Disposition of the Air Force Health Study

Committee on the Disposition of the Air Force Health Study

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C

Epidemiologic Studies of Vietnam Veterans Health

Table C-1 provides an overview of design aspects of the epidemiologic studies related to Vietnam veterans' health reviewed in the Institute of Medicine's Veterans and Agent Orange report series (IOM, 1994, 1996, 1999, 2001, 2003, 2005). The summaries include the study's design type, the numbers of subjects in the study and comparison populations, and a synopsis of how subjects were selected, how data were collected, what inclusion criteria were used, and how exposure was determined. The table was excerpted from Appendix A of the *Veterans and Agent Orange: Update 2004* report. More information on these studies may be found in the reports referenced.

TABLE C-1 Epidemiologic Studies of Vietnam Veterans

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
UNITED STATES STUDIES				
AFHS Studies Reviewed in *Update 2004*				
Akhtar et al., 2004	Cohort	Follow-up to Ketchum et al. (1999), comparing cancer incidence among Ranch Hands with Vietnam veterans who served in Southeast Asia but did not spray herbicides and with U.S. national cancer rates	1,189 net Ranch Hands for external analysis; 1,009 net Ranch Hands for internal analysis	1,776 net comparison subjects for external analysis; 1,429 net comparison subjects for internal analysis
Barrett et al., 2003	Cohort	Serum TCDD measurement and psychological functioning among Ranch Hand veterans	1,109	1,493
Michalek et al., 2003	Cohort	Correlation for TCDD elimination and Ranch Hands with diabetes	343	No comparison group
Pavuk et al., 2003	Cohort	Study to examine the relationship between serum TCDD and thyroid function in Ranch Hand veterans	1,009	1,429
AFHS Studies Reviewed in *Update 2002*				
Barrett et al., 2001	Cohort	Based on tests of cognitive functioning in 1982 and dioxin concentrations measured in 1987 and 1992, analyzed association between serum dioxin levels and cognitive functioning	937 Ranch Hands	1,052 Ranch Hand comparisons

Michalek et al., 2001a	Cohort	Based on physical examination through 1992 and medical records reviewed through March 1993, association between serum dioxin levels and hepatic abnormality	1,109 Ranch Hands	1,493 Ranch Hand comparisons
Michalek et al., 2001b	Cohort	Based on physical examination in 1982, 1985, 1987, 1992, and 1997, and medical records through 1997, association between serum dioxin and peripheral neuropathy	761 Ranch Hands	1,086 Ranch Hand comparisons
Michalek et al., 2001c	Cohort	Based on physical examination in 1982, 1985, 1987, and 1992, and medical records through 1997, association between serum dioxin and hematologic function	953 Ranch Hands	1,280 Ranch Hand comparisons
Steenland et al., 2001	Cohort	Reexamine and compare diabetes data from the NIOSH cohort and the United States Air Force (USAF) Ranch Hands in order to reconcile differences between the two study methods and protocols	267 NIOSH workers; 990 Ranch Hands	227 NIOSH comparisons 1,275 Ranch Hand comparisons
AFHS Studies Reviewed in *Update 2000*				
AFHS, 2000	Cohort	266 health-related endpoints, including assessments of 10 clinical areas: general health, neoplasia, neurologic, psychologic, gastrointestinal, cardiovascular, hematologic, endocrine, immunologic, pulmonary	995	1,299
Longnecker and Michalek, 2000	Cohort	Based on physical examination and medical records review through 1992, association between serum dioxin and diabetes mellitus among comparison group (no Ranch Hands)	—	1,197
Ketchum et al., 1999	Cohort	Based on physical examination and medical records review through 1992, association between serum dioxin and cancer, skin cancer, cancer other than skin cancer	980 Ranch Hands	1,275 Ranch Hand comparisons
Michalek et al., 1999a	Cohort	Further elucidate relationship between dioxin and diabetes mellitus, effect of dioxin body burden on sex-hormone-binding globulin and insulin and fasting glucose	871 Ranch Hands	1,121 Ranch Hand comparisons

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TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
Michalek et al., 1999b	Cohort	Based on physical examinations in 1982, 1985, 1987, and 1992, immunologic response and exposure to dioxin among Ranch Hand and comparison cohorts	914 Ranch Hands 372 (lymphocyte counts conducted)	1,186 Ranch Hand comparisons 491 (lymphocyte counts conducted)
Burton et al., 1998	Cohort	Based on physical examination and medical record review through 1992, association between serum dioxin and occurrence and timing (relative to Southeast Asia service) of chloracne and acne	930 Ranch Hands	1,200 Ranch Hand comparisons
Michalek et al., 1998b	Cohort	Updates, all-cause and cause-specific post-service mortality (through 1993) among veterans of Operation Ranch Hand, using standardized mortality ratios	1,261 Ranch Hands	19,080 Ranch Hand comparisons
Michalek et al., 1998c	Cohort	Prospective study, exposure and long-term health, survival, reproductive outcome	1,208 veterans; 903 offspring	1,549 veterans; 1,254 offspring
Michalek et al., 1998d	Cohort	Third report in a series investigating dioxin body burden and preterm birth, intrauterine growth retardation, infant death among offspring of Ranch Hand veterans	859	1,223
AFHS Studies Reviewed in *Update 1998*				
Michalek et al., 1998a	Cohort	Paternal serum dioxin levels and infant death among Ranch Hand offspring	859 children: 323 background exposure; 267 low exposure; 269 high exposure	1,223 children

Henriksen et al., 1997	Cohort	Relationship between serum dioxin and glucose, insulin, and diabetes mellitus in Ranch Hands through 1992	989	1,276
AFHS, 1996; Michalek et al., 1998b	Cohort	Mortality update, Ranch Hands through the end of 1993 in the AFHS cohort (1983, 1984b, 1985, 1986, 1989, 1991a, 1995)	1,261	19,080
Henriksen et al., 1996	Cohort	Serum dioxin and reproductive hormones in Ranch Hands, 1982, 1985, 1987, and 1992	1,045 participants (1982); 474 provided semen	1,224 participants (1982); 532 provided semen
AFHS Studies Reviewed in *Update 1996*				
AFHS, 1995	Cohort	Mortality updates of Ranch Hands who sprayed herbicides in Vietnam, compared with USAF C-130 air and ground crew veterans in Southeast Asia who did not spray herbicides	1,261, original cohort	19,101, original cohort
Wolfe et al., 1995	Cohort	Paternal serum dioxin and reproductive outcomes of Ranch Hand veterans, compared with USAF veterans from Southeast Asia who did not spray herbicides	932	1,202
AFHS Studies Reviewed in *VAO*				
AFHS, 1992	Cohort	Reproductive outcomes of AFHS participants	791	942
AFHS, 1984a, 1987, 1990, 1991b	Cohort	Baseline morbidity, follow-up examination results	1,208 baseline	1,668 baseline

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TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
AFHS, 1983, 1984b, 1985, 1986, 1989, 1991a	Cohort	Mortality updates, Ranch Hands who sprayed herbicides in Vietnam, compared with USAF C-130 air and ground crew veterans in Southeast Asia who did not spray herbicides	1,261 (original cohort)	19,101 (original cohort)
Michalek et al., 1990	Cohort	Mortality of Ranch Hands, compared with USAF C-130 air and ground crew veterans in Southeast Asia	1,261	19,101
Wolfe et al., 1990	Cohort	Health status of Ranch Hands at second follow-up, compared with USAF C-130 air and ground crew veterans in Southeast Asia	995	1,299
Centers for Disease Control and Prevention Studies Reviewed in *VAO*				
Decoufle et al., 1992	Cohort	Association between self-reported health outcomes and perception of exposure to herbicides based on Vietnam Experience Study	7,924	7,364
O'Brien et al., 1991	Cohort	Interview report and mortality for NHL based on Vietnam Experience Study	8,170	7,564
CDC, 1990a	Case-control	Selected Cancers Study: population-based case-control study of all men born 1921–1953; cases diagnosed area covered by eight cancer registries, controls selected by random-digit dialing	1,157 NHL; 342 STS; 310 HD; 48 nasal carcinoma; 80 nasopharyngeal carcinoma; 130 primary liver cancer	1,776

CDC, 1990b	Case-control	Selected Cancers Study: population-based case-control study of all men born 1921–1953; cases diagnosed in area covered by eight cancer registries, controls selected by random-digit dialing for NHL	1,157	1,776
CDC, 1990c	Case-control	Selected Cancers Study: STS	342	1,776
CDC, 1990d	Case-control	Selected Cancers Study: HD, nasal cancer, nasopharyngeal cancer, primary liver cancer	310 HD; 48 nasal carcinoma; 80 nasopharyngeal carcinoma; 130 primary liver cancer	1,776
CDC, 1989b	Cohort	Vietnam Experience Study: random sample, U.S. Army enlisted men, 1965–1971	2,490	1,972
CDC, 1988a	Cohort	Vietnam Experience Study: random sample, U.S. Army enlisted men, 1965–1971, psychosocial outcomes	2,490	1,972
CDC, 1988b	Cohort	Vietnam Experience Study: physical health outcomes	2,490	1,972
CDC, 1988c	Cohort	Vietnam Experience Study: reproductive outcomes	12,788 children	11,910 children
CDC, 1987; Boyle et al., 1987	Cohort	Vietnam Experience Study: mortality	9,324	8,989
Erickson et al., 1984 a,b	Case-control	CDC birth defects study, children born in the Atlanta, Georgia, area 1968–1980, comparing paternal Vietnam experience and potential Agent Orange exposure for birth defects cases and normal controls	7,133	4,246

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TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
Department of Veterans Affairs Studies Reviewed in *Update 2002*				
Kang et al., 2001	Cohort	Health of Army Chemical Corps Vietnam veterans, compared with Army Chemical Corps veterans who did not serve in Vietnam	2,872	2,737
Kang et al., 2000a	Cohort	Self-report pregnancy outcomes for female Vietnam veterans, compared with contemporary veterans not deployed to Vietnam; odds ratios calculated for reproductive history and various birth defects	3,392 women; 1,665 women with indexed pregnancy	3,038 women; 1,912 women with indexed pregnancy
Kang et al., 2000b	Cohort	Gynecologic cancers among female Vietnam veterans, compared with veteran controls	484	5,946
Department of Veterans Affairs Studies Reviewed in *Update 1998*				
Dalager and Kang, 1997	Cohort	Morbidity and mortality experience (1968–1987), Army Chemical Corps Vietnam veterans, compared with U.S. men; extension of Thomas and Kang (1990)	2,872	2,737
Mahan et al., 1997	Case-control	Lung cancer among Vietnam veterans (1983–1990)	329	269 111
McKinney et al., 1997	Cross-sectional	Tobacco use in veterans and nonveterans by 1987 NMES	15,000	—
Bullman and Kang, 1996	Cohort	Mortality of veterans with nonlethal (combat and noncombat) wounds sustained during the Vietnam war	34,534	—
Watanabe and Kang, 1996	Cohort	Mortality experience (1965–1988) of Army and Marine Corps Vietnam veterans; extension of Breslin et al. (1988) and Watanabe et al. (1991)	33,833	36,797

Dalager et al., 1995b	Case-control	HD cases diagnosed 1969–1985 among Vietnam-era veterans	283	404
Watanabe and Kang, 1995	Cohort	Postservice mortality among Marine Vietnam veterans	10,716	9,346
Department of Veterans Affairs Studies Reviewed in *Update 1996*				
Dalager et al., 1995a	Cohort	Update of Thomas et al. (1991) through Dec. 31, 1995	4,586	5,325
Bullman et al., 1994	Case-control	Association between testicular cancer and surrogate measures of exposure to Agent Orange in male Vietnam veterans	97	311
Department of Veterans Affairs Studies Reviewed in *VAO*				
Bullman et al., 1991	Case-control	PTSD cases in Vietnam veterans, compared with Vietnam veterans without PTSD, for association with traumatic combat experience	374	373
Dalager et al., 1991	Case-control	NHL cases diagnosed 1969–1985 among Vietnam-era veterans, compared with cases of other malignancies among Vietnam-era veterans, for association with Vietnam service	201	358
Eisen et al., 1991	Cohort	Health effects in male monozygotic twins serving in the armed forces during Vietnam era (1965–1975)	2,260	2,260
Thomas et al., 1991	Cohort	Mortality experience (1973–1987) among female Vietnam veterans, compared with female non-Vietnam veterans and for each cohort compared with U.S. women	4,582	5,324

continues

TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
Watanabe et al., 1991	Cohort	Mortality experience (1965–1984) in Army and Marine Corps Vietnam veterans, compared with: (1) branch-specific (Army and Marine) Vietnam-era veterans, (2) all Vietnam-era veterans combined, (3) the U.S. male population	24,145 Army 5,501 Marines	(1) 27,145 Army 4,505 Marines (2) 32,422 combined Vietnam era (3) U.S. male population
Bullman et al., 1990	Cohort	Mortality experience in Army I Corps Vietnam veterans, compared with Army Vietnam-era veterans	6,668 deaths	27,917 deaths
Farberow et al., 1990	Case-control	Psychological profiles, military factors associated with suicide and MVA fatalities in Los Angeles County Vietnam-era veterans (1977–1982)	22 Vietnam suicides; 19 Vietnam-era suicides	21 Vietnam MVA; 20 Vietnam-era MVA
Thomas and Kang, 1990	Cohort	Morbidity and mortality experience (1968–1987) in Army Chemical Corps Vietnam veterans compared with U.S. men	894	—
True et al., 1988	Cross-sectional	PTSD and Vietnam combat experience among Vietnam-era veterans	775	1,012
Breslin et al., 1988; Burt et al., 1987	Cohort	Mortality experience (1965–1982) in Army and Marine Corps Vietnam veterans, compared with Vietnam-era veterans who did not serve in Southeast Asia, standardized by age and race; nested NHL case-control study	24,235	26,685

Kang et al., 1987	Case-control	STS cases (1975–1980) diagnosed at the Armed Forces Institute of Pathology (AFIP), compared with controls identified from patient logs of referring pathologists or their departments, for association with Vietnam service and likelihood of Agent Orange exposure	217	599
Kang et al., 1986	Case-control	STS (1969–1983) in Vietnam-era veterans, for association with branch of Vietnam service as a surrogate for Agent Orange exposure	234	13,496
American Legion Studies Reviewed in *VAO*				
Snow et al., 1988	Cohort	PTSD in association with traumatic combat experience among American Legion members serving in Southeast Asia (1961–1975)	2,858	Study group subdivided for internal comparison
Stellman et al., 1988a	Cohort	Physical health, reproductive outcomes among American Legion members who served in Southeast Asia (1961–1975), for association with combat and herbicide exposure	2,858	3,933
Stellman et al., 1988b	Cohort	Social, behavioral outcomes among American Legion members who served in Southeast Asia (1961–1975), association with combat and herbicide exposure	2,858	3,933
State Studies Reviewed in *Update 1998*				
Clapp, 1997	Case-control	Selected cancers identified (1988–1993) among Massachusetts Vietnam veterans, compared with Massachusetts Vietnam-era veterans with cancers of other sites; update of Clapp et al., 1991	245	999
State Studies Reviewed in *Update 1996*				
Visintainer et al., 1995	Cohort	Mortality experience (1965–1971) in male Michigan Vietnam veterans, compared with non-Vietnam veterans from Michigan	3,364 deaths	5,229 deaths

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TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
State Studies Reviewed in *VAO*				
Fiedler and Gochfeld, 1992; Kahn et al., 1992a,b,c	Cohort	New Jersey: outcomes in select group of herbicide-exposed Army, Marine, and Navy Vietnam veterans, compared with veterans self-reported as unexposed	10 Pointman I 55 Pointman II	17 Pointman I 15 Pointman II
Clapp et al., 1991	Case-control	Massachusetts: selected cancers identified (1982–1988) among Vietnam veterans, compared with Massachusetts Vietnam-era veterans with cancers of other sites	214	727
Deprez et al., 1991	Descriptive	Maine: Vietnam veterans, compared with atomic test veterans and general population, for health status and reproductive outcomes	249	113 atomic test veterans
Levy, 1988	Cross-sectional	Massachusetts: PTSD in chloracne as indicator of exposure to TCDD; control Vietnam veterans	6	25
Anderson et al., 1986a	Cohort	Wisconsin: mortality experience, veterans compared with nonveterans (Phase 1); mortality experience of Vietnam veterans and Vietnam-era veterans, compared with nonveterans and other veterans (Phase 2)	110,815 white male veteran deaths; 2,494 white male Vietnam-era veteran deaths; 923 white male Vietnam veteran deaths	342,654 white male non-veteran deaths; 109,225 white male other veteran deaths

Anderson et al., 1986b	Cohort	Wisconsin: mortality experience in Vietnam-era veterans and Vietnam veterans, compared with U.S. men, Wisconsin men, Wisconsin nonveterans, and Wisconsin other veterans	122,238 Vietnam-era veterans; 43,398 Vietnam veterans	—
Goun and Kuller, 1986	Case-control	Pennsylvania: STS, NHL, selected rare cancer cases, compared with controls without cancer for Vietnam experience in men (1968–1983)	349	349 deceased
Holmes et al., 1986	Cohort	West Virginia: mortality experience (1968–1983) of veterans, Vietnam veterans, Vietnam-era veterans, compared with nonveterans; Vietnam veterans compared with Vietnam-era veterans	615 Vietnam veterans; 610 Vietnam-era veterans	—
Pollei et al., 1986	Cohort	New Mexico: chest radiographs of Agent Orange Registry Vietnam veterans, compared with radiographs of control USAF servicemen, for pulmonary and cardiovascular pathology	422	105
Kogan and Clapp, 1985, 1988	Cohort	Massachusetts: mortality experience (1972–1983) among white male Vietnam veterans, compared with non-Vietnam veterans and all other nonveteran white males in Massachusetts	840 deaths	2,515 deaths in Vietnam-era veterans
Lawrence et al., 1985	Cohort	New York: mortality experience in (1) Vietnam-era veterans, compared with nonveterans and (2) Vietnam veterans, compared with Vietnam-era veterans	(1) 4,558 (2) 555	17,936 941
Rellahan, 1985	Cohort	Hawaii: health outcomes in Vietnam-era (1962–1972) veterans residing in Hawaii, associated with Vietnam experience	232	186
Wendt, 1985	Descriptive	Iowa: health effects and potential exposure to Agent Orange among veterans who served in Southeast Asia	10,846	None

continues

TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
Greenwald et al., 1984	Case-control	New York: STS cases, compared with controls without cancer for Vietnam service and herbicide exposure including Agent Orange, dioxin, or 2,4,5-T	281	281 live controls; 130 deceased controls
Newell, 1984	Cross-sectional	Texas: preliminary (1) cytogenetic, (2) sperm, (3) immune response tests in Vietnam veterans, compared with controls	(1) 30; (2) 32; (3) 66	(1) 30; (2) 32; (3) 66
Other U.S. Veterans Studies Reviewed in *VAO*				
Tarone et al., 1991	Case-control	Testicular cancer (18–42 years old) cases, January 1976–June 1981, compared with hospital controls, for association with Vietnam service	137	130
Aschengrau and Monson, 1990	Case-control	Cases with late adverse pregnancy outcomes compared with normal control births, for association with paternal Vietnam service (1977–1980)	857 congenital anomalies 61 stillbirths; 48 neonatal deaths	998
Goldberg et al., 1990	Cohort	Male twin pairs who served in Vietnam era (1965–1975), for association between Vietnam service and PTSD	2,092	2,092
Aschengrau and Monson, 1989	Case-control	Association between husband's military service and spontaneous abortion at or by 27 weeks, compared with women delivering at 37 weeks	201	1,119

AUSTRALIAN VETERANS STUDIES

Australian Studies Reviewed in *Update 2000*

AIHW, 1999	Cohort	Validation of the male veterans study (CDVA, 1998a) by medical documents, doctors' certification, records on a disease or death registry	6,842	—
CDVA, 1998a	Cohort	Self-reported data on male members of the Australian Defence Force and the Citizen Military Force who landed in Vietnam or entered Vietnamese water. Questions on physical (including reproductive history) and mental health, and that of their partner(s) and children	49,944 mailed; 39,955 responded	—
CDVA, 1998b	Cohort	Self-reported data on female members of the Australian Defence Force and the Citizen Military Force who landed in Vietnam or entered Vietnamese water. Questions on physical (including reproductive history) and mental health, and that of their partner(s) and children	278 mailed 225 responded	—

Australian Studies Reviewed in *Update 1998*

Crane et al., 1997a	Cohort	Mortality experience (through 1994) of Australian veterans who served in Vietnam	59,036 men 484 women	—
Crane et al., 1997b	Cohort	Mortality experience (through 1994) of Australian national servicemen who served in Vietnam	18,949	24,646
O'Toole et al., 1996a,b,c	Cross-sectional	Survey of self-reported health status (1989–1990) of Australian Army Vietnam veterans	641	—

Australian Studies Reviewed in *VAO*

Field and Kerr, 1988	Cohort	Tasmanian Vietnam veterans, compared with neighborhood controls for adverse reproductive and childhood health outcomes	357	281

continues

TABLE C-1 *Continued*

Reference	Study Design	Description	Study Group (*N*)	Comparison Group (*N*)*
Fett et al., 1987a	Cohort	Mortality experience in Vietnam veterans, compared with Vietnam-era veterans through 1981	19,205	25,677
Fett et al., 1987b	Cohort	Cause-specific mortality experience in Vietnam veterans, compared with Vietnam veterans through 1981	19,205	25,677
Forcier et al., 1987	Cohort	Mortality in Vietnam veterans by job classification, location, time of service	19,205	Internal comparison
Donovan et al., 1983, 1984	Case-control	Congenital anomalies in children (1969–1979), compared with infants born without anomalies, for association with paternal Vietnam service	8,517	8,517
OTHER VIETNAM VETERANS' STUDIES				
Other New Vietnam Veterans' Studies Reviewed in *Update 2004*				
Kim H-A et al., 2003	Cohort	Immunotoxicologic effects of Agent Orange exposure on Korean Vietnam veterans	51 (24 veterans–patient; 27 veterans–normal)	36
Kim J-S et al., 2003	Cross-sectional	Agent Orange exposure and Korean Vietnam veterans	1,224	154
Mo et al., 2002	Cohort	Skin and general disease patterns among Korean Vietnam veterans	332	None

Other Vietnam Veterans Studies Reviewed in *Update 1998*

Chinh et al., 1996	Cohort	Antinuclear antibodies and sperm autoantibodies among Vietnamese veterans who served 5–10 years in a "dioxin-sprayed zone"	25	63; 36

NOTE: Abbreviations: 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; AFHS, Air Force Health Study; CDC, Centers for Disease Control and Prevention; CDVA, Commonwealth Department of Veterans' Affairs (Australia); HD, Hodgkin's disease; MVA, motor vehicle accidents; NIOSH, National Institute for Occupational Safety and Health; NHL, non-Hodgkin's lymphoma; NMES, National Medical Expenditure Survey; PTSD, post-traumatic stress disorder; SMR, standardized mortality ratio; STS, soft-tissue sarcoma; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; *Update 2004, Veterans and Agent Orange: Update 2004* (IOM, 2005); *Update 2000, Veterans and Agent Orange: Update 2000* (IOM, 2001); *Update 1998, Veterans and Agent Orange: Update 1998* (IOM, 1999); *Update 1996, Veterans and Agent Orange: Update 1996* (IOM, 1996); USAF, United States Air Force; and *VAO, Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam* (IOM, 1994).

*Comparison group based on a population (e.g., U.S. white males, country rates); details are given in the text for population specifics.

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