

Occupational cohort

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Methods to identify occupational diseases

- **Case series reports**
 - bladder cancer and "aniline" dyes
 - silicosis and underground metal miners
 - scrotal cancer and young chimney sweeps
- **Routinely collected population statistics, occupation and COD**
 - mineral oil mists and laryngeal cancer

Methods to identify occupational diseases

- **Formal Epidemiologic study designs**
 - association are not strong
 - health outcomes caused by multiple factors
 - cancer and gas works, dyestuff, asbestos

Mortality studies

- **Mainly historical**
 - prolonged induction and latency periods
 - cancer, cardiovascular, neurodegenerative diseases
- **Cancer mortality**
 - the focus of many occupational cohort studies
 - high fatality rates and accuracy of death certificates
 - Occupation often considered "high dose" situation
 - Occupation is assumed to cause 5-15% of all cancers

Mortality studies

- **Pooling mortality and exposure from multiple cohorts**
 - a method of increasing statistical precision
 - small risks or associations with rare diseases
 - dioxin, low-dose ionizing radiation, man-made vitreous fiber in IARC
 - DDx with meta-analysis : to increase study and to apply uniform data analysis protocol
 - problem point : if exposure data vary across cohorts then the effects became obscured or attenuated

Established occupational carcinogens*

Agent	Source(s)	Cancer site(s)
Arsenic	Smelters, mines	Lung, skin
Asbestos	Mining, mfg. products	Lung, pleura, peritoneum
Benzidine	Dyes, textiles	bladder
Beryllium	Ceramics	Lung
Cadmium	Mining, batteries	Lung
Chromates	Paints, pigments	Lung
Dioxin	Herbicides	Multiple (promoter)
Ethylene oxide	Medical	Leukemia
Ionizing radiation (X-, gamma-rays)	Nuclear	Leukemia
Radon	Underground mines	Lung
Silica (crystalline)	Mines, pottery, etc.	Lung
Vinyl chloride	PVC mfg.	Liver

*IARC Group 1 list

Morbidity studies

- **Disease incidence, symptoms, impaired physiologic functions**
- **Traditional method in morbidity studies**
 - Cross-sectional prevalence studies
 - selection bias
- **repeated measurements**
- **Linking occupational cohorts with population-based cancer registries**
 - case identification for rare and nonfatal cancers
 - Danish stone industry, Norwegian aluminum smelter workers, Icelandic stone masons : national cancer registries

Types of outcomes in cohort morbidity studies

Induction period/ reversibility	Event (dichotomous)	Change in status (continuous)
Short(days to months)		
Reversible	Asthma attack	Cross-shift function(FEV1)
	Tendonitis	Temporal threshold hearing shift
Irreversible	Contact dermatitis	Annual change in FEV1
	Asthma diagnosis	
	Spontaneous abortion	
	Amputation	
Long(years)		
Reversible	Chronic bronchitis	Sperm count
	Endometriosis	Blood pressure
Irreversible	Carpal tunnel syndrome	
	Silicosis	Noise induced hearing loss
	Myocardial infarction	Atherosclerosis
	Infertility	Hepatic fibrosis

Types of occupational cohorts

- Workers from single facility or multiple facilities in same industry : Radiation(IARC)
- Workers from multiple industries with similar exposures : Benzene
- Members of trade or professional associations : carpenters union, MD, RN radiologists,
- Workers with specific diseases : silicotics
- Administrative cohorts : HMOs

Cause-specific mortality among 5777 male workers in the French hard-metal industry, 1968-1991*

Cause of death	Observed	Expected†	Obs/Exp
All causes	591	644.6	0.92
Circulatory diseases	139	158.3	0.88
Respiratory diseases	22	29.21	0.75
Cancers (all sites)	209	203.1	1.03
lung cancer	61	47.22	1.29
pleural cancer	3	1.39	2.16
larynx	7	12.80	0.55
esophagus cancer	19	15.30	1.24
oral cancer	23	19.51	1.18
bladder cancer	4	5.43	0.74

* Moulin, et al., Am J Epidemiol 1998; 148:241-8

† Expected based on rates for French men

Leukemia Incidence Among Chinese Workers Exposed to Benzene Compared with Non-Exposed Workers: 1972-1987*

Occupational Group	No. Cases	Relative Risk
Non-exposed	9	1.0
Exposed		
-Coatings	17	2.2
-Rubber	1	1.3
-Chemical	7	3.6
-Shoe	4	2.5
-Other/mixed	9	2.5

* Hayes RB, et al. J Natl Cancer Inst 1997;89:1065-1071.

Breast cancer mortality relative risk among U.S. women radiologic technicians, by years certified and year first certified*

Year first certified	Number, years certified		
	<10	10-19	20-29
> 1960	1.0†	1.0	0
1950-59	1.1	1.4	1.0
1940-49	1.1	4.8	2.1
<1940	1.0	1.9	2.8
			>30
			3.5

* Doody MM, et al. Cancer Cause Control 1998;9:67-75.

† reference category

Lung Cancer Mortality Among Sillicotics Classified by Type of Industry*

Industry	Obs	Exp†	Obs/Exp
Mines	29	7.67	3.78
Foundries	33	10.85	3.04
Granite	6	2.94	2.04
Pottery	5	1.00	4.99
Other†	10	1.44	6.94

*Infante-Rivard C. et al. (1989). Lancet 2:1504-7

† Includes construction, shipyards, cables, paints, paper mills trades

‡ Based on rates in Quebec males

Census-based cohort study of occupational EMF exposure and breast cancer incidence in Norway*

Cumulative exposure (µt-yrs)	Relative risk	
	< age 50	> age 50
0.1 - 0.8	1.00†	1.00
0.9 - 1.4	1.07	1.10
1.5 - 3.0	1.09	1.30
> 3.0	1.05	1.27

*Klithiene J, et al. Am J Ind Med 1999; 36:147-54.

† Relative risk

Choice of occupational cohorts

- Research objectives
- Availability of data
- Exposure assessment
- Health outcome evaluation

Assessment of Exposure for Occupational Cohort

Exposure Assessment

“Determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure.”

DiNardi, S. (ed.). The Occupational Environment – Its Evaluation and Control. Fairfax, VA: AIHA Press, 1998, p. 1302.

Exposure Assessment

- Establish a connection between workplace exposure and health outcome
- Important in managing risk
- Qualitative association
 - employment/not employment
- Quantitative dose-response estimation : standard, risk assessment
 - detailed exposure assessment

Reconstruction of historical exposure

- A matrix of exposure level
 - cross-classified by job and time period linked to worker’s job assignment records
- Why needs?
 - workers personal exposure : not monitored throughout their period of employment
 - routine monitoring adopted in the past 20-30 years
 - Occupational hygiene measurement : test the compliance of mandated guidelines
 - In developing country : monitoring more recent and sporadic
 - qualitative and quantitative changes over time of exposure

Describing exposure

- Cumulative terms
 - PPM*years
- Exposed/not exposed
 - Potentially exposed
 - Chemicals available in workplace
- Exposure intensity
 - PPM
- Exposure scale
 - High, medium, low, no exposure

Estimating exposure

- Statistical tools – Mean, UCL
- Maximum, Peak
- Extrapolation
- Scaling factors
 - Engineering controls
 - Seniority

Measuring Exposure

- Fundamental activities of a cohort study
- Comparable for all members of the cohort
- Specific attention to the accuracy and precision of proposed measurements
 - Pilot studies often needed
- Measurement
 - Personal air sampling
 - Chart review, Interview
 - Blood tests or other specimens : Biomarkers
 - Other laboratory tests
 - radiographic evidence of pulmonary fibrosis
 - Sample storage : blood, hair

Study Biases

- Healthy worker effect
- Exposure misclassification
- Confounding

Healthy worker effect

- Typically cardiovascular and other nonmalignant diseases
- Sources in cohort mortality studies
 - The initial selection of relatively healthy individuals at time of hire and the survival of the healthiest individuals that permits long-term employment
 - The healthy worker survivor effect : tendency for the least healthy workers to leave the active workforce
 - The tendency for the least healthy workers to transfer from higher to lower exposed jobs within the same work place, when the exposure is recognized as a contributor to impaired health

Healthy worker effect

- Inappropriate choice of the general population as a reference
 - dose-response estimation : internal comparison
 - ** *uniform exposure or not accurate data*
- Minimize the healthy worker survivor effect
 - Exposure lagging
 - Restricting analyses to long-term workers
 - Stratified analyses : adjust for time since hire or active versus inactive employment
 - In prospective cohort : repeated measurement of exposure and health outcome on newly hired workers

Exposure misclassification

- Nondifferential, ordinary
 - Individual exposure is performed without knowledge of health outcome
- Differential misclassification
 - Exposure assessment more thoroughly for persons who manifest or report adverse health effects in morbidity study
- Additional information
 - A cohort mortality study of diatomaceous earth industry workers exposed to crystalline silica : qualitative index that incorporated ordinal exposure intensity rankings and duration of exposure, additional dust measurement data for earlier years of industry

Confounding

- Nonoccupational risk factors
 - Cigarette smoking, environmental air pollution
- Cigarette smoking
 - Seldom practical in mortality studies
 - Industry medical records
 - personal interviews of workers or their next-of-kin
 - To examine the patterns of all smoking-related diseases
- Hypothetical adjustments : specifying the magnitude of association between smoking and exposure
- Obtaining confounding data : more feasible in morbidity studies

Confounding

- Concurrent occupational exposure with in same industry
 - Lung cancer risk of radon and silica exposure
- Single agent from workplace and nonoccupational sources
- Poorly measured exposures to confounders
- Anticipated excess risk : small
 - Speculative criticism
 - A failure to distinguish confounding from effect modification

Occupational Cohort in Korea

Posco cohort

Posco

MH wha,

여천 화학공단 코호트

Chunnam national university

JD Moon, SG Kim,

인천 근로자 코호트

Inha university

YC Hong, SG Kim,

Korea Hydro and Nuclear Power Cohort

Radiation Health Research Institute

YW Jin, SG Kim, M Jeong, SH Sung, YK Jang,
IK Park, CH Yun, YK Lim, ES Kim, CS Kim

Two radiation exposure record system

National Dose Registry of Korea
(NDRK)

Since 1984
by the Ministry of Science and Technology

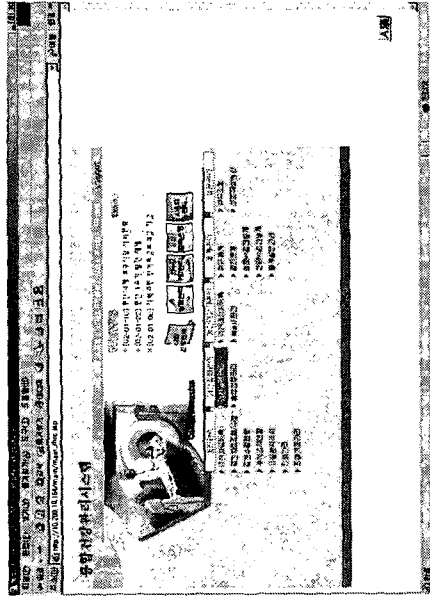
Nuclear Radiation Safety(NRS)
system

Since 1979
by Korea Hydro and Nuclear Power Co.

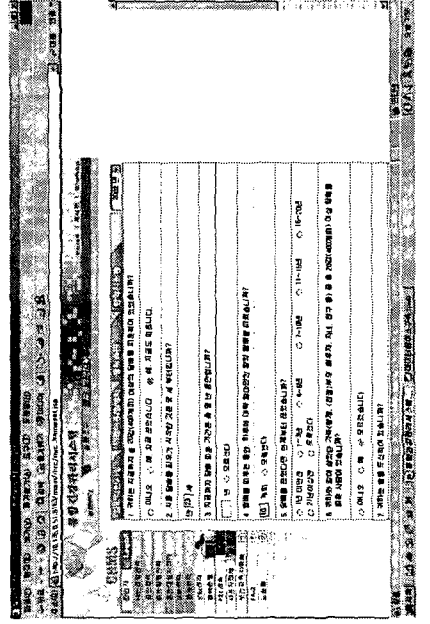
Comprehensive Health Management System (CHMS)

- Since 2000
- Annually check health status life style such as smoking, drinking, food habit, physical activity etc.
- Managed and accumulated by computerized system
- Serum and urine bank

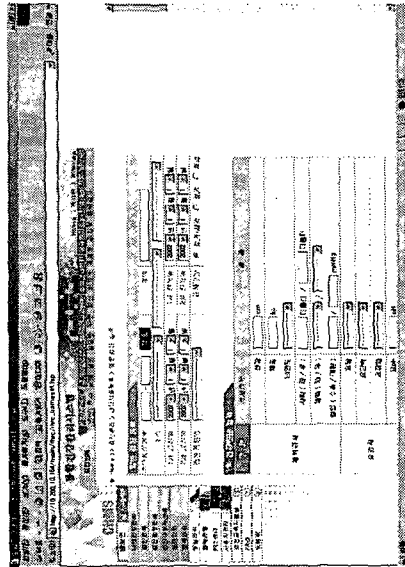
Main page of CHMS



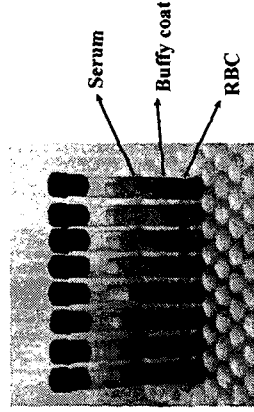
Page for questionnaire



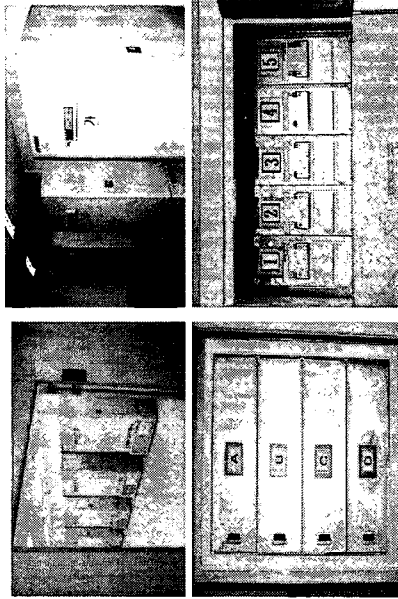
Page for clinical data



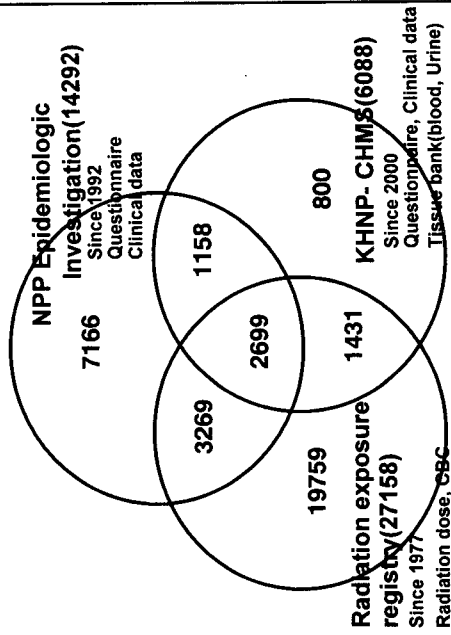
Blood Bank(I)



Blood Bank(II)



Data of RHRI



Distribution of death cases by cancer type and cumulative dose

Cause of death	Cumulative dose(mSv)						Total (7,641)
	0 (2,244)	0.1-4.99 (2,004)	5.0-9.99 (2,420)	10.0-19.99 (2,172)	20.0-49.99 (2,142)	50.0- (2,581)	
All cancers (10 person-year)	19 (64)	31 (103)	2 (7)	1 (4)	4 (16)	2 (8)	59 (204)
Non-Hodgkin's Lymphoma	2 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)
Stomach	5 (17)	7 (23)	0 (0)	0 (0)	0 (0)	0 (0)	12 (43)
Colon & rectum	2 (7)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	3 (11)
Liver	4 (13)	3 (10)	0 (0)	0 (0)	2 (8)	0 (0)	9 (31)
Pancreas	4 (13)	5 (16)	0 (0)	0 (0)	0 (0)	0 (0)	9 (31)
Lung	4 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (14)
Kidney and other retroperitoneal and soft tissue	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)
Bladder	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)
Oral cavity and pharynx	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	1 (4)
Larynx	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)
Secondary, unspecified	1 (4)	3 (10)	0 (0)	0 (0)	1 (4)	1 (4)	6 (21)
Non-cancer (10 person-year)	42 (138)	32 (103)	11 (35)	7 (22)	1 (4)	4 (13)	103 (324)
All cause of death (10 person-year)	61 (192)	73 (231)	13 (42)	8 (26)	5 (16)	6 (19)	172 (528)

*No cases of chronic myeloid leukemia

Evaluation and Discussion

- Multi-purpose cohort : Cancer, Cardiovascular etc.
- Data and specimen open to Biomedical research : review board
- Accuracy of diagnosis : review of medical record
- Cohort size : continuing recruitment and follow-up
- Control of confounding factors : questionnaire
- Changes in exposure : regular check-up
- Loss to follow-up : active and passive surveillance
- Exposure biomarkers : biologic specimen bank