

**AIR FORCE HEALTH STUDY
(PROJECT RANGE HAND II)**

**AN EPIDEMIOLOGIC INVESTIGATION OF HEALTH
EFFECTS IN AIR FORCE PERSONNEL FOLLOWING
EXPOSURE TO HERBICIDES**

BASELINE MORBIDITY STUDY RESULTS

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FINAL RANCH HAND REPORT

ONGOING REFINEMENTS

- HOUSEKEEPING: TYPOS, GLOSSARIES, ETC.
- SELECTED STATISTICAL POWER CALCULATIONS
- SELECTED RELATIVE RISKS, ODDS RATIOS, CONFIDENCE INTERVALS
- FERTILITY/REPRODUCTIVE ANALYSES USING TOTAL COMPARISON GROUP
- EXPANDED APPENDICES: DATA TABLES
- INCLUSION OF SCIENCE PANEL RECOMMENDATIONS

CARDIOVASCULAR EVALUATION SUMMARY

- PHYSICAL EXAMINATION SHOWED SIMILAR GROUP FINDINGS FOR
 - SYSTOLIC, DIASTOLIC BLOOD PRESSURES
 - ABNORMAL ECG'S
 - COMPARISON OF PAST ECG'S TO THE EXAM ECG
 - HEART SOUNDS
 - FUNDUSCOPIC ABNORMALITIES
 - CAROTID BRUITS
- AGE WAS A SIGNIFICANT COVARIATE IN ALL OF THE ABOVE PARAMETERS
- VERIFIED PAST HEART DISEASE CORRELATED WITH DETECTED ABNORMALITIES FOR SBP, DBP, AND ECG
- NO PREMATURE HEART DISEASE IN THE RANCH HANDERS
- OLDER, HEAVY SMOKING RANCH HANDER HAD MORE VERIFIED HEART DISEASE THAN EQUIVALENT COMPARISONS
- OLDER, LESS SMOKING RANCH HANDER HAD LESS VERIFIED HEART DISEASE THAN EQUIVALENT COMPARISONS

CARDIOVASCULAR EVALUATION SUMMARY

- ABNORMAL PERIPHERAL PULSES: RH > C, P = 0.05
- SUBSET ANALYSES SHOWED CORRELATION TO
 - INCREASED AGE
 - HEAVY PAST SMOKING
 - CURRENT SMOKING
 - HISTORY OF VERIFIED HEART DISEASE
- CAROTID AND FEMORAL ARTERY ABNORMALITIES, RH > C,
BUT MAY BE BIOLOGICALLY SIGNIFICANT IN VIEW OF SMALL VESSEL FINDINGS
- HERBICIDE EXPOSURE ANALYSES WERE ESSENTIALLY NEGATIVE FOR CENTRAL
AND PERIPHERAL CARDIOVASCULAR VARIABLES

DERMATOLOGIC EVALUATION SUMMARY

- **DERMATOLOGIC ASSESSMENT BY QUESTIONNAIRE SHOWED NO GROUP DIFFERENCES FOR**
 - **OCCURRENCE OF PAST ACNE**
 - **OCCURRENCE OF PAST ACNE RELATIVE TO INDIVIDUAL'S SEA TOUR**
 - **SEVERITY OR DURATION OF PAST ACNE**
 - **ANATOMIC LOCATION OF PAST ACNE SUGGESTING CHLORACNE**

DERMATOLOGIC EVALUATION SUMMARY

- **PHYSICAL EXAMINATION SHOWED**
 - **NO CLINICAL DIAGNOSES OF CHLORACNE**
 - **NO POSITIVE BIOPSIES FOR CHLORACNE**
 - **NO GROUP DIFFERENCES IN THE PREVALENCE OF THE 5 MOST COMMON DIAGNOSES**
- **THE COUNT OF DIAGNOSED SKIN ABNORMALITIES DID NOT DIFFER SIGNIFICANTLY BY HISTORICAL SUBSET (NO ACNE, ACNE < 1961, ACNE > 1961) BETWEEN GROUPS**
- **EXPOSURE INDEX ANALYSES WERE NEGATIVE**

RENAL FUNCTION SUMMARY

- BOTH GROUPS SIMILAR FOR
 - PRESENCE OF URINARY OCCULT BLOOD
 - PROTEINURIA
 - CREATININE CLEARANCE
 - BLOOD UREA NITROGEN (BUN)
 - URINE SPECIFIC GRAVITY
 - WBC'S/HPF
- AGE VERY SIGNIFICANT COVARIATE FOR BUN AND SPECIFIC GRAVITY;
BLOOD GLUCOSE SIGNIFICANT COVARIATE FOR SPECIFIC GRAVITY
- NONCOMPLIANCE TO 24-HOUR URINE COLLECTIONS SIGNIFICANTLY
HIGHER IN OLDER AGED PARTICIPANTS

RENAL FUNCTION SUMMARY

- RANCH HAND > COMPARISON ($P=0.039$) FOR HISTORY OF KIDNEY DISEASE
- CUMULATIVE ABNORMALITIES FOR BUN, CREATININE CLEARANCE, OCCULT BLOOD, WBC'S, AND PROTEIN WERE NOT CORRELATED TO A HISTORY OF PAST KIDNEY DISEASE
- HERBICIDE EXPOSURE ANALYSES WERE ESSENTIALLY NEGATIVE

MALIGNANCY

- SIGNIFICANTLY MORE POST-RVN SKIN CANCER IN THE RANCH HAND GROUP THAN IN THE ORIGINAL COMPARISONS ($p < 0.01$) WHO COMPLETED PHYSICAL EXAMINATION
 - OBSERVED DIFFERENCE ONLY BORDERLINE ($p = 0.07$) WITH ALL ORIGINAL COMPARISONS OR THE TOTAL COMPARISON GROUP
 - ANALYSES NOT FULLY ADJUSTED FOR SUN EXPOSURE (GEOGRAPHIC AREA OF RESIDENCE) AND ETHNICITY (RACE)
 - NON-MELANOMA CELL TYPE PREDOMINATES (91% RH, 93% C)
 - FACE, HEAD AND NECK PREDOMINANT DISTRIBUTION (84% RH, 80% C)
- NO SIGNIFICANT DIFFERENCE IN THE OCCURRENCE OF "SYSTEMIC" CANCER ($p = 0.68$)

MALIGNANCY (CONT'D)

- ANALYSES DEMONSTRATED ASSOCIATION BETWEEN SMOKING AND "SYSTEMIC" CANCER ($p=0.07$) AND INDUSTRIAL CHEMICAL EXPOSURE AND SKIN CANCER ($p=0.03$)
- A CLUSTER OF SEVEN GENITOURINARY CANCERS IN THE RANCH HAND GROUP. ALL OCCURRED AT YOUNGER AGE THAN THE THREE COMPARISON GROUP GENITOURINARY CANCERS
- EXPOSURE INDEX ANALYSES REVEALED NO STATISTICALLY SIGNIFICANT OR SUGGESTIVE ASSOCIATIONS BETWEEN HERBICIDE EXPOSURE AND OTHER SKIN OR "SYSTEMIC" MALIGNANCY

FERTILITY

SUMMARY OF GROUP DIFFERENCES

PHYSICAL EXAMINATION PARAMETERS

SPERM COUNT (p = 0.77)

SPERM ABNORMALITY (p = 0.71)

HISTORICAL DATA PARAMETERS

FERTILITY/INFERTILITY

NUMBER OF CONCEPTIONS (p = 0.93)

NUMBER OF CHILDLESS MARRIAGES (p = 0.33)

COUPLES WITH DESIRED NUMBER OF CHILDREN (p = 0.24)

INFERTILITY INDEX (p = 0.20)

FERTILITY INDEX (p = 0.25)

FERTILITY (CONT'D)
SUMMARY OF GROUP DIFFERENCES

CONCEPTION OUTCOMES

MISCARRIAGE	(p = 0.77)
STILLBIRTH	(p = 1.00)
INDUCED ABORTION	(p = 0.89)
LIVE BIRTH	(p = 0.95)

LIVEBIRTH OUTCOMES

LEARNING DISABILITY	(p = 0.17)
PHYSICAL HANDICAPS	(p = 0.73)
INFANT DEATH	(p = 1.0)
NEONATAL DEATH	(p = 0.18)
BIRTH DEFECTS	(p = 0.04)

FERTILITY (CONT'D)

- SIGNIFICANT GROUP DIFFERENTIALS NOTED FOR REPORTED NON-VERIFIED BIRTH DEFECTS ($p=0.04$)
 - SIGNIFICANCE LOST ($p=0.18$) WHEN SKIN ANOMALIES ARE REMOVED
- EXPOSURE ANALYSIS REVEALED SIGNIFICANCE IN OVERALL REPORTED BIRTH DEFECTS IN FLYING OFFICERS ($p=0.02$) AND FLYING ENLISTED PERSONNEL ($p=0.03$)
 - SIGNIFICANT ASSOCIATION BETWEEN INCREASING EXPOSURE AND MISCARRIAGE IN OFFICERS ($p=0.04$) PHYSICAL HANDICAPS IN OFFICERS ($p=0.05$) NEONATAL DEATH IN ENLISTED GROUND PERSONNEL ($p=0.02$)
 - DOSE RESPONSE PATTERN INCONSISTENT BETWEEN OCCUPATIONAL CATEGORIES

GENERAL HEALTH

- SIGNIFICANT GROUP DIFFERENCES FOUND IN SELF-PERCEPTION OF HEALTH ($p < .025$), WITH MORE RANCH HANDERS PERCEIVING THEMSELVES TO BE IN FAIR OR POOR HEALTH
 - NOT SUPPORTED BY EXPOSURE INDEX ANALYSES
- BORDERLINE SIGNIFICANT GROUP DIFFERENCE ($p=0.056$) IN THE EXAMINER'S ASSESSMENT OF ILLNESS OR DISTRESS ($RH > C$)
 - UNSUPPORTED BY THE EXPOSURE INDEX ANALYSIS
- NO SIGNIFICANT GROUP DIFFERENCE IN PERCENT BODY FAT OR HEMATOCRIT
- SIGNIFICANTLY MORE INDIVIDUALS WITH SEDIMENTATION RATE ABNORMALITIES IN THE YOUNGER (≤ 40) COMPARISONS (4.2%) THAN IN THE RANCH HANDERS (0.5%)
 - NO OVERALL DIFFERENCES OBSERVED ($p=0.25$)

NEUROLOGICAL

- NO SIGNIFICANT GROUP DIFFERENCES IN CRANIAL NERVE FUNCTION
- EXCEPT FOR A BORDERLINE DIFFERENCE IN BABINSKI REFLEX ($p=.10$), NO SIGNIFICANT GROUP DIFFERENCES IN TESTS OF PERIPHERAL NERVES
 - ASSOCIATIONS BETWEEN GLUCOSE AND ALCOHOL AND PERIPHERAL NERVE FUNCTION ABNORMALITY IDENTIFIED
- NO SIGNIFICANT GROUP DIFFERENCES IN NERVE CONDUCTION VELOCITY
- NO GROUP DIFFERENCES IN CENTRAL FUNCTION (TREMOR, COORDINATION, ROMBERG, GAIT)
 - TREMOR AND BALANCE ASSOCIATED WITH GLUCOSE AND ALCOHOL

NEUROLOGICAL (CONT'D)

- NO CONSISTENT DOSE RESPONSE ASSOCIATIONS IN NERVE CONDUCTION VELOCITY OR CRANIAL NERVE FUNCTION
- NO SIGNIFICANT ASSOCIATION BETWEEN PERIPHERAL OR CENTRAL FUNCTION AND HERBICIDE EXPOSURE LEVELS

PSYCHOLOGY

- ANALYSES STRATIFIED BY EDUCATION
 - EFFECT OF EDUCATION ON PSYCHOLOGICAL TESTING IS SUBSTANTIAL
 - MAY REFLECT HIGHER LEVEL OF PSYCHOLOGICAL DEFENSES AMONG COLLEGE EDUCATED INDIVIDUALS OR DIFFERENTIAL IMPACT OF MEDIA INTEREST
- SUBJECTIVE MEASURES (SELF-REPORTED PROBLEMS AND CORNELL INDEX) SHOWED SIGNIFICANT GROUP DIFFERENCES FOR HIGH SCHOOL EDUCATED PERSONNEL (FATIGUE, ANGER, EROSION, ANXIETY, CORNELL INDEX)
 - NOT OBSERVED IN THE COLLEGE EDUCATED INDIVIDUALS
 - DEPRESSION NOT SIGNIFICANTLY DIFFERENT BETWEEN GROUPS
 - SIGNIFICANT GROUP DIFFERENCES IN ISOLATION NOTED ($P < 0.01$) AFTER ADJUSTMENT FOR EDUCATION

PSYCHOLOGY (CONT'D)

- MMPI REVEALED SIGNIFICANT DIFFERENCES IN DENIAL (K SCALE) HYPOCHONDRIA, MASCULINITY/FEMININITY, MANIA/HYPOMANIA, AND SOCIAL INTROVERSION FOR HIGH SCHOOL EDUCATED PERSONNEL
 - COLLEGE LEVEL INDIVIDUALS ONLY DIFFERED IN THE INTROVERSION SCALE
 - LOG LINEAR ANALYSIS ADJUSTED FOR EDUCATION REVEALED SIGNIFICANT DIFFERENCES IN THE HYPOCHONDRIA, DEPRESSION, HYSTERIA, AND SCHIZOPHRENIA SCALES
- NO SIGNIFICANT GROUP DIFFERENCES IN HALSTEAD-REITAN OR IQ
- EXPOSURE INDEX ANALYSES: CORNELL INDEX NS
MMPI — NO CONSISTENT FINDINGS
- THE QUESTIONNAIRE, MMPI AND CORNELL INDEX RESULTS AMONG THE HIGH SCHOOL GROUPS COULD BE HERBICIDE RELATED, BUT COULD ALSO BE THE RESULT OF "MEDIA BIAS", POST-VIETNAM STRESS, OR DIFFERENTIAL REPORTING

PULMONARY FUNCTION AND DISEASE

- NO GROUP DIFFERENCES IN REPORTED DISEASE, FORCED VITAL CAPACITY, FORCES EXPIRATORY VOLUME (1 SECOND) OR FEV_1 /FVC RATIO
- NO CONSISTENT ASSOCIATIONS BETWEEN PULMONARY FUNCTION AND EXPOSURE LEVELS. SEVERAL AGE/SMOKING/EXPOSURE LEVEL INTERACTIONS OBSERVED BUT INCONSISTENT IN NATURE
- NO INDICATION THAT CURRENT PULMONARY FUNCTION WAS AFFECTED BY EXPOSURE TO HERBICIDES DURING THE VIETNAM WAR

EVALUATION OF HEPATIC STATUS

- OVERALL GROUP DIFFERENCES:

GGPT (RH > C), LDH (RH > C), CHOLESTEROL (RH < C)

- NO OVERALL GROUP DIFFERENCES:

SGOT, SGPT, ALK. PHOS. T. BILI, D. BILI, TRIGLYCERIDES, UROPORPHYRIN, COPROPORPHYRIN, D-ALA

- SIGNIFICANT INTERACTIONS:

SGOT * ALCOHOL * GROUP *

LDH * ALCOHOL * GROUP * 2

SGPT * INDUSTRIAL CHEM. * GROUP

LDH * DEGREASING CHEM. * GROUP

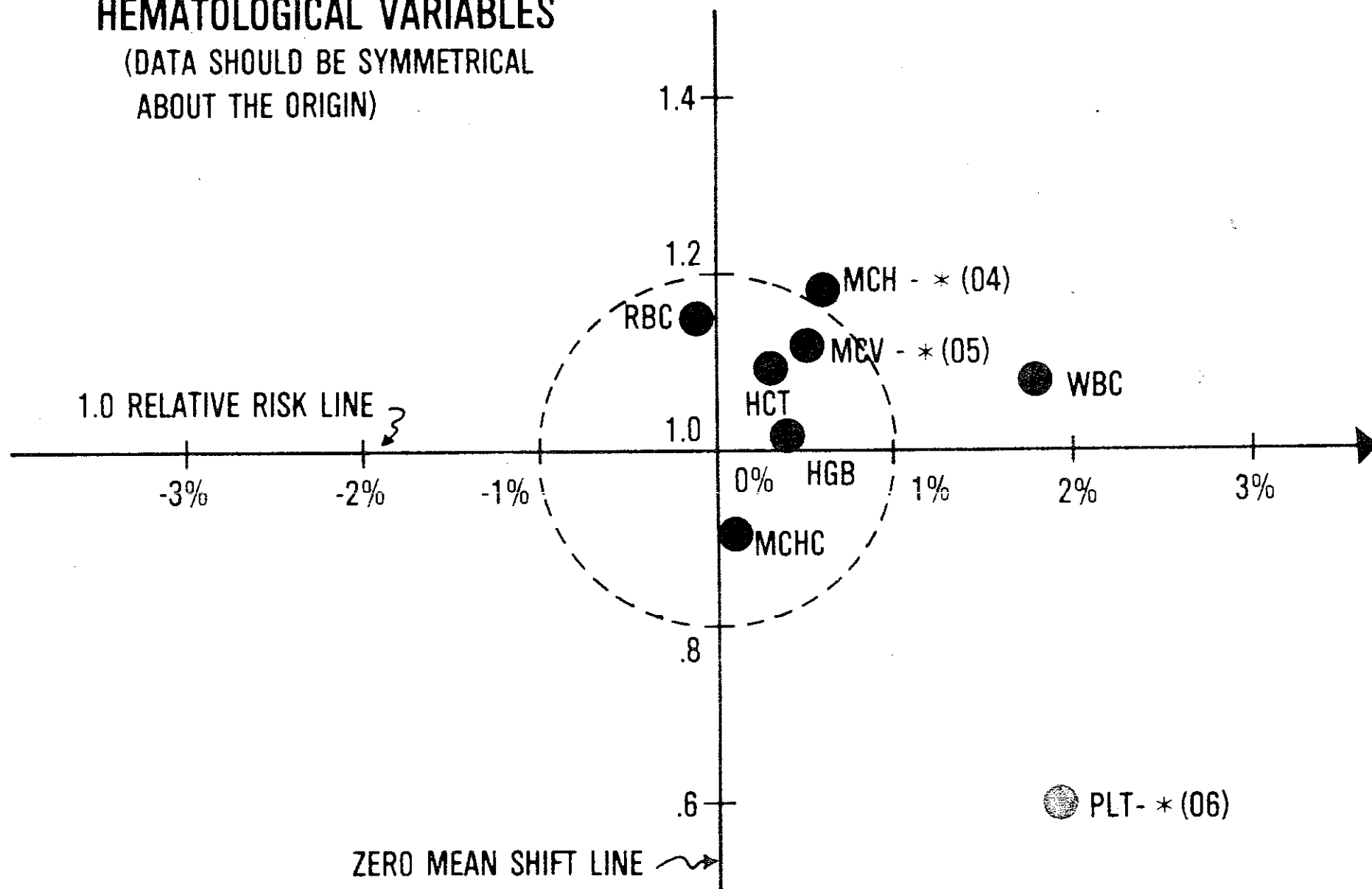
- NO EXPOSURE INDEX REGRESSIONS

EVALUATION OF HEPATIC STATUS

- HEPATOMEGALEY: 1.56% vs 0.78% (p 0.138)
- NONSPECIFIC LIVER DISORDERS: 1.53% vs 0.39% (p=0.004)
- SKIN PATCHES, BRUISES, SENSITIVITY: 44.2% vs 36.0% (p < 0.001)
- NO EXPOSURE INDEX REGRESSIONS

HEMATOLOGICAL VARIABLES

(DATA SHOULD BE SYMMETRICAL
ABOUT THE ORIGIN)



ENDOCRINE STATUS

- T3 }
T4 } RH > C
FTI }
- GLUCOSE 2 HR } RH NOT STATISTICALLY DIFFERENT FROM C
OVERALL, BUT GROUP BY AGE INTERACTION.
- TESTOSTERONE } RH = 637 ng/dl (P=0.06)
C = 652 ng/dl
- EXPOSURE INDEX REGRESSIONS DO NOT REINFORCE GROUP DIFFERENCES.

IMMUNOLOGICAL CELL COUNTS (THOUSANDS/mm³)
AND PERCENTAGES (%)

	<u>RH</u>	<u>COMP</u>
T11	1.29 (65.7%)	1.33 (65.0%)
T3	1.29 (65.1%)	1.36 (65.6%)
T4	0.85 (43.1%)	0.88 (42.1%)
T8	0.61 (30.8%)	0.66 (32.0%)
T4/T8	1.65 (NA)	1.54 (NA)
B1	0.10 (5.4%)	0.12 (5.8%)
LYMPHS	1.92 (NA)	2.00 (NA)

T AND B CELL FUNCTIONAL STUDIES
BY GROUP WITH P VALUES FOR TESTS BETWEEN GROUP MEANS

<u>VARIABLE</u>	<u>RH</u>	<u>COMP</u>	<u>P VALUE</u>
CONTROL 1	535	652	0.031
CON A	54637	57454	0.310 *
PHA	80433	83808	0.370 *
CONTROL 2	480	523	0.310
PW	33710	32092	0.370
TT	7051	6848	0.860

* STATISTICALLY SIGNIFICANT ALCOHOL BY GROUP DIFFERENCES

INDIVIDUAL HEALTH SUMMARY

- BOTH GROUPS SIMILAR IN
 - RISK TAKING ACTIVITIES (6)
 - RELIGIOUS PREFERENCE
 - EDUCATION
 - PERSONAL AND FAMILY INCOME
 - MILITARY STATUS
 - REPORTED INJURIES AND POISONINGS
 - CURRENT USE OF ALCOHOL
 - PAST HISTORY OF CIGARETTE, PIPE, CIGAR, AND MARIJUANA USAGE
- MORE RANCH HANDERS CURRENTLY SMOKE THAN COMPARISONS

INDIVIDUAL HEALTH SUMMARY

- NUMBER OF ABNORMALITIES BY ORGAN SYSTEM SHOWED SIGNIFICANCE FOR MALIGNANCY ($RH > C$, $P=0.01$) AND PULMONARY FUNCTION ($C > RH$, $P=0.05$)
- THE DISTRIBUTION OF IDENTIFIED ABNORMALITIES PER PERSON BY GROUP, AND A WEIGHTED SCORE OF THESE ABNORMALITIES, SHOWED NO DIFFERENCE BETWEEN GROUPS

CONCLUSIONS

- THE ASSERTION OF AN OVERALL HERBICIDE — HEALTH EFFECT CAUSE AND EFFECT RELATIONSHIP MUST CONSIDER
 - AGGREGATION OF ADVERSE ASSOCIATIONS IN THE RANCH HAND GROUP
 - SUBJECTIVE VERSUS OBJECTIVE FINDINGS
 - LACK OF DIAGNOSED STS, PCT, AND CHLORACNE
 - CLINICALLY IRRELEVANT OR QUESTIONABLE GROUP DIFFERENCES
 - PREDOMINANTLY NEGATIVE DOSE - RESPONSE RELATIONSHIPS
 - POTENTIAL SELECTION AND PARTICIPATION BIASES
 - LATENCY
 - "NEGATIVE" BASELINE MORTALITY STUDY
- THE RANCH HAND BASELINE MORBIDITY STUDY IS NOT NEGATIVE, NOR IS SUPPORTIVE OF AN HERBICIDE EFFECT. THE STUDY HAS DISCLOSED NUMEROUS FINDINGS THAT MERIT FOLLOW-UP IN ACCORDANCE WITH THE STUDY PROTOCOL.