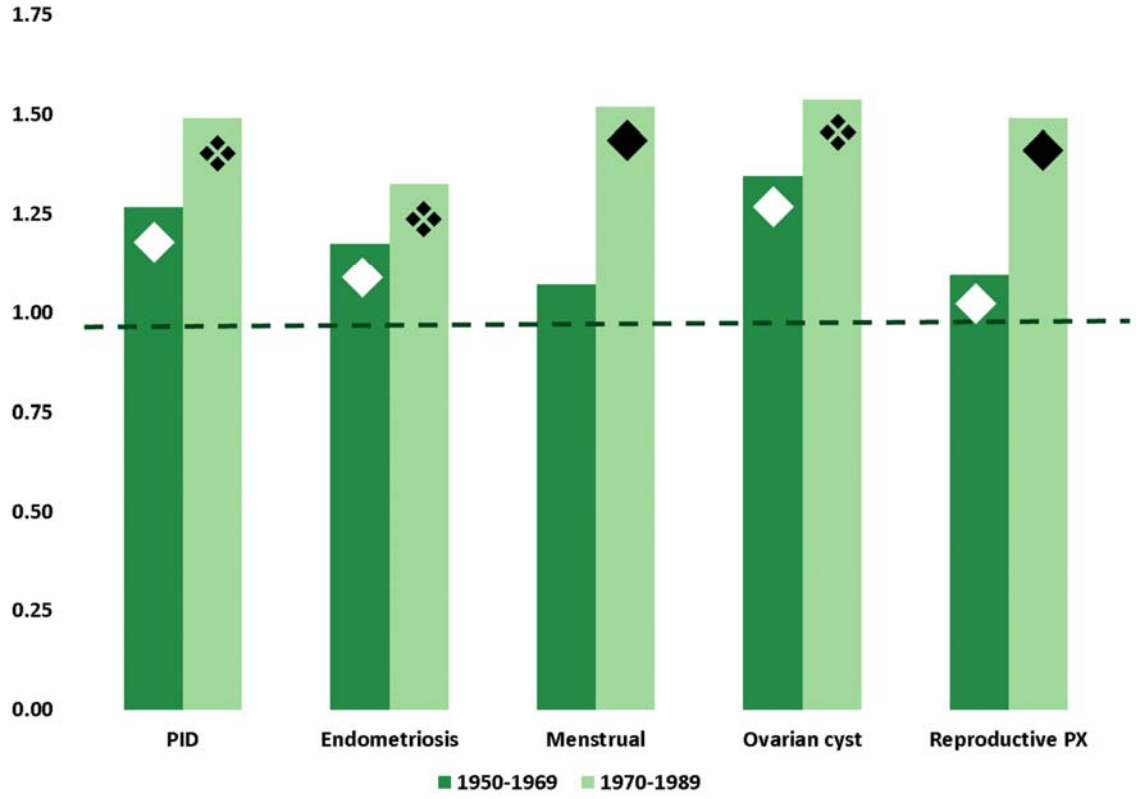
The Decennial Census no longer monitors long-term residential stability, so I am not able to update this. However, further supporting residential stability, a side analysis of the California Death Statistical Master file for the period 1991-2012 found 85 percent of decedents moved to the area before 2000, with about one year difference for women. See DTH2014.ZIP which I did as part of the analysis for the Environmental Health paper [10].

In response to Dr. Chang, in calculating numerators for this report, I assigned to each area (Willits or ROC) all people who ever lived in the area, summarizing their discharges on or after their first residence in each area. As in the July-2015 report, I again adjusted the numerator to account for the absence of SSNC.

Using the modified methodology, Figures 7 and 8 show the relative risk (RR) for the female NP life course model body systems that are directly relevant to plaintiff Danielle

Smith: genitourinary and neoplasm. I report results for other conditions in the file APPENDIX.XLSX (DXCHNP20). I did not modify any infant models.

Figure 7. Non-pregnant females -- genitourinary conditions – adjusted life course model



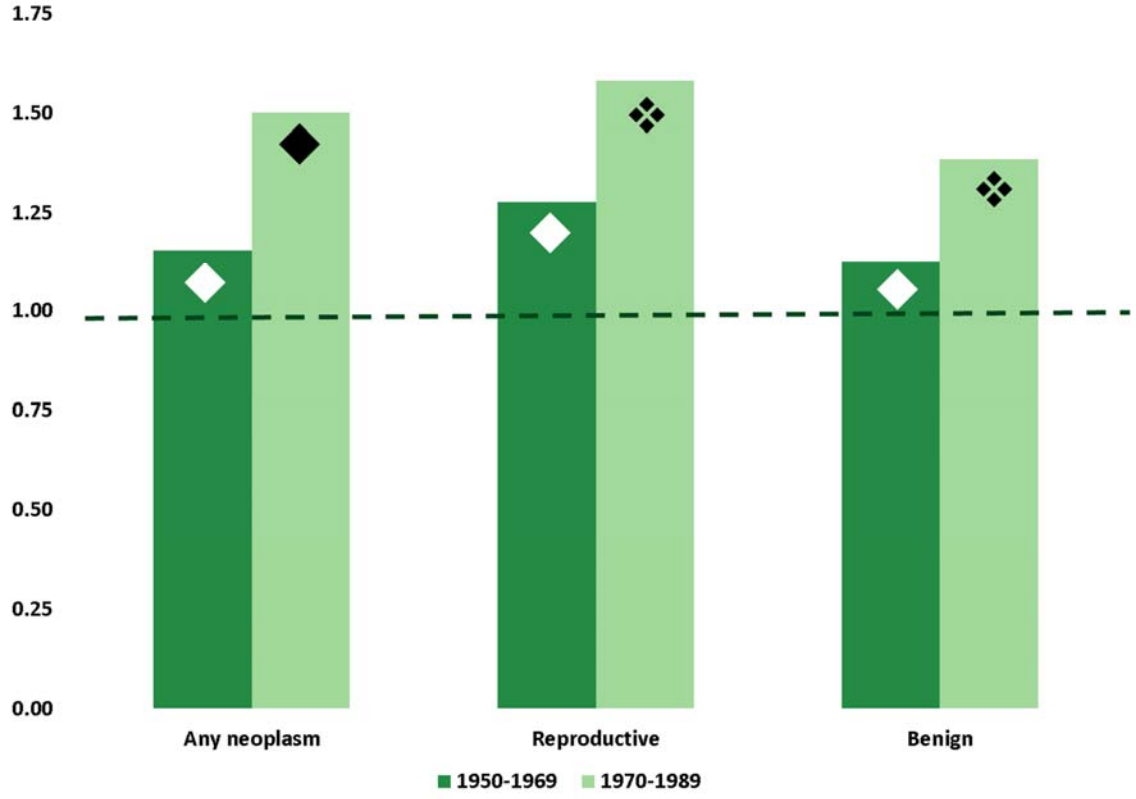
As in my July 2015 report, vertical bars show RR for each condition by period. The symbols are as follows:

- ( ) Difference is not statistically significant (P less than or equal to 0.05).
- ( ) In "mother generation" (1950-1969) geography (ROC, Willits) difference is significant. That is, Willits RR was statistically higher or lower than ROC.
- ( ) In "daughter generation" (1970-1989) geography is significant and time is significant in that RR changed from mother generation.
- ( ) In "daughter generation" geography is not significant but time is significant in that RR changed from mother generation.

(❖) In “daughter generation” geography is significant but the difference between generations is not.

Modifying the methodology responsive to Dr. Chang had little impact on results. In the July models, RR for any neoplasm was 1.28 (LCL =1.17, UCL = 1.40). In the models responsive to Dr. Change, RR statistics for this measure was 1.20 (LCL = 1.10, UCL = 1.31).

Figure 8. Non-pregnant females -- neoplasms – adjusted life course model



Summary

As expected, adjusting the methodology responsive to Dr. Chang had no important effect on the findings I have reported.

EVIDENCE-BASED CAUSATION

Statement

“Dr. Remy fails to consider standard epidemiologic criteria used to determine causation and therefore cannot claim that the results of her analysis

support a causal association between Remco activities and disease occurrence. (P. 5)"

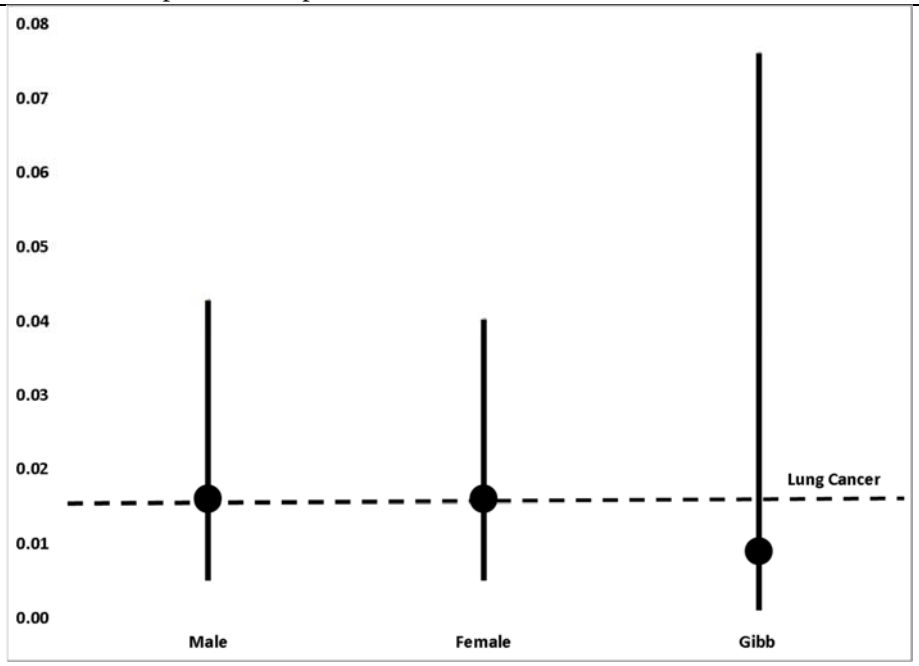
Response

My work combined with that of Vera Byers, MD, PHD and Rod O'Connor, PHD strongly supports causality between Remco activities and disease occurrence as outlined in the Hill guidelines for causality and Dr. Guzelian's outline for evidence-based causality.

Discussion

The source of exposure was hexavalent chromium Remco released from 1963-1989. At the population level, I use different time models to estimate exposure by residence in Willits. At the plaintiff level, Drs. O'Connor and Byers estimated exposure by visits to Luna Market using Gibbs methodology published in two studies examining cancer and non-cancer effects in occupationally exposed workers [28,29]. Figure 9, from work in progress by me, Byers, Clay, and O'Connor [30], shows Plaintiff exposure was not significantly different from Gibb's report for occupationally exposed workers, although the upper tail of the plaintiff distribution is shorter.

Figure 9. Plaintiff exposure compared with Gibb



ATSDR estimated community exposure, but those estimates were problematic. The population health methodology available to me does not allow me to directly estimate exposure for all people ever admitted to hospital from Willits. However, from Dr. Byers' plaintiff histories, Luna Market was the most frequently visited place in Willits, and exposure for the other residents in this small town probably was similar. While I do not know when people first moved to where they lived when admitted, the available data indicate that people tended to live only in one place and tended to stay for long periods. We know that is the situation for plaintiffs. The merging of plaintiff data with hospital data found few important differences between plaintiffs and other people admitted in Willits who did not join the litigation, suggesting equivalent exposure histories.

Both the population health data I analyzed and plaintiff data Dr. Byers gathered document the effects of toxicity to the reproductive system of women who lived in Willits. Dr. Byers has been responsible for collecting and evaluating the relevant scientific knowledge from related fields. She concludes that my analyses of health outcomes expand the knowledge base beyond the animal models. I understand from her that no other useful studies exist on the health impact of chromium to non-occupationally exposed females. Thus, we are unable to compare our results with others. ***No relevant work is published***.

My studies document that a significant health difference exists between women living in Willits and ROC consistent with the theory that Remco caused the increased illness rates. ATSDR and Dr. O'Connor both documented that Remco exposed the community and calculated exposure doses. ATSDR found it likely that Remco exposures probably had caused community health risks but did not examine data for evidence to support it, the very fact that drew me to this problem. Byers and O'Connor substantiated timing for the plaintiffs, and the population health data available to me generally support timing. Rates for conditions that Danielle Smith suffers are elevated in the population health data. Population health

models examining outcomes pre- and post- Remco closure support causality. No plausible alternate cause has ever been put forth to explain the excess illness in this community.

Summary

The information available to me support beyond a reasonable doubt that the presence of Remco in Willits caused a far-lasting impact on the health of people who lived in this small community.

I declare under penalty of perjury and the laws of the State of California that the foregoing is true and correct. The statements in this declaration are based on my personal knowledge and if called as a witness I could and would testify as to them under oath.

Executed at Belvedere, California as of October 9, 2015

1 # REFERENCES

1 Remy LL (2008) Declaration of Linda L. Remy, PhD. Donna M. Avila, et al, Plaintiffs, v. Willits Environmental Remediation Trust, et al., Case No.: C-99-3941 SI. United States District Court, Northern District of California (San Francisco Division). Dated 17-Mar-2008. WILLITS\WRITE\REMY1.PDF

2 Remy L (2008) A case study: Sick and sicker in Willits, California. UCSF Family Health Outcomes Project. Dated Sep-2008. WILLITS\WRITE\WILLITS_SUM.PDF

3 Remy LL (2009) Expert Report of Linda L Remy, PhD. Pursuant to Federal Rule of Civil Procedure 26(A)(2)(B). Donna M. Avila, et al, Plaintiffs, v. Willits Environmental Remediation Trust, et al., Case No.: C-99-3941 SI. United States District Court, Northern District of California (San Francisco Division). Dated 20-Jan-2009. WILLITS\WRITE\REMY3.PDF

4 Remy LL (2009) Declaration of Linda Remy, Phd Re: Report of January 19, 2009. Donna M. Avila, et al, Plaintiffs, v. Willits Environmental Remediation Trust, et al., Case No.: C-99-3941 SI. United States District Court, Northern District of California (San Francisco Division). Dated 30-Jan-2009. WILLITS\WRITE\REMY4.PDF

5 Remy LL (2009) Expert Report of Linda L Remy, PhD. Pursuant to Federal Rule of Civil Procedure 26(A)(2)(B). Donna M. Avila, et al, Plaintiffs, v. Willits Environmental Remediation Trust, et al., Case No.: C-99-3941 SI. United States District Court, Northern District of California (San Francisco Division). Dated 20-Aug-2010. WILLITS\WRITE\REMY5.DOC

6 Remy LL (2010) Expert Report of Linda L Remy, PhD. Pursuant to Federal Rule of Civil Procedure 26(A)(2)(B) Harry Whitlock, et al, Plaintiffs, v. Pepsi Americas, et al., Case No.: C-08-2742 SI. United States District Court, Northern District of California. Dated 10-Sep-2010. WHITLOCK\WRITE\REMY2.PDF

7 Remy, LL (2011) Rebuttal report of Linda L. Remy, PhD. Rebutting the opinion expressed by Michael A. Kelsh, PhD, in his report dated December 30, 2010. Harry Whitlock, et al, Plaintiffs, v. Pepsi Americas, et al., Case No.: C-08-2742 SI. United States District Court, Northern District of California. Dated 04-Mar- 2011. KELSH\WRITE\REMY3.PDF

8 Remy LL (2012) Expert Report of Linda L Remy, PhD. Pursuant to Federal Rule of Civil Procedure 26(A)(2)(B). Donna M. Avila, et al, Plaintiffs, v. Willits Environmental Remediation Trust, et al., Case No.: C-99-3941 SI. United States District Court, Northern District of California (San Francisco Division). Dated 15-Mar-2012. WILLMEND\WRITE\REMY5.PDF

9 Remy LL (2012) Rebuttal Report of Linda L. Remy, PhD dated July 6, 2012 Rebutting the Opinion Expressed by Jack S. Mandel, Phd in his Report Dated May 2012 C:\WILLMEND\REBUT\REMY6.DOCX

10 Remy LL, Clay T: (2014) **Longitudinal analysis of health outcomes after exposure to toxics, Willits California, 1991-2012: application of the cohort-period (cross-sequential) design**. *Environmental Health* 2014l **13**(88). Last accessed 10-Jul-2015 at: http://www.ehjournal.net/content/pdf/1476-069X-13-88.pdf

11 Remy L (2014) Memorandum to Vera Byers Re: Female health outcomes, Willits California, 1991-2012. Dated 18-Aug-2014.

12 Remy LL (2012) Expert Report of Linda L Remy, PhD. Pursuant to Federal Rule of Civil Procedure 26(A)(2)(B). Case No.: C-08-2742 SI. United States District Court, Northern District of California. Danielle Smith v. PepsiAmericas. Dated 16-Jul-2015. SMITH\WRITE\REMY6.PDF

13 Transcript of deposition of Linda L. Remy, Ph.D., November 9, 2010

14 Transcript of deposition of Linda L. Remy, Ph.D., August 26, 2015

15 Dean SV, Lassi ZS, Imam AM, Bhutta, ZA (2014) Preconception care: closing the gap in the continuum of care to accelerate improvements in maternal, newborn and child health. Reproductive Health 2014, 11(Suppl 3):S1.

16 U.S. Department of Health and Human Services. The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020. Phase I report: Recommendations for the framework and format of Healthy People 2020. Section IV. Advisory Committee findings and recommendations. Last accessed 18-Sep-2015 at: http://www.healthypeople.gov/2020/about/advisory/Reports

17 CDC (2011). CDC Health Disparities and Inequalities Report United States, 2011. Last accessed 18-Sep-2015 at: http://www.cdc.gov/mmwr/pdf/other/su6001.pdf

18. Hagenaars JA: *Categorical Longitudinal Data: Log-Linear Panel, Trend, and Cohort Analysis*. Newbury Park, Sage Publications, 1990.

19 See: http://quickfacts.census.gov/qfd/states/00000.html

20 See http://www.ed.gov/news/press-releases/new-state-state-college-attainment-numbers-show-progress-toward-2020-goal

21 http://www.city-data.com/city/Willits-California.html

22 http://www.city-data.com/county/Mendocino_County-CA.html

23 Romano P, Luft HS, Rainwater J, Remy L. (Sep 1996) Report of the California Hospital Outcomes Project: Maternal Outcomes Following Delivery, Risk-Adjusted Methodology and Preliminary Findings. California Health and Welfare Agency, Office of Statewide Health Planning and Development. This report is not available online and I do not have an electronic copy. I have a paper copy I can make available for inspection if needed.

24 Remy L, Oliva G, Clay T (2008). Maternal morbidity and outcomes including mortality, California 2001-2006. Family Health Outcomes Project, University of California San Francisco. For the Bay Area Data Collaborative. Available on request.

25 OSHPD (2010) Office of Statewide Health Planning and Development California Inpatient Data Reporting Manual, Medical Information Reporting For California, Seventh Edition, Section 97220. Last accessed 04-Oct-2015 at: http://www.oshpd.ca.gov/HID/MIRCal/Text_pdfs/ManualsGuides/IPManual/PatientSSN.pdf

26 See http://fhop.ucsf.edu/fhop-publications-data-analysis-methods-guidelines

27 Remy L, Oliva G (2008). Acute episodes of mental illness among the population of reproductive age 1991-2005. For the Maternal, Adolescent, and Child Health Branch, California Department of Health Services. Available on request.

28 Herman J. Gibb, Peter S. j. Lees, Paul F. Pinsky, and Brian C. Rooney, Clinical Findings of Irritation Among Chromium Chemical Production Workers, American Journal of Industrial Medicine 38:127-131 (2000)

29 Herman J. Gibb, Peter S. J. Lees, Paul F. Pinsky, and Brian C. Rooney, Lung Cancer Among Workers in Chromium Chemical Production, American Journal of Industrial Medicine 38:115-126 (2000)

30 Remy LL, Byers VS, O'Connor R, Clay T (2015) Reproductive Effects of Domestic Exposure to Hexavalent Chromium on the Population in Willits, CA. Gordon Invitational Conference August 2015.