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Overview of the 3M Company Study

"An Epidemiologic Analysis of Episodes of Care of
3M Decatur Chemical and Film Plant Employees, 1993-1998"

The analysis of administrative databases, including health insurance claims data, have been infrequently reported in occupational epidemiologic research studies. Often reported are the results from traditional occupational retrospective cohort mortality studies. However if the outcomes in question do not lead to mortality, then such research has limited value. Morbidity studies circumvent the mortality issue. Frequently involving self-reported questionnaires, these morbidity studies, too, have limited value unless they involve the time-intensive review and validation of the reported health outcomes through medical record review. Recently, the advent of high-speed computers and aggregation of large databases have provided increasing opportunities for another avenue of morbidity research, that of analysis of administrative databases, including health insurance claims data. As Wong stated in his recent commentary in the *Annals of Epidemiology* (see July 2001, volume 11, pages 281-284), "the increasing use of personal identifiers to record everyday transactions and health-related events and the computerization and archive of these transactions and events, the possibility of record linkage in epidemiologic research is endless. In theory at least, linking existing administrative data to health records represents a fast and inexpensive approach to data

collection. In particular, routine analyses of such data will serve as an effective tool for surveillance or hypothesis generation. However, because these databases are set up and maintained for administrative and not scientific purposes, caution must be exercised in their use and their limitation must be recognized."

The attached study entitled, "An Epidemiologic Analysis of Episodes of Care of 3M Decatur Chemical and Film Plant Employees, 1993-1998" utilizes a concept defined several decades ago, the 'episode of care' to examine an administrative health insurance claims database of 3M Decatur chemical and film plant employee and retiree records from January 1, 1993 through December 31, 1998. An episode of care is defined as a series of related health events with a beginning, an end and a course, all related to a particular health problem that exists continuously for a delineated period of time. Current commercialized computer software allows the stream of health claims data (e.g., inpatient, outpatient, pharmacy) to be examined in aggregate and categorized into episodes of care. The software code constructs an episode of a care around the index-eligible record by searching backward and forward in time for the health claims records that are related to the disease or condition on the index record. The index record consists of either procedure codes indicative of a face-to-face encounter or a pharmacy record for a delineating drug. More than 400 diseases and conditions were analyzed by the software (Clinical Care Groups™ developed by Ingenix Employer Group) used in this research study.

An important limitation of an episode of care study is the fact that the concept does not translate into well-defined epidemiologic endpoints as it may include incident cases, prevalent cases, tentatively diagnosed cases and misclassified cases that are the

routine consequence of the differential diagnoses that individuals may undergo in the course of disease diagnosis, treatment and management. Nevertheless, the episode of care concept may be a useful screening (i.e., surveillance) method for the potential risk of diseases and/or conditions that do not lead to traditional occupational epidemiologic study endpoints as stated previously.

The purpose of this episode of care study was to compare the observed to expected episodes of care experience of 652 chemical employees to the observed to expected episode of care experience of 659 film plant employees at the 3M Decatur manufacturing site. Health claims data were not available prior to 1993. Because the local medical care delivery system has a large influence on diagnoses rendered and hospitalizations incurred, this study design was able to adjust for this issue by directly comparing the Decatur chemical plant population episode of care experience to the Decatur film plant population episode of care experience. For each plant population, an expected number was calculated based on the 3M Company's U.S. employee population experience using indirect standardization techniques taking into account age, gender and calendar time period. The ratio of these two ratios (chemical plant's observed to expected experience divided by the film plant's observed to expected experience) may then be considered a relative risk ratio under certain assumptions. Employee comparison groups within the chemical plant population were defined according to their potential workplace exposure to perfluorooctane sulfonyl fluoride (POSF) fluorochemical production.

As Wong stated in his commentary (above), research studies such as this should be viewed as surveillance or hypothesis generating research endeavors. Based on a substantial body of literature including perfluorooctanesulfonate (PFOS) and

perfluorooctanoate (PFOA) toxicology and epidemiology research conducted, to date, the episodes of care that were considered *a priori* (i.e., surveillance) interests in this study were broadly defined to include liver and bladder cancer, endocrine disorders involving the thyroid gland and lipid metabolism, gastrointestinal disorders of the liver and biliary tract, and reproductive, pregnancy, congenital and perinatal disorders. In this regard, the episodes of care experience involving these outcomes was comparable between chemical and film plant employees. We did observe an association with cholelithiasis with acute cholecystitis but this was likely due to fewer expected number of episodes of care among the film plant employees rather than an excess of observed number of episodes of care among the chemical plant employees. It should be noted that other occupational epidemiologic research of medical surveillance data of the Decatur chemical plant employee population has not associated adverse clinical chemistry results with workplace exposure to POSF-based products.

As can be expected when there are more than 400 diseases and conditions analyzed in an epidemiologic study, non *a priori* associations were also observed which included colorectal cancer, benign colonic polyps and benign neoplasms of the skin. We urge considerable caution in the interpretation of these non *a priori* data as these associations were often the consequence of a few observed episodes of care reported among chemical plant employees and a fewer number of observed than expected episodes of care reported for film plant employees. Whether these non *a priori* findings have a biological rationale related to POSF-based exposure is doubtful as considerable toxicologic and epidemiologic research conducted, to date, does not provide support for these episode of care associations.

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ABSTRACT

A health care episode is defined as a series of related events with a beginning, an end, and a course, all related to a particular health problem that exists continuously for a delineated period of time. The episode of care concept does not translate into a well-defined epidemiologic endpoint as it may include incident cases, prevalent cases, tentatively diagnosed cases and misclassified cases that are the routine consequence of the differential diagnoses that individuals may undergo in the course of disease diagnosis, treatment and management. Nevertheless, the episode of care concept may be a useful screening method for the potential risk of diseases and/or conditions that do not lead to traditional occupational epidemiologic study endpoints such as mortality, or morbidity outcomes that would be difficult to assess without formal investigations involving comprehensive medical record reviews to validate the diagnoses.

The purpose of this study was to compare the observed to expected episodes of care experience of 652 chemical employees to the observed to expected episode of care experience of 659 film plant employees at the 3M Decatur manufacturing site. These employees worked between January 1, 1993 and December 31, 1998. We utilized the Clinical Care Groups™ (CCG) episode of care software developed by Ingenix Inc. to provide a comprehensive grouping of all visits (inpatient, outpatient), procedures, ancillary services and prescription drugs used in the diagnosis, treatment and management of more than 400 diseases or conditions. The software code constructs an episode of care around the index-eligible record by searching backward and forward in time for the health claims records that are related to the disease or condition on the index

record. The index record consists of either procedure codes indicative of a face-to-face encounter or a pharmacy record for a delineating drug.

Employee comparison groups were defined according to their potential workplace exposure to perfluorooctane sulfonyl fluoride (POSF) fluorochemical production. These comparison groups included those employees who only worked at the chemical or film plant, those employees who were considered to have had a high exposure job to POSF-based fluorochemicals and those employees who had worked the 10 years prior to study onset in jobs with high potential for exposure to POSF-based fluorochemicals. These POSF-based fluorochemicals may transform metabolically, to an undetermined degree, to perfluorooctanesulfonate (PFOS). Industrial hygiene and biological monitoring at the Decatur plant had shown a strong correlation between employee serum levels with PFOS and perfluorooctanoate (PFOA). At Decatur, PFOA exposures may be the result of a by-product of the electrolytic cell production, actual production of PFOA (began in 1998) or in its use as an elastomer in fluoropolymer production.

The risk ratio episode of care (RRE_pC) provided the estimate of risk between the observed to expected episodes of care experienced among chemical plant employees compared to the observed to expected episodes of care experienced among film plant employees (nonexposed). In essence, RRE_pC is a ratio of two indirect standardized ratios and is an unbiased estimator of the risk ratio if there are similar age- and gender-specific structures between the two comparison populations. The expected number of episodes of care for the chemical and film plant populations was calculated from the health claims experience of the 3M U.S. manufacturing population.

Based on a substantial body of literature including PFOS and PFOA toxicology and epidemiology research conducted, to date, the episodes of care that were considered *a priori* interests in this study included liver and bladder cancer, endocrine disorders involving the thyroid gland and lipid metabolism, gastrointestinal disorders of the liver and biliary tract, and reproductive, pregnancy, congenital and perinatal disorders.

In our study, the overall episodes of care experience was comparable between chemical and film plant employees for most diseases and conditions. Of our *a priori* concerns, we observed only one liver cancer episode of care, which was from a film plant employee. Among all employees we did not observe RRE_pCs that excluded the null hypothesis ($RRE_pC = 1.0$) for a variety of liver disorders, thyroid and lipid metabolism disorders and reproductive, pregnancy, congenital and perinatal disorders. We did observe an association with cholelithiasis with acute cholecystitis ($RRE_pC = 8.6$, 95% confidence interval 1.1-381); this may have been due, in part, to fewer expected number of episodes of care in the film plant. The RRE_pC for other biliary tract disorders did not exclude the null hypothesis in the confidence interval.

Because of a previously reported increased mortality risk for bladder cancer among the chemical plant employees, we focused particular attention on episodes of care which involved the urogenital tract. We found only one episode of care for bladder cancer reported for a film plant employee who had never worked in the chemical plant. We did observe a greater increased risk in episodes of care among chemical plant employees for lower urinary tract infections ($RRE_pC = 1.3$, 95% confidence interval 1.0-1.6). This increased risk of episodes of care was greater among the long-term high exposure chemical plant workers ($RRE_pC = 2.2$, 95% CI 1.4-3.3). There was also a

greater percentage of these long-term high exposure chemical plant workers who had recurring lower urinary tract infections (59%) than film plant workers (31%). It is not known whether this reoccurrence is a result of occupational exposure(s) or nonoccupational-related factors. We do note that the prevalence of episodes of care for lower and unspecified urinary tract infections (number of unique individuals divided by population at risk) was comparable between the chemical (9.5%) and film (9.9%) plant employees.

Other associations observed, that were not *a priori* concerns, among all study subjects included increased RRE_pCs for cancers and benign growths (RRE_pC = 1.3, 95% CI 1.1-1.6) that was contributed to by increased RRE_pCs (which did not exclude the null hypothesis) for benign colonic polyps (RRE_pC = 1.4, 95% CI 0.9-2.1), malignant neoplasms of the colorectal tract (RRE_pC = 5.4, 95% CI 0.5-265), malignant neoplasms of the rectum (RRE_pC = 1.8, 95% CI 0.3-12), malignant neoplasms of the prostate (RRE_pC = 7.7, 95% CI 0.9-364) and benign neoplasms of the skin (RRE_pC = 1.3, 95% CI 0.9-1.7).

We urge caution in the interpretation of our study data as these RRE_pCs represent the risk ratio for episodes of care, not for disease incidence. Those RRE_pCs with values greater than 2.0 were often the consequence of a few observed episodes of care reported among chemical plant employees and a greater number of expected than observed episodes of care reported for film plant employees. This led to wide confidence intervals as reported above for malignant neoplasms of the colorectal tract and prostate. Our analysis was limited by the study time period of six years. Health claims data were not available prior to 1993. Whether our non *a priori* findings have a biological rationale

related to POSF-based or PFOA exposure is doubtful as considerable toxicologic and epidemiologic research conducted, to date, does not provide support for these episode of care associations.

INTRODUCTION

3M Perfluorooctanyl Chemistry, Toxicology and Epidemiology

Fluorinated organic compounds have been used for decades in a wide variety of industrial and commercial applications. The 3M company has produced fluorochemicals by an electrochemical process at its Decatur (Alabama) manufacturing facility that exchanges all of the hydrogen atoms of an organic feedstock with fluorine atoms from hydrogen fluoride [3M Company, 2000]. The highest volume perfluorochemical produced in this way is perfluorooctane sulfonyl fluoride (POSF). Using POSF as a basic building block, unique chemistries can be created by further reaction with functionalized hydrocarbon molecules. These perfluorinated compounds are used in applications such as specialty lubricants, semiconductor manufacturing, protective barriers or coatings, surfactants, fire retardants and non-conductive coolants. Exposure to POSF-based fluorochemicals may transform metabolically, to an undetermined degree, to perfluorooctanesulfonate (PFOS; $C_8F_{17}SO_3^-$) as an end-stage metabolite. Information related to human and environmental exposures to PFOS have been developed providing evidence of widespread distribution in humans and the environment.

A detailed description of industrial hygiene and biological monitoring of several fluorochemicals, including PFOS and perfluorooctanoate (PFOA, $C_7F_{15}COO^-$), at the Decatur plant, has been reported [Logan et al, 2001; Olsen et al, 2001]. At the Decatur site, PFOA exposures may be the result of it being produced as a by-product of the electrochemical cell production, of actual production of PFOA (which began in 1998) or of its use as an elastomer in fluoropolymer production. Employees may be exposed by

one or all routes (i.e., inhalation, skin contact/absorption, and ingestion) to PFOS and PFOA. The primary route of exposure may be different for each employee and depends on several different factors such as: process conditions, job tasks, work location, personal hygiene, personal habits and general work practices [Logan et al, 2001] Inhalation was considered the primary route of exposure from POSF-based production processes and fugitive sources [Logan et al, 2001].

Serum levels of PFOS from cell chemical operators engaged in POSF-based fluorochemical production have averaged between 1 and 2 ppm with the highest values reported at 10 ppm. Employees engaged in indirect production activity, such as engineers and laboratory workers, had serum fluorochemical levels that averaged less than 0.5 ppm. At the Decatur site's film plant where nonfluorochemical production occurs, located approximately 300 yards from the chemical plant, employees' serum PFOS levels averaged 0.1 ppm. Although observed at slightly lower levels, the Decatur employees' serum PFOA levels correlated with their serum PFOS levels [Olsen et al, 2001]. Unlike serum PFOS, serum PFOA levels did not exceed 5 ppm. Total serum organic fluorine was correlated with the organic fluorine calculated in employees' serum PFOS and PFOA levels.

There is substantial toxicologic and epidemiologic literature regarding PFOA. Briefly, PFOA is a moderate inducer of peroxisome proliferation related to an increased incidence of hepatic, pancreas, and Leydig cell adenomas in lifetime feeding bioassays of rats [Sibinski, 1987; Cook et al, 1994; Biegel et al, 1995, Obourn et al, 1997]. Repeated daily exposure of cynomolgus primates to ammonium perfluorooctanoate for 26 weeks by gastric intubation resulted in severe toxicity among animals in the highest dose group

(30 mg/kg/day subsequently reduced to 20 mg/kg/day) during the course of the study [Butenhoff et al, 2001]. Dose-related increased liver weights without macroscopic or microscopic changes occurred at the lowest dosage (3 mg/kg/day), which was associated with serum PFOA levels of approximately 50 ppm. Epidemiologic studies have not associated clinical chemistries, hormones or mortality outcomes of workers with occupational exposures to PFOA [Gilliland and Mandel, 1993; 1996; Olsen et al, 1998; 2000; Alexander, 2001a]. Several production employees at the 3M Cottage Grove plant, which manufactures ammonium perfluorooctanoate, have exceeded 30 ppm (range 0.0 - 114 ppm) [Olsen et al, 1998].

Regarding the toxicology of PFOS, several repeat dose studies have consistently demonstrated that the liver is the primary target organ [3M Company, 2000]. Liver tissue response to high doses of PFOS included the enlargement of the liver and apparent alterations in metabolic processes with the reduction in serum cholesterol levels observed as the earliest clinical response to PFOS [Seacat et al, 2001a]. These effects occurred in cynomolgus primates at serum PFOS levels at 100 ppm. Also at high doses, PFOS adversely affected survival of rat pups in the neonatal period of life as a result of maternal exposure during fetal development [3M Company, 2000]. Reduced weight gain, absorptions and resorptions were observed at the higher dose groups tested (1.6 mg/kg/day and 3.2 mg/kg/day). There were no effects on post-natal neurological development or on fertility and estrous cycling in offspring in multi-generation studies. Multiple genotoxicity assays suggested PFOS does not present a hazard from interaction with genetic material. Results from a two-year rat bioassay cancer study will be reported in 2001.

Serum PFOS levels in 3M's fluorochemical production workers have not been associated with abnormalities in clinical testing that included lipids, hematologic parameters and 11 different hormone values [Olsen et al, 1999]. An update of a retrospective cohort mortality study of 2,083 Decatur chemical and film plant employees with at least one cumulative year of work experience was recently completed [Alexander, 2001b]. Standardized mortality ratios (SMRs) were reported for three exposure subgroups: high exposure to POSF-based chemicals (e.g., cell and chemical operators), low exposure to POSF-based chemicals (engineers, laboratory workers in chemical plant) and minimal/nonexposure (film plant employees). The SMRs for total causes of death, all malignant neoplasms and all heart disease for each exposure sub-cohorts were lower than expected based on Alabama mortality rates. Two deaths from liver cancer were observed in the workers with at least one year of the combined employment in low and high exposure subcohorts (SMR = 3.1, 95% CI 0.4-11.1). Three bladder cancer deaths were reported among workers with at least one year of employment in the high exposure subcohort (SMR 16.1, 95% CI 3.2-47.1). Two of these three employees had worked for extensive periods of time in both the chemical and film plants. It was not clear whether these employee bladder cancer deaths could be attributed to fluorochemical exposures, another bladder carcinogen(s) encountered during their Decatur or non-Decatur work history careers or other nonoccupational factors, including the unknown possibility of an increased risk for mortality but perhaps not incidence of bladder cancer in this worker population.

A major strength of a retrospective cohort mortality study is the fact that, if the complete study population is identified, a comprehensive analysis of the occupational

cohort's death experience can be ascertained. However, if the occupational exposure is likely to lead to a non-mortality outcome, then the findings of the mortality study may be limited. Because the Decatur employees' PFOS serum levels were, on average, 2 orders of magnitude below the known earliest clinical effect (lowered serum cholesterol levels) in subchronic primate toxicity studies, it was not anticipated that disease outcomes would be associated with POSF-based fluorochemical exposures. Another reason for this epidemiologic investigation was to provide an additional perspective, that being morbidity of the Decatur chemical and film plant employees.

Morbidity studies (whether prospective or retrospective, longitudinal or cross-sectional) have their own important limitations. In particular, self-reports of diseases or conditions without medical record confirmation may provide biased findings. Several important tasks must occur for medical record review to happen. First, patient/physician confidentiality issues must be addressed in order to gain access to the records. Second, the medical records must then be found. Patients often visit multiple care givers and hospitals/clinics. Records may be lost or destroyed over time. Third, the medical records must be abstracted, coded and computerized for data analyses with subsequent quality assurance processes in place. All of these are resource-intensive, time consuming tasks. Fourth, there may be potentially numerous *a priori* hypotheses to examine. Non *a priori* hypotheses simply may not be examined due to time and cost constraints.

In order to minimize some of these limitations, we decided to examine what is referred to as an "episodes of care" experience of Decatur chemical and film plant employees. An analysis of episodes of care should be considered a screening study for

morbidity outcomes. As this episode of care concept is not generally well-known and rarely reported in occupational epidemiologic research, a detailed description follows.

Concept of an Episode of Care

The health care episode concept was conceived less than forty years ago [Solon et al 1967]. A health care episode is defined as a series of related events with a beginning, an end, and a course, all related to a particular health problem that exists continuously for a delineated period of time [Hornbrook et al., 1985]. An episode, as a measure of output, covers every service, and only those services, required to diagnose and treat each well-defined health problem.

Hornbrook et al [1985] differentiated four types of health care episodes: illness (patient perspective), disease (provider perspective), episode of care (payer perspective) and health maintenance. An episode of illness was defined as a single, unbroken interval of time during which the patient suffers from a continuous series of signs and/or symptoms that are perceived as ill-heath. An episode of disease begins with clinical specification that a disease is present and ends with specification that it is resolved. Episodes of disease may exist independent of episodes of illness. For example, although the illness symptoms may remain continuous, a physician may interpret the clinical evidence to reveal that the patient's initial disease has been superceded by another disease. Hornbrook et al [1985] defined an episode of care as a series of temporally continuous health care services related to treatment of a given illness or provided in response to a specific request by the patient. An episode of care is characterized by an onset, interim and a solution of the health problem for acute diseases and a resolution for

chronic diseases. One specific episode of care may involve more than one episode of illness and/or disease. The final type of episode Hornbrook et al [1985] described was a health maintenance episode which incorporates a comprehensive scheme for categorizing reasons for a person's contact with the health care system which can include both non-disease (e.g., immunizations, birth control, preplacement exams, health promotion activity) as well as disease-related conditions.

In general, it is much easier to measure episodes of care than episodes of illness or disease because medical records and insurance claims provide profiles of types and times of services more often than actual clinical data [Greene and Gunselman, 1984]. Episodes of care can commence upon an appointment scheduled, first patient-provider encounter, establishment of a diagnosis, or patient history of a chronic illness that was diagnosed previously. An episode of care terminates upon evidence that the particular disease, illness or care process was completed. For acute diseases, this is fairly straightforward. For chronic diseases, there may be no resolution of the disease, multiple beginnings and endings of the illness, and possibly only one or multiple episodes of care. This depends upon how the algorithm is constructed for the episode of care.

Because the episode of care can be measured (i.e., defined with a beginning, course, and end), several proprietary software products have been created which allow for the grouping of episodes of care via variable patient classification algorithms. Rosen and Mayer-Oake [1999] reviewed four of the most prominent first generation proprietary episode software products. Characteristics of these proprietary software products were the definition of an episode, number of grouped categories, case-mix adjustment, comprehensiveness of the claims included, clinical flexibility, onset and resolution

determinations and time between episodes. The lack of readily available data has hindered some of the complex methodological problems encountered when attempting to construct episode of care measures [Wingert et al, 1995].

A variety of methodological issues need to be considered when using an episode of care software product. Most importantly, among the various software programs there is no uniform approach to the software construction (i.e., grouping) of an episode of care. Thus, types and counts of episodes of care may differ by the software used. An episode of care may begin with a clear diagnosis by a provider; some providers, however, base an initial diagnosis on the patient's signs and symptoms whereas others assign a diagnosis only after a confirmed procedure. It is possible that two different diagnoses may be assigned to the same episode. A diagnosis that is categorized as confirmed, may in fact be tentative, or even incorrect (i.e., only a rule-out diagnosis). Thus, from an epidemiologic perspective an episode of care could represent any and all of the incident cases (newly diagnosed), prevalent cases (existing cases) and/or misclassified cases (both directions, false positive and false negative). Therefore, it is important that the term episode of care not be confused with incidence or prevalence as it can be a measure of both and also have an undetermined degree of misclassification. It is best to view episodes of care as its own unique metric. Second, there is variability in the comprehensiveness of the services that are included in the construction of the health care episode. Generally inpatient and outpatient services are considered but other services including prescriptions and laboratory work-up may, or may not, be included. Third, the endpoint of an episode can also vary among these software programs. An endpoint can be a predetermined time period for a defined condition or it may be determined through

the use of "clean periods" or "clean windows" which are defined as gaps in time between health care services necessary to separate possible recurring episodes. Finally, the clinical flexibility of the algorithm may differ depending upon the software program used [Cave 1995; Dang et al, 1996a; 1996b; Rosen and Mayer-Oakes, 1999].

Study Purpose

The purpose of this study was to utilize Clinical Care Groups™ (CCG) software, developed by Ingenix Employer Group (Ingenix) to analyze the episode of care experience among Decatur chemical and film plant employees. CCG represents state-of-the-art episode of care methodology [Valdivia and Van Vorst; 2000]. The overall methodologic strategy was to calculate, for more than 400 CCG disease and condition descriptions (defined in the Methods section), the risk ratio of the observed to expected episodes of care experience of Decatur chemical plant employees who worked between January 1, 1993 and December 31, 1998 compared to the observed to expected episodes of care experience of film plant employees who worked during the same time period. Based on toxicology and epidemiology research conducted, to date, on the PFOA and POSF-based chemistry, episodes of care that were considered *a priori* interests in this study included liver and bladder cancer, endocrine disorders involving the thyroid gland and lipid metabolism, gastrointestinal disorders of the liver and biliary tract, and reproductive, pregnancy, congenital and perinatal disorders.

METHODS

Presented below are detailed methodologic descriptions of the CCG software used in this study; the eligible Decatur employee study population; the databases used and data extraction techniques employed by Ingenix; and the statistical analyses that were used to construct the risk ratio episode of care.

Specifics of CCG Software

The CCG software involves a comprehensive grouping of all visits (inpatient, outpatient), procedures, ancillary services and prescription drugs used in the diagnosis treatment and management of more than 400 diseases or conditions. Within CCG, an episode of care is constructed by four main sections: episode initiation; incorporation of pharmacy claims; backward and forward searching; and claim record labeling. Unlike other episodes of care software, CCG pre-processes drug claims in an attempt to assign one or more diagnosis codes to each record based on diagnosis codes found in the patient's medical claims stream. This is called the Drug-Disease Matcher (DDM^{TM}).

The software code (called a grouper by CCG) constructs an episode around the index-eligible record by searching backward and forward in time for records that are related to the disease in question. Acute conditions have anterior and posterior clear windows which determine the number of days that can be searched prior to (anterior window) and after (posterior window) the index event. This window is reset if related claims are found. Because of their nature, chronic conditions do not have clear windows. Rather a predetermined 999 day interval is set that can be reset 999 days from events that would be associated with the index event.

The CCG grouper labels the claim records to one of the five following record types: index, associated, precursor, sign/symptom, and V-code. An index record consisted of either procedure codes indicative of a face-to-face encounter or a pharmacy record for a delineating drug (drugs that treat a specific disease, e.g., insulin for diabetes). Although claim records often list multiple diagnosis codes for a single encounter, the CCG program contained logic that determined the diagnosis code most likely the reason for the encounter. This primary diagnosis code on the index record determined which Class description (defined below) the record was assigned, thereby opening either a new episode of care or adding to an already existing episode. The other four claim record labels that the CCG software uses were: 1) precursor (contains one or more diagnosis codes representing a clinical precursor to the more clinically significant disease that had been episoded); 2) sign/symptom (contains nonspecific diagnosis code that can be considered to part of a more specific disease); 3) V-code (supplementary factors that influenced health status but were not classified into more specific disease categories (e.g., alcoholism could refer to several different disease conditions)); and 4) associated records (non-index eligible procedure codes that occurred outside of a patient-provider encounter).

The CCG software assigns an episode of care to a CCG Class description of a disease or condition. A CCG Class has several important qualities. It is: 1) clinically homogenous; 2) exhaustive; 3) part of a disease hierarchy; and 4) classified as a chronic or acute condition. Several CCG Classes may define a CCG Category. Several CCG Categories constitute a CCG Specialty Category. Altogether, the CCG grouper software

allows for 20 Specialty Categories that are subdivided into 103 CCG Categories. The CCG Categories are then further subdivided into 442 CCG Class descriptions.

The CCG software analysis provided a summary output file with one record per episode of care. For example, a claims stream for one patient that resulted in the primary diagnosis of acute myocardial infarction could have resulted in one Specialty Category episode (Disease of the Circulatory System), several CCG Category episodes (e.g., atherosclerotic coronary vascular disease, hypertension, disorders of heart valve) and many more CCG Class episodes within each CCG Category (e.g., the CCG Category atherosclerotic coronary vascular disease may have shock, ischemic heart disease and acute myocardial infarction included as its CCG Class episodes of care).

Ingenix Inc. has evaluated its CCG software performance against a sample of 450,000 members obtained from twelve health plans [Valdivia and Van Vorst, 2000]. Of 2.3 million medical and pharmacy claim records, 84% were grouped into clinical care groups. The proportion grouped represented 90% of the total costs paid by the health plans. A greater percentage of the medical claims were grouped (91%) compared to pharmacy claims (72%) which represented 93% and 77% of total costs for medical and pharmacy claims, respectively

Decatur Study Population

Although chemical production at Decatur began in 1961, our initial study population consisted of all full-time and inactive employees at the Decatur site as identified in the 3M Epidemiology's work history database for Decatur as of January 1, 1993. There was a one-year eligibility employment criterion to be included in this

database. All employees hired subsequently were included in the study as long as they met the criterion to be eligible for this database. In other words, employees who worked for less than one year during the study time period were not included in this analysis. Employees hired, terminated (voluntary or involuntary termination) or died while employed from the company during the study (1/1/93 through 12/31/98) had their Decatur episodes of care experience limited to their Decatur time of employment. Full-time active employees who retired during the study period continued to have their episodes of care experience examined through the end of study; Medicare, however, becomes the employee's primary provider upon the employee's 65th birthday and thus Ingenix did not have most of these Medicare claims. Similarly, claim records for employees who went on long term disability (LTD) were covered primarily by Medicare after 18 months of LTD status. There were some employees ($n < 40$) who chose HMO coverage between 1996 and 1998. HMO records were not incorporated in the Ingenix database coverage for the Decatur site. Altogether, there were 1,311 Decatur employees (97%) eligible for the episode of care analysis during the 1993 - 1998 time period.

Analysis of the episode of care experience was examined by whether the employee was considered a chemical plant or film plant employee. Each employee's work history record was examined by the investigators (JMB, GWO, MMB) to determine whether the employee: 1) ever worked in the chemical plant, film plant or both; 2) worked in the chemical plant, film plant or both during the study time period of January 1, 1993 through December 31, 1998; and 3) worked continuously in the chemical plant or film plant for the entire 10 years prior to the onset of the study time period, January 1, 1993 ('long-term' workers). For those employees who had work experience in

both the chemical and film plants, records were reviewed to identify which plant each employee primarily worked at in his or her career at the 3M Decatur site. Both chemical and film plant employees were categorized in the analyses as to whether they have, or have not, worked in both plants. The majority of film plant employees with prior work experience in the chemical plant worked at the chemical plant for a brief period of time (1 to 3 months) and this usually occurred during the first year of their employment. These employees were categorized as film plant employees. Likewise, the majority of chemical plant employees with prior work experience in the film plant worked at the film plant for a brief period of time and this usually occurred during the first year of their employment. These employees were categorized as chemical plant employees. Employees who had site-wide responsibilities (those who may work daily in both chemical and film plants, such as environmental, health and safety specialists) were assigned to the chemical plant because of their greater likelihood of exposure to POSF-based chemicals than those employees who only worked in the film plant.

Each employee was assigned a job title that described the person's usual job activity while a Decatur employee. These job titles were: boiler operator, environmental health and safety specialist, engineer, mill operator, maintenance, office worker, operator (e.g., cell, chemical), quality control worker, shipping clerk and supervisor. Based on the findings from the Decatur serum fluorochemical assessment study [Olsen et al., 1999], three subcohort groups were categorized as to their potential for high, low and minimum/nonexposed POSF-based exposure.. These were the same categorizations used in the Decatur retrospective cohort mortality study [Alexander, 2001b]. For example, cell operators, chemical operators and maintenance workers at the chemical plant were

categorized as high exposure. Engineers and laboratory workers at the chemical plant were categorized as low exposure. Film plant workers were categorized as minimal/nonexposed.

Four study employee comparison groups were identified for the episodes of care analyses. The rationale for these four categories was to increase the likelihood of the chemical plant cohort to have long-term high fluorochemical exposure jobs. These four comparisons were:

Group A Comparison: all chemical plant employees with or without prior film plant experience (n = 652) compared to all film plant employees with or without a prior chemical plant experience (n = 659).

Group B Comparison: all chemical plant employees who never worked in the film plant (n = 388) compared to all film plant employees who never worked in the chemical plant (n = 424). Group B is a subset of Group A.

Group C Comparison: all high (defined above) fluorochemical exposure chemical plant employees (n = 498) compared to their job counterparts (considered least exposed) in the film plant, (n = 490). Group C is a subset of Group A.

Group D Comparison: all long-term (defined above), high fluorochemical exposure chemical plant workers (n = 211) compared to their job counterparts (considered least exposed) in the film plant (n = 345). Group D is a subset of Group C, which is a subset of Group A .

Ingenix Databases and Data Extraction

Aside from developing the CCG product, Ingenix also provides data warehouse, reporting, consulting and analysis to 3M. On a quarterly basis, Ingenix receives member eligibility information, as well as, medical and prescription claim detail from each one of 3M's benefit plan vendors. Ingenix then uses this data to create the following databases:

The Medical Focused Database provides access to the highest level of detail for both inpatient and outpatient data. The database is comprised of individual service records, meaning that every line item on each claim is broken out into its own individual record. This would allow you to drill down, for example, to a specific service provided by a specific physician for a specific patient on a specific day.

The Monthly Cost and Utilization (MCU) Database contains summarized claim data. Claims are aggregated in a fashion that allows a customer to easily report by grouping meaningful to the customer, such as by location or aggregations of location, by paid and incurred month, and by service categories.

The Inpatient Confinement Database is the result of Ingenix methodology which links all services related to a hospital confinement and groups them into one record. The record contains a host of information necessary for analysis of inpatient services, including, but not limited to, length of stay, MDC, DRG, major specific diagnosis, surgery performed, and physician and facility provider.

Prescription Drug Database is designed to capture drug specific details available from prescription mail order and drug card plans. The drug database includes claimant and expense information, prescription number, physician DEA number, pharmacy number and type, an indicator to identify how and why the drug was dispensed, and the National Drug Code (NDC). Additionally, Ingenix adds information specific to the particular drug that was dispensed that is not supplied by the vendor. This information is taken from First Databank's National Data File (NDDF), which includes:

- Blue Book Average Wholesale Price (AWP)
- Federal Maximum Allowable cost (MAC Price)
- Controlled Substance Indicator
- Brand/Generic Indicator

The Eligibility Database is derived from 3M's enrollment data. The Eligibility database provides a routine way to access population, either on a summarized level or by individual member. Furthermore, enrollment data can be used in conjunction with other Ingenix databases to produce information such as admission rates, services per employee or covered life, and average benefits per employee or member.

Extracts from the above medical and prescription drug databases were created for the entire 3M population (employee data and claim experience only). These extracts were tested against the source databases to ensure that the population subset for the extraction was correct. The testing method involved running various statistical reports (e.g. number of claimants, dollars paid, dates of service) from both the source and extracted data. Once the quality assurance checks had been satisfactorily completed, the extracted data was then run through the CCG grouping software to create the 3M specific episodes of care for the six-year study period.

Data Analysis

Because of confidentiality concerns regarding employee medical information, the Ingenix investigators were the only researchers who knew the identification of the employees' episodes of care experience. Each study cohort's personal identifiers were provided to Ingenix for record linkage purposes to determine and extract the reported number of health claims per covered employee. For each person within each cohort (chemical or film, groups (A-D), Ingenix determined, based on the eligibility database described above, whether or not the person belonged to a 3M sponsored health plan that could result in the possibility of claims, regardless of type, for the 72 month study period (1993-1998). The actual number of days (i.e., time) in which an employee was enrolled within the company health plans was not known. We only knew whether employees were eligible on a month to month basis via the data available through the Ingenix Eligibility Database. Therefore, we chose to examine the comparison of episodes of care experience between chemical and film plant to have a Poisson distribution and then

subsequently compared the ratio of these two Poisson variables via the methods outlined by Ederer and Mantel [1974].

The observed number of claims based on the CCG algorithm for the Specialty Category, Category and Class descriptions was compared to an expected value using indirect standardization methods [Tsai and Wen, 1986] to adjust for three age categories (<40, 40-49 and >=50 years) and gender (male, female). Two normative databases were used to calculate the expected number of claims: 1) the entire U.S. 3M population health claims experience from 1993-1998 excluding the Cottage Grove and Cordova sites due to their fluorochemical production activities; and 2) the U.S. 3M population health claims experience from 1993-1998 excluding employees at the St. Paul, Woodbury, Cottage Grove, and Cordova sites. The latter database, hereafter called the 3M manufacturing plant normative database, provided a comparison database that was more representative of 3M manufacturing plant employees, in general, as it excluded the St. Paul 3M Center corporate and research employees. However, it also excluded the downtown St. Paul manufacturing plant as the 3M St. Paul manufacturing and corporate/research sites share identical location codes. [Note: A third normative database, which consisted of other companies that belong to the Ingenix aggregate database, was not considered appropriate because the different health insurance plans that these other companies use may greatly influence the type and degree of health care.] For each of the four comparison group's chemical and film plant populations, we calculated the observed and expected number of episodes of care experience for the CCG's Specialty Category, Category and Class descriptions.

A Standardized Episodes of Care Ratio (SE_pCR) was calculated separately for the chemical and film plants for each respective cohort. That is,

$$SE_pCR_{chemical} = \sum Observed_{chemical} / \sum Expected_{chemical}$$

$$SE_pCR_{film} = \sum Observed_{film} / \sum Expected_{film}$$

However, it is the ratio of the two plant indirect standardized ratios for each comparison group, which we defined as the Risk Ratio Episodes of Care (RRE_pC), provides the measure of risk between the two study populations. That is,

$$RRE_pC = SE_pCR_{chemical} / SE_pCR_{film}$$

$$= [\sum Observed_{chemical} / \sum Expected_{chemical}] / [\sum Observed_{film} / \sum Expected_{film}]$$

This direct comparison of two indirect standardized ratios is an unbiased estimator of the risk ratio (i.e., relative risk) if there are similar age-specific structures between the two comparison populations [Tsai and Wen, 1986]. Because the chemical and film plant cohorts had slightly different age structures used for the indirect standardization, the ratio of the two indirect standardized ratios for the chemical and film plant populations was not necessarily directly comparable. Therefore, we used the methods by Tsai and Wen [1986] to compare whether the ratio of two indirect standardized ratios, corrected for their age structure, was similar to an unadjusted ratio of

two indirect standardized ratios. That is,

$$RRE_pC_{corrected} = SE_pCR_{chemical\text{-}corrected} / SE_pCR_{film\text{-}corrected}$$

where

$$SE_pCR_{chemical\text{-}corrected} = \sum Observed_{chemical} / \sum Expected_{chemical\text{-}corrected}$$

and

$$SE_pCR_{film\text{-}corrected} = \sum Observed_{film} / \sum Expected_{film\text{-}corrected}$$

The age- and gender- adjusted $SE_pCR_{chemical\text{-}corrected}$ is the sum of the age-specific episodes of care for the chemical plant standardized to the sum of the chemical and film plant expected episodes of care. Likewise, the age- and gender-adjusted $SE_pCR_{film\text{-}corrected}$ $_{corrected}$ is the sum of the age-specific episodes of care for the film plant standardized to the sum of the chemical and film plant expected episodes of care. It is important to note that each $SE_pCR_{corrected}$ is not meaningful by itself, only their ratio, $RRE_pC_{corrected}$, which is an unbiased estimator of the relative risk [Tsia and Wen, 1986].

Although Tsai and Wen [1986] suggested that a 95 percent confidence interval (95% CI) of $RRE_pC_{corrected}$ can be readily calculated using the procedures developed by Ederer and Mantel [1974] for the ratio of two Poisson variables, such methods, in fact, cannot be used without great difficulty. Unlike RRE_pC which is a ratio of two Poisson variables ($\sum Observed_{chemical} / \sum Observed_{film}$) multiplied by a constant ($\sum Expected_{film} / \sum Expected_{chemical}$), the calculation of a confidence interval for

$RRE_pC_{corrected}$ is not readily apparent as each $Observed_{corrected\text{-}chem}/Observed_{corrected\text{-}film}$ subgroup is not a Poisson variable and neither is their sum.

Consequently, our analysis strategy was to calculate both a RRE_pC and a $RRE_pC_{corrected}$. If the two risk ratios were comparable, which we suspected they would be given the fact that the chemical and film plant age structures were not substantially different, then we assumed that RRE_pC was a minimally biased risk ratio estimate and we calculated the 95% CI of RRE_pC using the methods of Ederer and Mantel [1974]. Cumulative binomial tables [Documenta Geigy, 1967] were used to calculate the 95% CI when the number of total observations was less than 30. We used the normal approximation to the binomial when the total number of observations was greater than or equal to 30. RRE_pC and RRE_pC_{cr} were not calculated when there were two or fewer total observed episodes of care for the chemical and film plants combined.

RRE_pC may be greater than the null hypothesis (as defined in this study as the exclusion of the null hypothesis value (1.0) from the 95% CI for three possible reasons. An increased RRE_pC may be due to: 1) a greater observed to expected episode of care experience in the chemical plant (than compared to the film plant); 2) a greater expected than observed experience in the film plant (than compared to the chemical plant) or 3) a combination of both 1 and 2. In other words, the first instance occurs when $SE_pCR_{chemical}$ is > 1.0 and SE_pCR_{film} is $\geq$1.0, but if SE_pCR_{film} is > 1.0 it is still less than $SE_pCR_{chemical}$. The second instance occurs when $SE_pCR_{chemical}$ is $\leq$ 1.0 and SE_pCR_{film} is < 1.0 but if $SE_pCR_{chemical}$ is < 1.0 it is still greater than SE_pCR_{film}. The potential for the greatest magnification of the RRE_pC may occur in the third instance when $SE_pCR_{chemical}$ is > 1.0 and SE_pCR_{film} is < 1.0 The RRE_pC that is increased in the first instance might be

attributed to the possibility of potential workplace exposure in the chemical plant whereas the RRE_pC that is increased in the second instance may be due to an unexplained less than expected number of observed episodes of care in the film plant (and not as the possibility of potential workplace exposures in the chemical plant). The third instance may be the possibility of either or both explanations.

RESULTS

Presented in Table 1 are the demographic characteristics of the four study group comparisons. Among all 1,311 study subjects (study group A), 36 percent of the 659 film plant workers were 50 years of age or older compared to 53 percent of the 659 chemical plant workers. Sixty percent of the employees had worked only in the chemical plant (n = 388) or only in the film plant (n = 424). This was defined as study comparison group B. Seventy-six percent (n = 498) of the 652 chemical plant employees worked in a job(s) with a high potential for POSF-based exposure. This defined study comparison group C. Among the 211 long-term high exposure chemical employees, comprising study comparison group D, 61 percent had worked only in the chemical or film plant since 1983.

Provided in Table 2 is the employment status at the beginning and end of study for comparison group A stratified by gender. For all 1,311 study subjects, 31 percent of the chemical plant and 26 percent of the film plant employees were not yet hired as of the study onset (January 1, 1993). By the end of the study (December 31, 1998), 78 percent of the chemical plant employees were actively employed and 11 percent had retired. Among the film plant employees, 71 percent were actively employed and 17 percent had

retired. Percentages of inactive, terminated, deceased and transferred employees were comparable between the chemical and film plant employees. Provided in Tables 3 through 5 are similar percentages for the comparison groups B through D. Because of its definition of long-term workers since 1983, it is to be expected that comparison group D had the highest percentage (24 percent) of any comparison group for the number of retired employees at end of study.

Presented in Appendix A is the employment status for each comparison group (A through D) by individual year (as of January 1st). The number of active chemical plant employees was relatively constant (i.e., never varied by more than 7 employees between years) until 1997 when there was an increase of 83 employees form January 1, 1997 to January 1, 1998 (19 percent increase). During the six year study time period the number of film plant employees never varied by more than 30 employees between any two successive years.

The ratio of total number of outpatient to inpatient claims per plant within each comparison group (A-D) was greater than 150 to 1 (Table 6). For each comparison group, the average number of outpatient claims per person per year was higher among film plant employees compared to chemical plant employees. The average number of inpatient claims was comparable.

Provided in Tables 7 through 10 are the observed and expected numbers of episodes of care by plant for the CCG Specialty Category, Category and Class descriptions for the four study comparison groups A through D, respectively. The expected results were slightly higher when the 3M manufacturing population was used but this was true for both chemical and film plant populations; thus the RRE_pC and

RRE_pC_{cr} were similar regardless of which normative population was used. Therefore, for purposes of brevity we have only shown the analyses when the 3M manufacturing normative population was used. Presented in tables 7 through 10 are the number of unique individuals who constituted the total number of episodes of care for each CCG description. The RRE_pC and RRE_pC_{cr} were comparable for most CCG descriptions and therefore the results will focus on the RRE_pC and its 95% CI. The CCG Specialty Categories are presented in a hierarchical order similar to ICD-9 codes, beginning with Infectious Diseases, then Cancers and Benign Growth, Endocrine Disorders, etc. Twenty Specialty Categories are presented (bold print) which are then subdivided into 97 Categories (directly under Specialty Category description) and these are further subdivided into Classes (indented under the Category description in the tables). For the Specialty Category of Cancers and Benign Growth, all Categories and Classes are presented. For the remaining Specialty Categories, all CCG Categories are presented but not all Class descriptions (although all Class descriptions provided by the CCG grouper were analyzed). In particular, Class descriptions were generally not provided under those Specialty Categories that had no *a priori* hypotheses (e.g., Psychiatric Disorders, Cardiovascular Disorders, Dermatologic Disorders, Musculoskeletal Disorders). RRE_pC and RRE_pC_{cr} were not calculated when there were two or fewer total observed episodes of care for the chemical and film plants combined.

For study comparison group A (Table 7), there were 10,608 episodes of care (sum of the 20 Specialty Categories) for the 652 chemical plant employees during the six year study period (average of 2.7 episodes of care per chemical plant employee per year). For

the 659 film plant employees, they had 11,957 episodes of care (average of 3.0 episodes of care per film plant employee per year).

In Table 7, the Specialty Category of Cancers and Benign Growths had an RRE_pC of 1.3 (95% CI 1.1-1.6). Within its Categories, neoplasms of the male reproductive system had an RRE_pC of 10.0 (95% CI 1.3 - 447). This RRE_pC was the consequence of a disparity in observed to expected episodes of care of malignant neoplasms of the prostate in chemical and film plant employees. There were 5 observed versus 3.1 expected episodes of care of malignant neoplasms of the prostate among the chemical plant employees compared to 1 observed and 4.7 expected episodes of care in the film plant.

The RRE_pC was 1.5 (95% CI 1.0-2.2) for neoplasms of the gastrointestinal tract (Table 7). More than eighty percent of these gastrointestinal tract episodes of care for both the chemical and film plant were for benign colonic polyps. There was an increased RRE_pC for both malignant neoplasms of the colon (5.4, 95% CI 0.5-265) and malignant neoplasms of rectum and anus (1.8, 95% CI 0.3-12.4). There was a total of 5 unique chemical plant employees who constituted the 8 episodes of care for these two conditions.

Neoplasms of skin had an RRE_pC of 1.3 (95% CI 1.0-1.6). This increased RRE_pC was due to RRE_pCs for malignant melanoma of the skin (>2.3, 95% CI 1.0-63) and benign neoplasms of skin (1.3, 95% CI 0.9-1.7).

Among the Specialty Category of Endocrine Disorders, the Category of diabetes Type I with complications had an RRE_pC of 5.1 (95% CI 0.5-247), which was due to the disparity of more observed than expected episodes of care in the chemical plant and vice versa in the film plant. However, the RRE_pC for Diabetes Type I without complications

was not elevated (1.0, 95% CI 0.4-2.6). There was no increased RRE_pC found for the Categories of disorders of the thyroid (1.1, 95% CI 0.6-1.8), lipid metabolism (1.0, 95% CI 0.8-1.3) or other endocrine or nutritional disorders (1.0, 95% CI 0.7-1.3). Although there were few episodes of care for disorders of the liver (Specialty Category is Gastrointestinal Disorders), there was an increased RRE_pC for cholelithiasis with acute cholecystitis (8.6, 95% CI 1.1-380.7) under the Category of disorders of the biliary tract (1.7, 95% CI 0.8 - 2.9). The elevated RRE_pC for cholelithiasis with acute cholecystitis was the consequence of observed to expected disparities between the chemical and film plant populations. No other class description regarding cholecystitis or chloelithiasis had an RRE_pC that excluded the null hypothesis. Episodes of care for acute pancreatitis was elevated among chemical plant employees (2.6, 95% CI 0.6-16). All six episodes of care were from one unique individual.

In Table 7, the Specialty Categories of Cardiovascular Disorders, Pulmonary Disorders, Ear, Nose and Throat Disorders and Urologic Disorders did not have any RRE_pC with a 95% CI that excluded the null hypothesis. The highest RRE_pC was for the Category descriptions of disorders of renal function (3.1, 95% CI 0.5-32.9) and disorders of renal parenchyma (3.7, 95% CI 0.3-192). Again, these were based on a disparity of observed and expected values between the chemical and film plant populations. The Category of lower and unspecified urinary tract infections had an RRE_pC of 1.3 (95% CI 1.0-1.6) with RRE_pCs for the Class descriptions of cystitis of 1.5 (95% CI 1.0-2.2) and urinary tract, unspecified of 1.1 (95% CI (0.8-1.6). Whereas the prevalence of unique individuals with an episode of care of cystitis was higher film plant employees (31/659 = 4.7 percent) compared to chemical plant employees (19/652 = 2.9 percent), the

recurrence of the episodes of care of cystitis was much higher among chemical plant employees (66%) compared to film plant employees (22%) and this was the result of a greater percentage of recurrence among female chemical plant employees. Of the 56 observed episodes of care for cystitis among chemical employees, 50 (89 percent) belonged to 14 (74 percent) female employees (data not shown) of the 19 total unique individuals who had such episodes of care. Of the 40 observed episodes of care for cystitis among the film plant employees, only 21 (52 percent) belonged to the 15 (48 percent) female employees (data not shown) of the 31 total unique individuals who had such episodes of care. The recurrence of the lower urinary tract, not specified infections was comparable between chemical and film plant employees as well as between female chemical and film plant employees. There was not an increased RRE_pC for calculi of the upper urinary tract (1.0, 95% CI 0.8-1.4).

In Table 7, the Specialty Categories of Gynecologic and Reproductive Disorders, Pregnancy, Congenital Anomalies and Perinatal Disorders did not have any RRE_pC with a 95% CI that excluded the null hypothesis. The highest RRE_pC (3.6, 95% CI 0.5-172) was for the Class description of preterm labor (Category is complicated pregnancy or delivery under the Specialty Category of Pregnancy). This RRE_pC was the result of 7 episodes of care from 3 unique chemical plant employees.

Among the Miscellaneous Specialty Category in Table 7, there were no substantial differences for signs and symptoms (abdominal pain, chest pain, fever, headache with radiology, malaise, syncope, and ill-defined signs and symptoms) between episodes of care observed for the chemical and film plant employees.

Comparable RRE_pC results were observed when the entire study population was restricted to those employees who had only worked in either the chemical plant or film plant but not both (study comparison group B, Table 8). It should be noted that, unlike Table 7, the RRE_pC for lower and unspecified urinary tract infections excluded the null hypothesis (1.5, 95% CI 1.1-2.1). The percentage of chemical plant employees with recurrence of episodes of care for cystitis was 72 percent compared to 26 percent for film plant employees. Also observed was a higher RRE_pC for the Category of menopausal and menstrual disorders (2.0, 95% CI 1.1-4.0).

The episodes of care data presented in Table 9 are of those employees who were identified to have worked in high potential fluorochemical jobs (e.g., cell operators, chemical operators) in the chemical plant and were compared to their job counterparts (film operators, process operators) in the film plant (i.e., study comparison group C). The RRE_pC for the Specialty Category of Cancers and Benign Growths was 1.8 (95% CI 1.2-3.0). CCG Categories that contributed higher RRE_pCs included those reported previously in Tables 7 and 8: 1) neoplasms of the gastrointestinal tract (1.8, 95% CI 1.2-3.0); neoplasms of the skin (1.1, 95% CI 0.8-1.5); and neoplasms of the male reproductive tract (7.6, 95% CI 0.9-359). Only one Class description, benign colonic polyps, had an RRE_pC which excluded the null hypothesis in its confidence interval (1.9, 95% CI 1.1-3.2). Increased RRE_pCs that did not exclude the null hypothesis in the 95% CI included malignant neoplasms of colon (4.5, 95% CI 0.4-238), malignant melanoma of the skin (>2.5, 95% CI 0.8-51.0), malignant neoplasms of prostate (6.7, 95% CI 0.6-325). and benign ovarian cysts (2.6, 95% CI 0.6-15.1).

Of the non-cancer Specialty Categories presented in Table 9, only two contained a Category or Class description whose RRE_pC excluded the null hypothesis in its 95% CI. In the Specialty Category of Psychiatric Disorders, the Category of affective disorders had an RRE_pC of 1.4 (95% CI 1.1-1.9). In the Specialty Category of Gastrointestinal Disorders, the Class description of cholelithiasis with acute cholecystitis had an RRE_pC of 9.2 (95% CI 1.2-407). Again, this was the result of a greater number of observed episodes of care than expected among chemical plant employees (7 versus 2.5) compared to fewer observed than expected episodes of care (1 versus 3.2) among film plant employees. Unlike the results in Table 8, we did not observe an increased RRE_pC for the Category of menopausal and menstrual disorders (1.1, 95% CI 0.7-2.0).

Provided in Table 10 are the episodes of care analyses for those long-term high exposure job employees in the chemical plant along with their counterpart long-term (least exposed) employees in the film plant (study comparison group D). The Specialty Category of Cancers and Benign Growths continued to have an increased RRE_pC which excluded the null hypothesis in its 95% confidence interval (1.6, 95% CI 1.2-2.1). As seen previously with the other study comparison groups (Tables 7-9), increased Category RRE_pCs (under the Specialty Category of Cancers and Benign Growths) were observed for neoplasms of the gastrointestinal tract (2.9, 95% CI 1.7-5.2), neoplasms of the male reproductive tract (9.7, 95% CI 1.1-458), and neoplasms of skin (1.2, 95% CI 0.8-1.9). Increased Class RRE_pCs were observed for malignant neoplasm of colon (>3.8, 95% CI 0.9-60.0), malignant neoplasms of the rectum and anus (> 5.0, 95% CI 0.9-62.0), benign colonic polyps (2.4, 95% CI 1.3-4.5), malignant melanomas of the skin (>3.0, 95% CI 0.8-52) and malignant neoplasms of the prostate (8.2, 95% CI 0.8-399). Except for

benign colonic polyps, these Classes had three or fewer episodes of care among chemical plant employees.

Non-cancer Categories which had a 95% CI that excluded the null hypothesis in Table 10 included disorders of the pancreas (6.4, 95% CI 1.2-63), which was due to acute pancreatitis (5.5, 95% CI 1.0-56). As mentioned previously, the six episodes of care for acute pancreatitis were from one individual. The Category of lower and unspecified urinary tract infections also excluded the null hypothesis (2.2, 95% CI 1.4-3.3). Increased RRE_pC were observed for both the episode of care described as cystitis (2.4, 95% CI 1.2-4.8) and that of urinary tract infection, not specified (2.1, 95% CI 1.2-3.5). The percentage of recurrence of cystitis was greater among chemical plant (61 percent) than film plant 24 percent) employees. Class descriptions that had a null hypothesis excluded in the 95% CI of its RRE_pC were cholelithiasis with acute cholecystitis (>4.0, 95% CI 2.1-128) and abdominal pain (1.6, 95% CI 1.2-2.1) under the Category of symptoms or signs (1.2, 95% CI 1.1-1.4) of the Specialty Category described as Miscellaneous (1.2, 95% CI 1.1-1.4). All other Class descriptions under the Category symptoms or signs had RRE_pCs that were at or greater than the null hypothesis although none had 95% CIs that excluded the null hypothesis.

Table 11 provides a summary of the Specialty Categories, Categories and Classes which had an RRE_pC that excluded the null hypothesis in the 95% confidence interval for at least one of the four comparison groups, A through D, as discussed above in Tables 7 through 10. The only CCG description that had the null hypothesis excluded in all four comparison groups was the CCG Specialty Category of Cancers and Benign Growths.

DISCUSSION

The episode of care concept does not translate into a well-defined epidemiologic measure. An episode of care may include incident cases (i.e., newly diagnosed cases), prevalent cases (existing cases), tentatively diagnosed cases and misclassified cases that are the routine consequence of the differential diagnoses that individuals may undergo in the course of disease diagnosis, treatment and management. Acute episode of care conditions may include the same individual multiple times. Therefore a large RRE_pC may not infer a high incidence risk. Likewise, a high RRE_pC could be masked as a consequence of a large observed to expected ratio in the film plant that is not the result of incident episodes of care although the numerator (chemical plant) is. The number of episodes of care can also be influenced by the practice patterns of the local medical community and the varying health plans available to members of the community. Episodes of care are hierarchical. Therefore, one person may contribute episodes of care to several Classes which represent fewer Categories of the same Specialty Category. All of these are constraints to the use of episodes of care methodology in occupational epidemiology investigations.

On the other hand, episodes of care may be considered a reasonable screening method for the potential risk of diseases and/or conditions when there are two study populations from the same company, covered by the same medical plan, who live within the same community, and who differ primarily only in their workplace exposure. This scenario existed with the employees at 3M's Decatur manufacturing site.

We addressed POSF-based workplace exposure with the construction of the four study comparison groups. We were able to subdivide the study population into those

employees who were primarily in the chemical or film plants throughout their Decatur career (comparison group A), only in the chemical or film plants throughout their career (comparison group B), those who had worked in a high potential exposure job (comparison group C), and those who had worked long-term (at least 10 years prior to the onset of the study) in a high potential exposure job (comparison group D).

Our study included individuals who were on long-term disability at the beginning and throughout the course of the study time period as well as those employees who retired subsequent to January 1, 1993. We recognize that neither of these groups provided a comprehensive episodes of care assessment due to the eligibility criteria for Medicare. Medicare does not cover employees' long term disability claims until 18 months after diagnosis. Thus, employees who went on long term disability during the course of the study would have had their initial disease or condition identified through company claims data. This may not be true, however, for the 20 chemical and 26 film plant employees who were already on long-term disability at the onset of the study (Table 2). The majority of employees during the course of the study retired prior to age 65 and therefore their health claims would have been considered in the construction of the episodes of care through age 64.

Our *a priori* interests included liver and bladder cancer, endocrine disorders involving the thyroid gland and lipid metabolism, gastrointestinal disorders of the liver and biliary tract, and reproductive, pregnancy, congenital and perinatal disorders. Because of the many multiple comparisons which were not of *a priori* interests, chance findings might arise, although this assumes the universal null hypothesis (i.e,. that chance is the first-order explanation for all observed phenomenon) [Borak and Bidulescu, 2000;

Rothman, 1992]. We agree with Rothman's treatise [1990] that it is preferable not to provide adjustments for multiple comparisons in empirical research because it may lead to fewer errors of interpretation when the data are not random, but instead actual observations of nature. The intent of this study was to use the episodes of care methodology as a screen for morbidity outcomes associated with long-term high exposure to POSF-based production. An adjustment procedure would only increase the type II error for those associations that are not null and thereby we could dismiss non *a priori* findings that should require further insight.

A major *a priori* consideration was the bladder cancer association (3 observed 0.2 expected among a high POSF-exposed subcohort) reported in the Decatur retrospective cohort mortality study [Alexander, 2001b]. Two of these employees had also worked in the film plant during the course of their Decatur career. In our study, we observed no episodes of care for neoplasm of the bladder among chemical plant employees and one among the film plant employees. A review of the inpatient, outpatient and pharmacy claims confirmed this was a bladder cancer diagnosis during the course of the study. Because of confidentiality requirements, we do not know the specific jobs this person performed although our data did provide this was a female employee not employed as a film plant production operator or maintenance worker since this episode of care of bladder cancer was not reported for comparison groups C or D. It is not possible for this episode of care of bladder cancer to be one of the three employees who had died from bladder cancer in the mortality study as these three individuals had either quit or retired from the company prior to the onset of our study.

Among the Specialty Category of Urologic Disorders, we did observe a higher RRE_pC for disorders of renal function, renal parenchyma and lower and unspecified urinary tract infections. Among the latter, the percentage of episodes of care that represented recurrences was higher among all chemical plant employees (55 percent) compared to all film plant employees (38 percent). Among long-term high exposed employees, this recurrence percentage increased to 59 percent among the chemical plant employees with episodes of care for lower and urinary tract infections compared to 31 percent among film plant employees. Although the RRE_pC was 2.2 (95% CI 1.4-3.3), the question then arises as to whether this two-fold increase is a result of non-related occupational factors associated with recurring lower urinary tract infections in the chemical plant employee population or as a consequence of an ongoing workplace exposure. Female chemical plant employees had a greater proportion of recurrence than female film plant employees. Nevertheless, the prevalence of episodes of care of the Category defined as lower and unspecified urinary tract infections was comparable for the unique long-term, high exposure chemical plant employees (20/211 = 9.5 percent) and the film plant employees (34/345 = 9.8 percent). There was no increased risk observed for upper urinary tract calculi. Laboratory results have not suggested animals were at increased risk for urinary tract infections in either a 2-year feeding study of rats or a 6-month feeding study of cynomolgus primates for PFOS [3M Company, 2000]. A major exposure route for serum PFOS levels assayed in Decatur employees, however, is the inhalation of POSF [Logan et al, 2001]. To date, there is minimal information regarding the toxicology of POSF via inhalation. Urinalysis findings have not been

reported in previous medical surveillance reports on this plant population [Olsen et al, 1999].

The increased RRE_pC for the Specialty Category of Cancers and Benign Growths was primarily attributed to neoplasms of the gastrointestinal tract and neoplasms of the skin. No episode of care of malignant neoplasm of the liver was reported among chemical plant employees compared to one episode of care in the film plant. Among all study subjects, the observed to expected number of benign colonic polyps was twice the expected for the chemical plant (48 versus 24.6) and forty percent higher than expected among film plant employees (47 versus 33.7). Whether this was the result of increased incidence, prevalence and/or that of heightened awareness through a screening program is not certain. We are aware that a chemical plant manager was diagnosed with colorectal cancer in 1997 and this may have heightened increased awareness among some employees for colorectal cancer screening in the latter two years of this study (Table 12). It should be noted that the RRE_pC for benign colonic polyps was increased for high exposure employees (1.9, 95% CI 1.1-3.2) and for those long-term high exposure chemical plant employees (2.4, 95% CI 1.3-4.5). The frequency of adenomatous polyps often parallels colorectal cancer incidence and colorectal cancer is generally not viewed as an occupational disease [Schottenfeld and Winawer, 1996]. In the updated retrospective cohort mortality study of this Decatur workforce there were no observed colorectal cancer deaths compared to 1.6 expected among employees ever employed in a high exposure job, 1 colorectal cancer death compared to 0.8 expected among employees ever employed in a low exposure job (but never a high exposure job) and 0 colorectal cancer deaths compared to 1.5 expected among employees who only worked in the film

plant. There was no evidence reported of colorectal pathology in a six-month primate feeding study of PFOS [Seacat et al, 2001]. Results from a two-year PFOS bioassay study in rats is pending [3M Company, 2000] but there was no pathology reported in the interim 14 week analysis[Seacat et al, 2001].

The increased RRE_pC observed for neoplasms of the skin were primarily attributed by malignant melanoma of the skin and benign neoplasms. Exposure to sunlight is considered a major cause of malignant melanoma in susceptible populations [Armstrong and English, 1996]. There was no increased RRE_pC for nonmalignant melanomas of the skin (i.e., basal cell and squamous cell carcinomas). There was an increased RRE_pC for benign neoplasm of the skin. However, histopathology was not available and thus these benign neoplasm findings are difficult to interpret.

We did observe an increased RRE_pC for malignant neoplasm of the prostate among all subjects (10.0, 95% CI 1.3-447). This increased RRE_pC was largely due to a deficit of observed episodes of care among the film plant employees (1 observed versus 5.3 expected) rather than as a consequence of a large excess of observed episodes of care among the chemical plant employees (5 observed versus 3.1 expected). The total evidence suggests that a prior history of prostatic diseases may be associated with an increased risk of prostate cancer [Ross and Schottenfeld, 1996]. In our study we did not observe an increased RRE_pC with prostatic hyperplasia nor for acute prostatitis. Among the long-term high exposure comparison population, the RRE_pC for prostatic hyperplasia was 1.0(95% CI 0.6-1.5) and for acute prostatitis the RRE_pC was 1.4 (95% CI 0.9-2.2). In addition, there were no observed deaths reported for prostate cancer in the 37 year follow-up of the retrospective cohort mortality study [Alexander, 2001b] at the Decatur

site. Nor was there an increased SMR for prostate cancer mortality that was recently reported among Cottage Grove employees who historically have had the highest serum PFOA levels among the 3M fluorochemical manufacturing sites [Alexander, 2001a].

Decreased cholesterol was the most sensitive clinical response, occurring only at serum PFOS levels > 100 ppm, in a six month oral dosing study of cynomolgus primates [Seacat et al, 2001]. Although there was no Specialty Category, Category or Class descriptions for hypolipidemia in our study, we did not observe any decreased RRE_pCs for hyperlipidemia. Among long-term high exposed workers, the RRE_pC for hyperlipidemia was 0.9 (95% CI 0.7-1.3). A lack of an association was expected as serum PFOS levels in these Decatur chemical plant employees have not been found to be generally above 10 ppm [Olsen et al, 2001] nor associated with decreased serum cholesterol in biennial medical surveillance examinations [Olsen et al, 1999].

Except for the episode of care described as cholelithiasis with acute cholecystitis, we observed no increased RRE_pC for other disorders of the biliary tract or for disorders of the liver. This single association was due to a combination of increased observed to expected episodes of care among the chemical plant employees (7 versus 4.2) and the opposite occurrence among film plant employees (1 observed versus 5.2 expected). This magnitude of association for cholelithiasis with acute cholecystitis remained for long-term high exposed employees ($RRE_pC > 4.0$, 95% CI 2.1-128). Laboratory evidence is unlikely to provide substantial additional perspective. The biliary tract of the rat is substantially different than humans. At necropsy, there were no gallstones reported in a 6 month feeding study of cynomolgus primates [Seacat et al, 2001].

There was minimal evidence for an increased risk of episodes of care among female chemical employees for pregnancy outcomes and complications, congenital anomalies and perinatal disorders. The RRE_pC for preterm labor was 3.0 (95% CI 0.3-144) based on 4 episodes of care. However, these 4 episodes of care arose from one employee. Although we observed an increased RRE_pC for menopausal and menstrual disorders among those employees who only worked in the chemical plant compared to their film plant counterparts, this association was based on observed to expected ratios that were less than one for both plants. This finding was not replicated among the analyses for the high exposed and long-term high exposed comparison groups.

Although we found no increased RRE_pC for Parkinson's disease, we were perplexed by the large number of unique episodes of care reported (17 chemical employees, 19 film employees) as the prevalence in the general population is estimated at 0.1 percent [Tanner and Goldman, 1996]. Our prevalence of episodes of care, based on these 36 unique episodes, was 2.8 percent. Further investigation revealed that the CCG grouping process for Parkinson's Disease took into account prescription drugs (via the CCG Drug Disease Matcher) as well as medical claims. An individual prescribed a drug that is considered a delineating drug for Parkinson's would be categorized as such in the episode of care algorithm although there was no ICD-9 code to substantiate a diagnosis. A review of the claims and pharmacy records of these 36 individuals revealed that only 5 individuals (3 chemical, 2 film) had outpatient claims with ICD-9 codes (332, 333) that would be consistent with a diagnosis of Parkinson's Disease. However, two of these five individuals (both with ICD-9 codes of 333 and not 332) only had one claim for a prescription in this six year time period. Nineteen of the 36 individuals had their only

episode of care as a prescription for amantadine hydrochloride. We suspect that these 19 were prescribed amantadine hydrochloride for its anti-influenza A effects. There were, however, no ICD-9 codes for respiratory claims within the 30 day time period of the prescription. Therefore, we can only suspect that these prescriptions were done without a face-to-face encounter. No single physician was the predominant prescriber of these prescriptions. Of the remaining 12 individuals, only three had multiple prescriptions for Sinemet™. The remaining nine were also identified with single prescriptions considered in the Drug Disease Matching program for Parkinson's Disease without any evidence of a face-to-face physician encounter. Therefore, we believe there was a minimum of 3 individuals (2 chemical, 1 film) and no more than 8 individuals (4 chemical, 4 film) that could have been diagnosed with Parkinson's Disease (4 chemical, 4 film) among the 36 individuals (17 chemical, 19 film) who were identified by the CCG grouper to have episodes of care for Parkinson's Disease. This assumption would represent a study population prevalence of 0.2 and 0.6 percent, respectively for Parkinson's Disease.

In summary, we conducted an analysis of the episodes of care of 652 chemical and 659 film plant employees at the Decatur manufacturing site from 1993-1998. Although the analyses of episodes of care does not translate into a well-defined epidemiologic measure, it can be used as a screening method to determine if a study population could be at an increased risk for a disease or condition. Our analysis was further limited by the study time period of six years, 1993-1998. Further investigation would always be required to determine whether an increase in incidence or prevalence actually exists based on the episodes of care reported. In our study the overall episodes of care experience was comparable between chemical and film plant employees for most

Specialty Categories, Categories and Class diseases and conditions. Where increased RRE_pCs were observed, they were often attributed to a deficit of observed episodes of care in the film plant as much as any observed excess of episodes of care in the chemical plant. These high RRE_pC values often had very wide 95% confidence intervals which did not exclude, or barely excluded, the null value. Of our *a priori* concerns, we did not observe positive associations that excluded the null hypothesis for malignant neoplasm of the liver, liver disorders, thyroid and lipid metabolism disorders and reproductive, pregnancy, congenital and perinatal disorders. We did observe an association with cholelithiasis with acute cholecystitis; this was due, in part, to a greater than expected number of episodes of care in the film plant. Other biliary tract disorders did not exclude the null hypothesis in the confidence interval.

Because of the previously reported increased mortality risk for bladder cancer among the chemical plant employees, we focused particular attention on episodes of care which involved the urogenital tract. We found one episode of care for bladder cancer reported for a film plant employee who had never worked in the chemical plant. We did observe a greater increased risk in episodes of care among chemical plant employees for lower urinary tract infections but this was largely due to increased percentages of these employees having recurring episodes of care, rather than a greater prevalence of individuals having episodes of care. This increased risk of episodes of care was greater among the long-term high exposure chemical plant workers. It is not known whether this recurrence is a result of occupational exposure or nonoccupational-related factors. Other associations observed, that were not *a priori* concerns, included increased risk of episodes of care for benign colonic polyps and malignant neoplasms of the colorectal

tract as well as malignant neoplasms of prostate. Whether these associations have a biological rationale is questionable as other toxicologic and epidemiologic research does not offer support in relation to the serum PFOS and/or PFOA levels measured in Decatur chemical plant employees.

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REFERENCES

Alexander BH (2001a). Mortality study of workers employed at the 3M Cottage Grove facility. Minneapolis:University of Minnesota (unpublished report) April 26, 2001.

Alexander BH (2001b). Mortality study of workers employed at the 3M Decatur facility. Minneapolis:University of Minnesota (unpublished report) April 26, 2001.

Armstrong BK, English DR (1996). Cutaneous malignant melanoma. (In) Cancer Epidemiology and Prevention (second edition) , eds Schottenfeld D, Fraumeni JF. New York:Oxford University Press, pages 1282-1312.

Borak J, Bidulescu A (2000). Some thoughts on multiple comparisons and their correction. OEM Report 14:65-71.

Cook JC, Murray SM, Frame SR, Hurtt ME (1992). Induction of Leydig cell adenomas by ammonium perfluorooctanoate: a possible endocrine-related mechanism. Toxicol Appl Pharmacol 113:209-217.

Biegel LG, Liu RCM, Hurtt ME, Cook JC (1995). Effects of ammonium perfluorooctanoate on Leydig cell function: in vitro, in vivo , and ex vivo studies. Toxicol Appl Pharmacol 134:18-25.

Butenhoff J, Costa G, Clecombe C, Farrar D, Hansen K, Iwai H, Jung R, Kennedy G, Lieder P, Olsen G, Thomford P. Toxicity of ammonium perfluorooctanoate in cynomolgus monkeys after 26 weeks of oral dosing. St. Paul:3M Company (unpublished report).

Cave DG (1995). Profiling physician practice patterns using diagnostic episode clusters. Med Care 35:463-486.

Dang DK, Pont JM, Portnoy MA (1996a). Episode treatment groups: an illness classification and episode building system. Part I. Med Int 1996 (March):118-122.

Dang DK, Pont JM, Portnoy MA (1996b). Episode treatment groups: an illness classification and episode building system. Part II. Med Int 1996 (April):122-128.

Documenta Geigy Scientific Tables (1967). Seventh edition. Editors Diem K, Lenter K. Ciba-Geigy Limited; Basle, Switzerland.

Ederer F, Mantel N (1974). Confidence limits on the ratio of two Poisson variables. Am J Epidemiol 100:165-167.

Fetter R, Shin Y, Freemen J, Averill R, Thomspon J (1980). Case mix definition by diagnosis-related groups. Med Care 18(2 suppl):1-53.

Gilliland FD, Mandel JS (1993). Mortality among employees of a perfluorooctanoic acid production plant. J Occup Med 35:950-954.

Gilliland FD, Mandel JS (1996). Serum perfluorooctanoic acid and hepatic enzymes, lipoproteins and cholesterol: a study of occupationally exposed men. Am J Ind Med 129:560-568.

Greene SB, Gunselman DL (1984). Conversion of claims files to an episode data base: a tool for management and research. Inquiry 21:189-194.

Hornbrook MC, Hurtado A, Johnson R: Health care episodes: Definition, measurement and use. Med Care Rev 1985;42:163-218.

Logan PW, Johnson TM, Olsen GW, Reagen WK, Mulhausen JR (2001). An industrial hygiene exposure assessment of a fluorochemical manufacturing plant. Am Ind Hyg Assoc J (submitted).

Obourn JD, Frame SR, Bell RH, Longnecker DS, Elliott GS, Cook JC (1997). Mechanisms for the pancreatic oncogenic effects of the perixosme proliferator Wyeth-14,643. Toxicol Appl Pharmacol 145:425-436.

Olsen GW, Gilliland FD, Burlew MM, Burris JM, Mandel JS, Mandel JH (1998). An epidemiologic investigation of reproductive hormones in men with occupational exposure to perfluorooctanoic acid J Occup Env Med 40:614-622.

Olsen GW, Burris JM, Mandel JH, Zobel LR (1999). Serum perfluorooctane sulfonate and hepatic and lipid clinical chemistry tests in fluorochemical production employees. JOEM 41:799-806.

Olsen GW, Burris JM, Burlew MM, Mandel JH (2000). Plasma cholecystokinin and hepatic enzymes, cholesterol and lipoproteins in ammonium perfluorooctanoate production workers. Drug Chem Toxicol 23:603-620.

Olsen GW, Logan PW, Hansen KJ, Simpson CA, Burris JM, Burlew MM, Vorarath SP, Venkateswarlu P, Schumpert JC, Mandel JH. Serum fluorochemicals in a random sample of production employees (2001). Am Ind Hyg Assoc J (submitted)

Rosen AK, Mayer-Oakes A (1999). Episodes of Care: Theoretical frameworks versus current operational realities. J Quality Improvement 25:111-128.

Ross RK, Schottenfeld D (1996). Prostate Cancer. (In) Cancer Epidemiology and Prevention (second edition) , eds Schottenfeld D, Fraumeni JF. New York:Oxford University Press, pages 1180-1206.

Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology 1990;1:43-46.

Schneider K, Linchtenstein J, Freeman JL, Newbold RC, Fetter RB, Gottleib L, Leaf PJ, Portlock CS (1988). J Ambulatory Care Manage 11(3)1-12.

Schottenfeld D, Winawer SJ (1996). Cancers of the large intestine. (In) Cancer Epidemiology and Prevention (second edition) , eds Schottenfeld D, Fraumeni JF. New York:Oxford University Press, pages 813-840.

Scotto J, Fears TR, Kkraemer KH, Fraumeni JF (1996). Nonmelanoma skin cancer. (In) Cancer Epidemiology and Prevention (second edition) , eds Schottenfeld D, Fraumeni JF. New York:Oxford University Press, pages 1313-1330.

Seacat AM, Thomford PJ, Hansen KJ, Olsen GW, Case MT, Butenhoff JL (2001a). Investigation of the no observable effect level for perfluorooctanesulfonic acid potassium salt in cynomolgus monkeys after twenty-six weeks of oral dosing and one year of recovery. Toxicol Sciences (submitted).

Seacat AM, Thomford PJ, Hansen KJ, Clemen LA, Case MT, Butenhoff JL (2001). Sub-chronic dietary toxicity of potassium perfluorooctanesulfonic acid in rats. Toxicol Sciences (submitted).

Sibinski LJ (1987). Two-year oral (diet) toxicity/carcinogenicity study of fluorochemical FC-143 in rats. St. Paul:Riker Laboratories.

3M Company (2000). SIDS Initial Assessment Report Pefluorooctane Sulfonic Acid and Its Salts. Minneapolis:3M Company, Sept 20, 2000.

Solon JA (1967). Delineating episodes of medical care. Am J Public Health 57:401-408.

Tanner CM, Goldman SM (1996). Epidemiology of Parkinson's disease. Neuroepidemiology 14:317-335.

Tsai SP, Wen CP (1986). A review of methodological issues of the standardized mortality ratio (SMR) in occupational cohort studies. Int J Epidemiol 15:8-21.

Valdivia T, Van Vorst K (2000). Clinical Care Groups™ Methodology. Ingenix:Minneapolis.

Wingert TD, Kralewski JE, Lindquist TJ, Knutson DJ (1995). Constructing episodes of care from encounter and claims data: some methodological issues. Inquiry 32:430-443 (Winter 1995/96).

Table 1
Demographic Characteristics of the Four Comparison Group Analysis Between Decatur Chemical and Film Plant Employees

	Study Group 1		Study Group 3		Study Group 5		Study Group 6	
Variable	Chemical	Film	Chemical	Film	Chemical	Film	Chemical	Film
N	652	659	388	424	498	490	211	345
Male	530 (81)	558 (85)	311 (80)	364 (86)	423 (85)	425 (87)	196 (89)	308 (93)
Female	122 (19)	101 (15)	77 (20)	60 (14)	75 (15)	65 (13)	15 (11)	37 (7)
Age (end of study)								
< 30	59 (9)	36 (5)	51 (13)	34 (8)	43 (9)	19 (4)	0 (0)	0 (0)
30 – 39	124 (19)	82 (12)	83 (21)	62 (15)	104 (21)	65 (13)	1 (0)	10 (3)
40 – 49	238 (37)	194 (29)	118 (30)	149 (35)	194 (39)	151 (31)	99 (47)	112 (32)
50 – 59	182 (28)	267 (41)	107 (28)	152 (36)	122 (25)	194 (40)	86 (41)	173 (50)
≥ 60	49 (8)	80 (12)	29 (7)	27 (6)	35 (7)	61 (12)	25 (12)	50 (15)
Average Age (yrs)	45.1	48.6	44.0	46.3	44.5	49.0	50.7	52.3
Only worked in Chemical Plant	388 (60)	424 (64)	388 (100)	424 (100)	298 (60)	322 (66)	128 (61)	212 (61)
High exposure job	498 (76)	508 (77)	298 (77)	322 (76)	498 (100)	490 (100)	211 (100)	345 (100)
Worked only in Chemical (or Film) Plant and, at least, from 1983 – 1998	177 (27)	269 (41)	177 (46)	269 (63)	128 (26)	212 (43)	128 (61)	212 (61)

Table 2

Employment Status by Gender and Plant of Study Comparison Group A,
January 1, 1993 and December 31, 1998

	Chemical			Film		
	Male	Female	Total	Male	Female	Total
January 1, 1993						
Active	361 (68)	66 (54)	427 (65)	433 (78)	69 (68)	502 (76)
Inactive	12 (2)	8 (7)	20 (3)	22 (4)	4 (4)	26 (4)
Not yet hired	157 (30)	48 (39)	205 (31)	103 (18)	28 (28)	131 (26)
Retired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Terminated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deceased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transferred	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL	530 (100)	122 (100)	652 (100)	558 (100)	101 (100)	659 (100)
December 31, 1998						
Active	419 (79)	92 (75)	511 (78)	396 (71)	74 (73)	470 (71)
Inactive	17 (3)	12 (10)	29 (4)	26 (5)	13 (13)	39 (6)
Not yet hired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retired	62 (12)	10 (8)	72 (11)	105 (19)	7 (7)	112 (17)
Terminated	18 (3)	5 (4)	23 (4)	17 (3)	5 (5)	22 (3)
Deceased	7 (1)	0 (0)	7 (1)	8 (1)	0 (0)	8 (1)
Transferred	7 (1)	3 (2)	10 (2)	6 (1)	2 (2)	8 (1)
TOTAL	530 (100)	122 (100)	652 (100)	558 (100)	101 (100)	659 (100)

Table 3

Employment Status by Gender and Plant of Study Comparison Group B,
January 1, 1993 and December 31, 1998

	Chemical			Film		
	Male	Female	Total	Male	Female	Total
January 1, 1993						
Active	169 (54)	33 (43)	202 (52)	260 (71)	36 (60)	296 (70)
Inactive	8 (3)	3 (4)	11 (3)	12 (3)	0 (0)	12 (3)
Not yet hired	134 (43)	41 (53)	175 (45)	92 (25)	24 (40)	116 (27)
Retired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Terminated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deceased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transferred	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL	311 (100)	77 (100)	388 (100)	364 (100)	60 (100)	424 (100)
December 31, 1998						
Active	243 (78)	58 (75)	301 (78)	289 (79)	49 (82)	338 (80)
Inactive	12 (4)	7 (9)	19 (5)	17 (5)	7 (12)	24 (6)
Not yet hired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retired	37 (12)	8 (10)	45 (12)	35 (10)	0 (0)	35 (8)
Terminated	11 (4)	2 (3)	13 (3)	13 (4)	2 (3)	15 (4)
Deceased	2 (1)	0 (0)	2 (1)	4 (1)	0 (0)	4 (1)
Transferred	6 (2)	2 (3)	8 (2)	6 (2)	2 (3)	8 (2)
TOTAL	311 (100)	77 (100)	388 (100)	364 (100)	60 (100)	424 (100)

Table 4

Employment Status by Gender and Plant Comparison Group C,
January 1, 1993 and December 31,1998

	Chemical			Film		
	Male	Female	Total	Male	Female	Total
January 1, 1993						
Active	273 (65)	35 (47)	308 (62)	323 (76)	47 (72)	370 (76)
Inactive	11 (3)	7 (9)	18 (1)	20 (5)	2 (3)	22 (4)
Not yet hired	139 (33)	33 (44)	172 (35)	82 (19)	16 (25)	98 (20)
Retired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Terminated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deceased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transferred	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL	423 (100)	75 (100)	490 (100)	425 (100)	65 (100)	498 (100)
December 31, 1998						
Active	345 (82)	55 (73)	400 (80)	299 (70)	47 (72)	346 (71)
Inactive	14 (3)	8 (11)	22 (4)	24 (6)	9 (14)	33 (7)
Not yet hired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retired	42 (10)	6 (8)	48 (10)	80 (19)	4 (6)	84 (12)
Terminated	15 (4)	5 (7)	20 (4)	14 (3)	5 (8)	19 (4)
Deceased	6 (1)	0 (0)	6 (1)	8 (0)	0 (0)	8 (0)
Transferred	1 (0)	1 (1)	2 (0)	0 (0)	0 (0)	0 (0)
TOTAL	423 (100)	75 (100)	490 (100)	425 (100)	65 (100)	498 (100)

Table 5

Employment Status by Gender and Plant of Study Comparison Group D,
January 1, 1993 and December 31, 1998

	Chemical			Film		
	Male	Female	Total	Male	Female	Total
January 1, 1993						
Active	195 (99)	15 (100)	196 (93)	308 (100)	37 (100)	345 (100)
Inactive	1 (1)	0 (0)	15 (7)	0 (0)	0 (0)	0 (0)
Not yet hired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Terminated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deceased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transferred	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL	196 (100)	15 (100)	211 (100)	308 (100)	37 (100)	345 (100)
December 31, 1998						
Active	147 (75)	9 (60)	156 (74)	212 (69)	25 (68)	237 (69)
Inactive	6 (3)	1 (7)	7 (3)	13 (4)	7 (19)	20 (6)
Not yet hired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retired	34 (17)	5 (33)	39 (18)	74 (24)	3 (8)	77 (22)
Terminated	5 (3)	0 (0)	5 (2)	5 (2)	2 (5)	7 (2)
Deceased	4 (2)	0 (0)	4 (2)	4 (1)	0 (0)	4 (1)
Transferred	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL	196 (100)	15 (100)	211 (100)	308 (100)	37 (100)	345 (100)

Table 6

Number of Inpatient and Outpatient Claims by Plant by Four Study Groups
1993 – 1998

	Chemical Plant					Film Plant				
	Cohort Size	Total Number of Claims		Average Person/Year		Cohort Size	Total Number of Claims		Average Person/Year	
		Inpatient	Outpatient	Inpatient	Outpatient		Inpatient	Outpatient	Inpatient	Outpatient
Study Group A	652	204	34,053	0.05	8.7	659	237	40,174	0.06	10.2
Study Group B	388	91	17,655	0.04	7.6	424	152	24,051	0.06	9.5
Study Group C	498	156	24,036	0.05	8.0	490	183	30,010	0.06	10.2
Study Group D	211	81	13,743	0.06	10.9	345	131	23,572	0.06	11.4

Table 7

Observed, Expected and Unique Number of Individuals by Plant with Risk Ratios of Episode of Care (with and without correction factor) and 95% Confidence Interval of Risk Ratio (not corrected) for CCG Specialty Category, Category, and Class Descriptions

Study Comparison Group A (All Employee Study Subjects)

CCG Specialty Category, Category and Class Description	Chemical			Film			RRE_pC_{cr}	RRE_pC	95% CI
	Obs	Exp	Unique Number of Individuals (%)	Obs	Exp	Unique Number of Individuals (%)			
1. Infectious Diseases	582	599.6	402 (69)	680	612.7	432 (64)	1.0	0.9	**0.8 – 1.0**
Mycoses	3	1.7	3 (100)	5	2.0	5 (100)	0.7	0.7	**0.1 – 3.6**
Septicemia	1	3.0	1 (100)	4	3.8	4 (100)	0.3	0.3	**0.0 – 3.2**
Tuberculosis	1	1.2	1 (100)	1	1.3	1 (100)	-	-	-
HIV	0	0.6	0 (-)	0	0.6	0 (-)	-	-	-
Viral Infections, other	0	1.9	0 (-)	0	1.8	0 (-)	-	-	-
Other infections	577	591.1	401(69)	670	603.2	430 (64)	1.0	0.9	**0.8 – 1.0**
2. Cancers and Benign Growths	303	270.7	192 (63)	273	320.4	174 (64)	1.4	1.3	**1.1 – 1.6**
Neoplasms of the head and neck	3	1.3	3 (100)	0	1.8	0 (-)	> 2.3	> 2.3	**0.6 - 1000**
Neoplasms of the gastrointestinal tract	58	29.8	39 (67)	53	40.8	41 (77)	1.6	1.5	**1.0 – 2.2**
Malignant neoplasm of colon	4	1.8	4 (100)	1	2.4	1 (100)	6.5	5.4	**0.5 – 265**
Malignant neoplasm of liver	0	0.5	0 (-)	1	0.6	1 (100)	-	-	-
Malignant neoplasm of pancreas	1	0.4	1 (100)	0	0.6	0 (-)	-	-	-
Malignant neoplasm of rectum and anus	4	1.3	4 (100)	3	1.8	3 (100)	2.2	1.8	**0.3 – 12.4**
Carcinoma *in situ,* digestive tract	1	0.5	1 (100)	1	0.7	1 (100)	-	-	-

Table 7 (continued)

Benign colonic polyps	48	24.6	37 (77)	47	33.7	38 (81)	1.5	1.4	**0.9 – 2.1**
Neoplasms of the respiratory tract	2	2.5	2 (100)	1	3.3	1 (100)	3.3	2.6	**0.1 – 155**
Malignant neoplasm of lower respiratory tract	2	2.1	2 (100)	1	2.8	1 (100)	3.3	2.7	**0.1 – 158**
Neoplasms of bones and connective tissue	1	0.6	1 (100)	0	0.8	0 (-)	-	-	-
Malignant neoplasm of bone	1	0.6	1 (100)	0	0.8	0 (-)	-	-	-
Neoplasms of skin	116	97.9	105 (91)	108	114.1	93 (86)	1.3	1.3	**1.0 – 1.6**
Malignant melanoma of skin	5	2.2	5 (100)	0	2.6	0 (-)	> 2.3	> 2.3	**1.0 – 63**
Malignant neoplasm of skin other than melanoma	17	23.8	14 (82)	26	31.6	22 (85)	0.9	0.9	**0.5 – 1.7**
Benign neoplasm of skin	94	71.9	93 (99)	82	79.8	79 (96)	1.3	1.3	**0.9 – 1.7**
Neoplasms of the breast and female reproductive system	33	40.8	30 (91)	24	41.6	22(92)	1.4	1.4	**0.8 – 2.5**
Malignant neoplasm of female breast	2	3.5	2 (100)	0	4.0	0 (-)	-	-	-
Malignant neoplasm of body of uterus	1	0.4	1 (100)	0	0.4	0 (-)	-	-	-
Benign neoplasm of breast	10	16.8	9 (90)	10	17.6	10 (100)	1.1	1.1	**0.4 – 2.8**
Benign ovarian cyst	12	8.6	12 (100)	5	7.7	5 (100)	2.0	2.2	**0.7 – 7.8**
Benign neoplasm of ovary other than cyst	1	0.9	1 (100)	0	0.8	0 (-)	-	-	-
Uterine leiomyoma	7	9.7	7 (100)	9	10.1	9 (100)	0.8	0.8	**0.3 – 2.4**
Neoplasms of the urinary tract	0	1.8	0 (-)	2	2.4	2 (100)	0.0	0.0	**0.0 – 7.2**
Malignant neoplasm of bladder	0	1.0	0 (-)	1	1.5	1 (100)	-	-	-
Malignant neoplasm of kidney	0	0.7	0 (-)	1	0.9	1 (100)	-	-	-

Table 7 (continued)

Neoplasms of male reproductive system	7	3.7	7 (100)	1	5.3	1 (100)	10.1	10.0	**1.3 – 447**
Malignant neoplasm of prostate	5	3.1	5 (100)	1	4.7	1 (100)	7.8	7.7	**0.9-364**
Malignant neoplasm of testicle	2	0.6	2 (100)	0	0.6	0 (-)	-	-	-
Neoplasms of the nervous system	1	1.6	1 (100)	1	1.9	1 (100)	-	-	-
Malignant neoplasm of CNS, primary	1	1.3	1 (100	1	1.6	1 (100)	-	-	-
Neoplasms of endocrine organs	1	1.0	1 (100)	0	1.1	0 (-)	-	-	-
Malignant neoplasm of thyroid	1	1.0	1 (100)	0	1.1	0 (-)	-	-	-
Other neoplasms	77	85.3	71 (92)	74	101.9	67 (91)	1.3	1.2	**0.9 – 1.7**
Malignant neoplasm, other	5	5.5	5 (100)	4	6.7	4 (100)	1.6	1.5	**0.3 – 7.7**
Malignent neoplasm, unspecified and secondary	0	0.8	0 (-)	1	1.0	1 (100)	-	-	-
Metastatic cancers other than lymph nodes	6	4.4	6 (100)	5	5.6	5 (100)	1.6	1.6	**0.4 – 6.4**
Carcinoma *in situ* other than skin, respiratory or gastrointestinal	0	3.0	0 (-)	1	3.3	1 (100)	-	-	-
Other benign or unspecified neoplasm	66	71.7	64 (97)	63	85.4	63 (100)	1.3	1.3	**0.9 – 1.8**
Neoplasms of the hematologic system	4	4.4	4 (100)	9	5.2	8 (89)	0.6	0.5	**0.1 – 1.9**
Leukemia, chronic	0	0.8	0 (-)	3	1.1	3 (100)	0.0	0.0	**0.0 – 3.1**
Lymphoma	3	2.4	3 (100)	3	2.8	3 (100)	1.4	1.2	**0.2 – 8.7**
Multiple myeloma	1	0.4	1 (100)	1	0.5	1 (100)	-	-	-
Myeloproliferative syndrome	0	0.4	0 (-)	2	0.4	2 (100)	-	-	-
3. Endocrine Disorders	370	367.3	224 (61)	453	438.8	266 (59)	1.0	1.0	**0.9 – 1.1**
Disorders of the thyroid	31	51.2	22 (71)	33	57.1	28 (85)	1.1	1.1	**0.6 – 1.8**

Table 7 (continued)

Acquired hypothyroidism with surgery	24	38.8	21 (88)	23	43.4	23 (100)	1.2	1.2	**0.6 – 2.1**
Hyperthyroidism other than in pregnancy	4	6.7	4 (100)	5	7.5	5 (100)	0.9	0.9	**0.2 – 4.1**
Thyroid nodule, benign nontoxic	1	3.2	1 (100)	3	3.5	3 (100)	0.4	0.4	**0.0 – 4.6**
Thyroiditis	2	2.5	2 (100)	2	2.7	2 (100)	1.0	1.1	**0.1 – 15.1**
Diabetes	69	66.7	41 (59)	91	84.4	62 (68)	1.0	1.0	**0.7 – 1.3**
Diabetes Type I with complications	4	2.5	4 (100)	1	3.2	1 (100)	5.8	5.1	**0.5 – 247**
Diabetes Type I without complications	10	10.0	10 (100)	12	12.3	12 (100)	1.1	1.0	**0.4 – 2.6**
Diabetes Type II with complications	11	14.6	11 (100)	15	19.1	15 (100)	1.0	1.0	**0.4 – 2.2**
Diabetes Type II without complications	44	39.5	40 (91)	63	49.9	60 (95)	0.9	0.9	**0.6 – 1.3**
Disorders of lipid metabolism (hyperlipidemia)	157	139.2	141 (90)	194	172.7	173 (89)	1.0	1.0	**0.8 – 1.3**
Fluid and electrolyte disorders	21	17.9	16 (76)	28	20.9	23 (82)	0.9	0.9	**0.5 – 1.6**
Other endocrine or nutritional disorders	92	92.4	78 (85)	107	103.7	86 (80)	1.0	1.0	**0.7 – 1.3**
Adrenal insufficiency	0	0.5	0 (-)	1	0.5	1 (100)	-	-	-
Hyperparathyroidism	1	0.7	1 (100)	2	0.8	2 (100)	0.8	0.6	**0.0 – 12**
Hypoglycemia	8	6.9	7 (88)	12	7.6	10 (75)	0.8	0.7	**0.3 – 2.0**
Obesity	43	41.4	42 (98)	46	45.0	43 (93)	1.1	1.0	**0.7 – 1.6**
Osteoporosis	2	2.9	2 (100)	3	3.4	3 (100)	0.9	0.8	**0.1 – 7.0**
Other endocrine, nutritional and metabolic disorders	38	40.0	37 (97)	43	46.1	41 (93)	1.0	1.0	**0.6 – 1.6**
4. Hematologic Disorders	44	46.4	36 (82)	43	53.0	39 (91)	1.2	1.2	**0.8 – 1.8**
Anemia, acquired	9	8.6	9 (100)	5	9.8	5 (100)	1.9	2.1	**0.6 – 7.8**

Table 7 (continued)

	Disorders of hemostatic function	2	0.9	1 (50)	0	1.1	0 (-)	-	-	0.2 - 1000
	Other hematologic disorders	33	36.7	30 (91)	38	42.0	36 (95)	1.1	1.0	0.6 – 1.6
5.	**Psychiatric Disorders**	389	398.4	218 (56)	368	427.9	204 (55)	1.2	1.1	1.0 – 1.3
	Affective disorders	138	150.8	105 (76)	113	158.1	84 (74)	1.4	1.3	1.0 – 1.7
	Depression, major without psychotic behavior	81	60.3	77 (95)	66	64.1	63 (95)	1.4	1.3	0.9 – 1.8
	Depression, minor	47	76.8	45 (96)	36	79.5	34 (94)	1.5	1.4	0.9 – 2.1
	Dissociative and personality disorders	3	4.0	3 (100)	3	4.0	3 (100)	1.1	1.0	0.1 – 7.4
	Neurotic disorders (anxiety disorders)	45	55.4	42 (93)	46	59.1	43 (93)	1.1	1.0	0.7 – 1.6
	Organic mental disorders	1	2.2	1 (100)	1	3.0	1 (100)	-	-	-
	Psychotic disorders	0	3.2	0 (-)	2	3.4	2 (100)	-	-	-
	Substance abuse	201	178.8	155 (77)	200	196.3	144 (72)	1.2	1.1	0.9 – 1.4
6a.	**Neurologic Disorders**	186	211.4	129 (69)	236	236.9	160 (68)	0.9	0.9	0.7 – 1.1
	Congenital or acquired central degenerative disorders	19	13.3	17 (89)	22	14.9	21 (95)	1.0	1.0	0.5 – 1.9
	Benign essential tremor	2	1.9	2 (100)	2	2.3	2 (100)	1.1	1.2	0.1 – 16.4
	Parkinson's disease	17	9.1	17 (100)	19	10.1	19 (100)	1.0	1.0	0.5 – 2.0
	Hemorrhage, cerebrovascular, or other major CNS disorders	18	18.3	13 (72))	26	24	19 (73)	1.0	0.9	0.5 – 1.7
	Other diseases of the nervous system	86	94.3	69 (80)	100	101.5	82 (82)	0.9	0.9	0.7 – 1.3
	Migraine	42	37.1	37 (88)	36	37.8	31 (86)	1.1	1.2	0.8 – 1.9
	Tension headache	6	10.4	4 (67)	5	10.9	4 (80)	1.2	1.3	0.3 – 5.2
	Peripheral neuromuscular disorders	63	82.4	57 (90)	87	92.9	79 (91)	0.9	0.8	0.6 – 1.1

Table 7 (continued)

	Neuralgia, neuritis, radicolitis	42	59.8	42 (100)	66	67.7	62 (94)	0.8	0.7	0.5 – 1.1
	Carpal tunnel syndrome	18	18.7	18 (100)	20	20.8	20 (100)	1.0	1.0	0.5 – 2.0
6b.	**Opthamologic Disorders**	166	267.7	116 (70)	220	302.3	155 (70)	0.9	0.9	0.7 – 1.1
	Disorders of the eye	166	267.7	116 (70)	220	302.3	155 (70)	0.9	0.9	0.7 – 1.1
	Cataract	14	15.3	14 (100)	14	20.7	13 (93)	1.4	1.4	0.6 – 3.1
	Conjunctivitis, acute	20	46.7	20 (100)	31	50.2	29 (94)	0.7	0.7	0.4 – 1.3
	Glaucoma	8	17.9	8 (100)	19	22.4	18 (95)	0.6	0.5	0.2 – 1.3
7.	**Cardiovascular Disorders**	413	423	234 (57)	571	533	282 (49)	1.0	0.9	0.8 – 1.0
	Hypertension	157	149.4	145 (92)	203	185.4	186 (92)	1.0	1.0	0.8 – 1.2
	Atherosclerotic coronary vascular disease and cardiac arrest	82	76.1	51 (62)	134	102.6	65 (49)	0.9	0.8	0.6 – 1.1
	Carditis and cardiomyopathy/CHF	8	11.9	7 (88)	15	16.2	11 (73)	0.7	0.7	0.3 – 1.8
	Disorders of heart valves	20	12.3	19 (95)	20	15.3	20 (100)	1.2	1.2	0.6 – 2.4
	Dysrhythmia and conduction disorders	14	22.8	12 (86)	18	29.8	17 (94)	1.2	1.0	0.5 – 2.1
	Large arterial and peripheral vascular disorders	3	5.2	3 (100)	4	7.2	4 (100)	1.1	1.1	0.2 – 6.2
	Large vein thromboembolic disorders	5	9.0	3 (60)	9	10.8	8 (89)	0.8	0.7	0.2 – 2.2
	Minor venous/arterial disorders	2	15.2	2 (100)	1	17.2	1 (100)	2.2	2.3	0.1 – 133
	Other cardiovascular disorders	122	120.5	102 (84)	167	147.9	130 (78)	1.0	0.9	0.7 – 1.1
8a.	**Pulmonary Disorders**	849	691.8	381 (45)	897	757.6	394 (44)	1.1	1.0	0.9 – 1.1
	Lower respiratory infections	315	305.0	181 (57)	327	337.9	181 (55)	1.1	1.1	0.9 – 1.3
	Obstructive pulmonary diseases	53	60.2	46 (87)	60	68.7	55 (92)	1.1	1.0	0.7 – 1.5

Table 7 (continued)

Asthma	23	36.9	22 (96)	28	39.5	27 (96)	1.0	0.9	0.5 – 1.6
Chronic obstructive pulmonary disease	30	23.3	30 (100)	32	29.2	31 (97)	1.2	1.2	0.7 – 2.0
Other pulmonary disorders	459	307.7	329 (72)	482	327.5	344 (71)	1.1	1.0	0.9 – 1.2
Atelectasis	4	3.6	4 (100)	4	4.6	4 (100)	1.2	1.3	0.2 – 7.0
Painful respiration	29	21.8	21 (72)	35	24.7	33 (94)	1.1	0.9	0.6 – 1.6
Pleurisy with or without effusion	7	10.4	3 (43)	14	12.1	9 (64)	0.7	0.6	0.2 – 1.5
Pulmonary eosinophilia	7	3.1	7 (100)	10	3.9	10 (100)	0.9	0.9	0.3 – 2.6
Other disorders of the respiratory system	409	264.3	311 (76)	411	276.8	327 (80)	1.1	1.0	0.9 – 1.2
Pulmonary edema	2	7.4	2 (100)	3	9.5	3 (100)	0.8	0.9	0.1 – 7.4
Respiratory failure	0	0.4	0 (-)	1	0.5	1 (100)	-	-	-
Sleep disorders	20	11.1	20 (100)	24	13.6	23 (96)	1.1	1.0	0.5 – 1.9
8b. Ear, Nose and Throat Disorders	1443	1347.3	398 (28)	1620	1437.8	418 (26)	1.0	1.0	0.9 – 1.0
Disorders of the ear and vestibular apparatus	233	267.3	137 (59)	267	293.2	160 (60)	1.0	1.0	0.8 – 1.2
Upper respiratory infections	1020	888.1	328 (32)	1116	940.1	355 (32)	1.0	1.0	0.9 – 1.1
Pharyngitis, acute	223	212.2	119 (53)	202	215.8	116 (57)	1.2	1.1	0.9 – 1.4
Sinusitis, acute	384	271.9	116 (43)	426	290.2	166 (39)	1.0	1.0	0.8 – 1.1
Chronic sinusitis, with surgery	95	82.2	93 (98)	108	89.0	106 (98)	1.1	1.0	0.7 – 1.3
Upper respiratory infection and common cold, acute	299	302.5	128 (43)	368	326.8	152 (41)	1.0	0.9	0.8 – 1.0
Other upper respiratory disorders	190	191.8	162 (85)	237	204.4	184 (78)	0.9	0.9	0.7 – 1.0

Table 7 (continued)

Allergic rhinitis	162	163.5	149 (92)	193	173.3	170 (88)	0.9	0.9	0.7 – 1.1
9. Gastrointestinal Disorders	631	520.5	264 (42)	755	604.3	306 (41)	1.0	1.0	0.9 – 1.1
Disorders of esophagus	80	51.7	68 (85)	109	61.2	89 (82)	0.9	0.9	0.6 – 1.2
Disorders of stomach and duodenum	65	48.0	53 (82)	112	55.7	75 (40)	0.7	0.7	0.5 – 0.9
Disorders of the small intestine	2	4.4	2 (100)	4	4.6	3 (75)	0.6	0.5	0.1 – 3.6
Hernias	27	34.3	23 (85)	59	42.0	49 (83)	0.6	0.6	0.4 – 0.9
Inflammatory bowel disease	13	8.6	13 (100)	7	9.6	7 (100)	2.1	2.1	0.8 – 6.1
Disorders of the large intestine	153	107.8	107 (70)	176	129.9	121 (69)	1.1	1.1	0.8 – 1.3
Disorders of the liver	3	6.0	3 (100)	3	6.9	3 (100)	1.3	1.2	0.2 – 8.6
Cirrhosis of liver without mention of alcohol	2	0.9	2 (100)	0	1.1	0 (-)	-	-	-
Hepatitis, acute alcoholic	0	0.3	0 (-)	1	0.4	1 (100)	-	-	-
Hepatitis, acute without hepatic coma	0	2.5	0 (-)	2	2.7	2 (100)	-	-	-
Hepatitis, chronic without hepatic coma	1	1.6	1 (100)	0	1.8	0 (-)	-	-	-
Disorders of the biliary tract	26	25.7	13 (50)	20	30.6	12 (60)	1.7	1.6	0.8 – 2.9
Cholecystitis without cholelithiasis, acute	1	2.2	1 (100)	2	2.7	2 (100)	0.7	0.6	0.0 – 12
Cholecystitits without choleithiasis, chronic or other	5	4.0	5 (100)	4	4.7	4 (100)	1.6	1.5	0.3 – 7.3
Cholelithiasis with acute cholecystitits	7	4.2	5 (71)	1	5.2	1 (100)	10.1	8.6	1.1 – 380.7
Cholelithiasis with chronic or unspecified cholecystitits	8	9.1	8 (100)	6	10.7	6 (100)	1.7	1.6	0.5 – 5.5
Cholelithiasis without cholecystitis	5	6.1	5 (100)	7	7.3	7 (100)	0.9	0.9	0.2 – 3.1

Table 7 (continued)

	Disorders of the pancreas	7	4.2	1 (14)	3	5.4	2 (67)	2.5	3.0	**0.7 – 18**
	Pancreatis, acute	6	3.6	1 (17)	3	4.7	2 (67)	2.1	2.6	**0.6 – 15.8**
	Pancreatis, chronic	1	0.6	1 (100)	0	0.7	0 (-)	-	-	-
	Other gastrointestinal disorders	255	229.9	200 (78)	262	258.5	208 (79)	1.2	1.1	**0.9 – 1.3**
10a.	**Urologic Disorders**	411	269.0	163 (40)	481	318.4	205 (43)	1.1	1.0	**0.9 – 1.2**
	Disorders of renal function	5	3.9	4 (80)	2	4.9	2 (100)	3.2	3.1	**0.5 – 33**
	Chronic renal failure	4	2.6	4 (100)	1	3.1	1 (100)	5.2	4.9	**0.5 – 238**
	Disorders of renal parenchyma	3	1.7	3 (100)	1	2.1	1 (100)	3.5	3.7	**0.3 – 192**
	Renal cyst	3	1.7	3 (100)	1	2.1	1 (100)	3.5	3.7	**0.3 – 192**
	Lower and unspecified urinary tract infections	127	94.5	57 (45)	107	99.3	66 (62)	1.3	1.3	**1.0 – 1.6**
	Cystitis	56	23.3	19 (34)	40	24.3	31 (78)	1.5	1.5	**1.0 – 2.2**
	Urinary tract, not specified	71	71.2	47 (66)	67	75.1	45 (67)	1.1	1.1	**0.8 – 1.6**
	Other disorders of the lower urinary tract	2	4.3	2 (100)	15	4.9	14 (93)	0.2	0.2	**0.0 – 0.7**
	Urethra stricture	2	4.3	2 (100)	15	4.9	14 (93)	0.2	0.2	**0.0 – 0.7**
	Other disorders of the upper urinary tract	73	32.2	34 (47)	85	38.9	44 (52)	1.1	1.0	**0.8 – 1.4**
	Calculus of urinary tract	73	32.2	34 (47)	85	38.9	44 (52)	1.1	1.0	**0.8 – 1.4**
	Other genitourinary disorders	62	48.5	60 (97)	81	57.1	79 (98)	1.0	0.9	**0.6 – 1.3**
	Other diseases with surgery	62	48.5	60 (97)	81	57.1	79 (98)	1.0	0.9	**0.6 – 1.3**
	Upper urinary tract infections	7	4.0	6 (86)	7	4.3	5 (71)	1.1	1.1	**0.3 – 3.5**
	Acute pyelonephritis	7	4.0	6 (86)	7	4.3	5 (71)	1.1	1.1	**0.3 – 3.5**
	Disorders of the prostate	132	79.8	83 (63)	183	106.8	113 (62)	1.0	1.0	**0.8 – 1.2**

Table 7 (continued)

	Prostatic hyperplasia	59	40.6	53 (95)	83	58.1	79 (95)	1.0	1.0	0.7 – 1.4
	Prostatitis, acute	73	39.2	55 (58)	100	48.7	60 (60)	1.0	0.9	0.7 – 1.2
10b.	**Gynecologic and Reproductive Disorders**	354	378.4	182 (51)	323	374.1	193 (60)	1.2	1.1	0.9 – 1.3
	Disorders of the female breast (non-malignant)	32	29.8	28 (88)	21	31.3	19 (90)	1.6	1.6	0.9 – 2.9
	Fibrocystic disease of breast	27	21.4	26 (96)	16	22.3	16 (100)	1.8	1.8	0.9 – 3.4
	Infections of the female genital tract	32	44.7	22 (69)	24	39.7	18 (75)	1.3	1.2	0.7 – 2.1
	Menopausal and menstrual disorders	44	74.0	34 (77)	42	75.8	31 (74)	1.1	1.1	0.7 – 1.7
	Other gynecologic disorders	112	106.1	75 (67)	81	101.3	61 (75)	1.3	1.3	1.0 – 1.8
	Endometriosis	11	6.1	11 (100)	6	5.5	6 (100)	1.7	1.7	0.6 – 5.4
	Fertility and infertility management	134	123.8	109 (81)	155	126.0	125 (81)	1.0	0.9	0.7 – 1.1
	Contraceptive or procreative management	41	51.8	40 (98)	28	38.6	28 (100)	1.1	1.1	0.7 – 1.8
	Infertility female	2	4.2	2 (100)	2	2.9	2 (100)	0.6	0.7	0.1 – 9.7
	Impotence of organic origin	47	26.3	45 (96)	51	36.0	50 (98)	1.2	1.3	0.8 – 1.9
	Other disorders of the male reproductive system	44	41.6	42 (95)	74	48.5	71 (96)	0.8	0.7	0.5 – 1.0
11.	**Pregnancy**	40	44.7	13 (33)	23	26.3	8 (35)	1.0	1.0	0.6 – 1.8
	Complicated pregnancy or delivery	29	30.2	12 (41)	16	18.6	8 (50)	1.0	1.1	0.6 – 2.2
	Diabetes, gestational	1	0.6	1 (100)	0	0.3	0 (-)	-	-	-
	Multiple gestational	1	0.5	1 (100)	0	0.2	0 (-)	-	-	-
	Postpartum hemorrhage	1	1.8	1 (100)	1	1.3	1 (100)	-	-	-
	Pregnancy with abortion	3	2.8	3 (100)	1	1.8	1 (100)	1.5	1.9	0.2 – 101

Table 7 (continued)

	Pregnancy, ectopic	1	0.4	1 (100)	0	0.2	0 (-)	-	-	-
	Preterm labor	7	3.1	3 (43)	1	1.7	1 (100)	3.6	3.9	0.5 – 172
	Other conditions during pregnancy	15	20.5	12 (80)	13	12.6	8 (62)	0.6	0.7	0.3 – 1.6
	Normal or unspecified pregnancy and delivery	11	14.5	9 (82)	7	7.7	5 (71)	0.9	0.8	0.3 – 2.6
	Spontaneous abortion	2	1.2	2 (100)	0	0.7	0 (-)	-	-	-
	Pregnancy	9	13.3	9 (100)	7	7.0	5 (71)	0.7	0.7	0.2 – 2.2
12.	**Dermatologic Disorders**	870	936.5	351 (40)	929	1035.5	369 (40)	1.1	1.0	0.9 – 1.1
	Dermatologic infections	282	289.3	164 (58)	286	320.6	165 (58)	1.2	1.1	0.9 – 1.3
	Disorders of the hair and nails	15	32.8	13 (87)	20	36.6	17 (85)	1.0	0.8	0.4 – 1.7
	Immune mediated skin conditions	134	160.0	85 (63)	133	175.2	82 (62)	1.2	1.1	0.9 – 1.4
	Other dermatologic conditions	439	454.4	266 (61)	490	503.2	290 (59)	1.1	1.0	0.9 – 1.1
13.	**Musculoskeletal Disorders**	1396	1420.0	365 (26)	1741	1587.1	426 (24)	1.0	0.9	0.8 – 1.0
	Acute or unspecified arthropathies and minor tendonitis	128	169.7	87 (68)	205	193.4	125 (61)	0.8	0.7	0.6 – 0.9
	Crystalline arthritis	17	15.2	16 (94)	25	19.1	22 (88)	0.9	0.9	0.4 – 1.6
	Degenerative joint disorders, other than spine	65	80.8	50 (77)	115	96.6	97 (84)	0.7	0.7	0.5 – 0.9
	Disorders of the spine	388	351.7	209 (54)	499	389.4	235 (47)	0.9	0.9	0.8 – 1.0
	Vasculitis and connective tissue disorders	13	9.5	13 (100)	18	11.1	16 (89)	0.9	0.9	0.4 – 1.8
	Other	785	793.2	295 (38)	879	877.5	340 (39)	1.1	1.0	0.9 – 1.1
14.	**Congenital Anomalies**	25	28.4	25 (100)	27	31.2	26 (96)	1.1	1.0	0.6-1.8
	Congenital Anomalies	25	28.4	25 (100)	27	31.2	26 (96)	1.1	1.0	0.6-1.8

Table 7 (continued)

	Atrial septal defect	0	0.3	0 (-)	1	0.4	1 (100)	-	-	-
	Other cardiovascular congenital abnormalities	2	3.0	2 (100)	5	3.8	5 (100)	0.6	0.5	0.1 – 3.1
	Other congenital abnormalities with admittance	22	24.3	22 (100)	20	26.2	20 (100)	1.2	1.2	0.6 – 2.3
	Other respiratory congenital abnormalities	1	0.6	1 (100)	1	0.7	1 (100)	-	-	-
15.	**Perinatal Disorders**	1	2.7	1 (100)	4	2.6	4 (100)	0.2	0.2	0.0 – 2.4
	Conditions originating in the perinatal period	1	2.7	1 (100)	4	2.6	4 (100)	0.2	0.2	0.0 – 2.4
16.	**Miscellaneous**	1620	1692.1	506 (31)	1697	1867.3	525 (31)	1.1	1.1	1.0 – 1.1
	Other miscellaneous conditions	427	707.6	287 (67)	455	773.0	319 (70)	1.1	1.0	0.9 – 1.2
	Routine health care	235	308.3	220 (94)	254	328.4	233 (92)	1.0	1.0	0.8 – 1.2
	Symptoms or signs	1193	984.5	461 (39)	1242	1094.3	480 (39)	1.1	1.1	1.0 – 1.2
	Abdominal pain	199	143.3	139 (70)	180	159.9	127 (71)	1.4	1.2	1.0 – 1.5
	Chest pain, unspecified	186	133.1	125 (67)	209	162.3	132 (63)	1.1	1.1	0.9 – 1.3
	Fever	20	16.5	20 (100)	28	18.2	28 (100)	0.8	0.8	0.4 – 1.5
	Headache with radiology	130	114.0	76 (58)	120	120.2	70 (58)	1.2	1.1	0.9 – 1.5
	Malaise and fatigue	65	66.6	55 (85)	66	73.4	57 (86)	1.1	1.0	0.8 – 1.6
	Syncope and collapse	19	18.6	15 (79)	19	22.0	15 (79)	1.2	1.2	0.6 – 2.3
	Symptoms, signs and ill – defined conditions	574	490.9	409 (71)	620	536.3	431 (70)	1.1	1.0	0.9 – 1.1
17.	**Injury and Poisoning**	515	787.3	259 (50)	616	844.5	294 (48)	1.0	0.9	0.8 – 1.0
	Major traumatic injury	121	224.2	85 (70)	140	241.0	106 (76)	1.0	0.9	0.7 – 1.2

Table 7 (continued)

Minor traumatic injury	284	445.1	178 (63)	363	473.4	219 (60)	0.9	0.8	0.7 – 1.0
Other injury	110	118.1	97 (88)	113	130.1	94 (83)	1.2	1.1	0.8 – 1.4

Table 8

Observed, Expected and Unique Number of Individuals by Plant with Risk Ratios of Episode of Care (with and without correction factor) and 95% Confidence Interval of Risk Ratio (not corrected) for CCG Specialty Category, Category, and Class Descriptions

Study Comparison Group B (Only Chemical or Only Film Employees)

	Chemical			Film					
CCG Specialty Category, Category and Class Description	Obs	Exp	Unique Number of Individuals (%)	Obs	Exp	Unique Number of Individuals (%)	RRE_pC_{cr}	RRE_pC	95% CI
1. Infectious Diseases	315	315.5	225 (71)	437	385.7	285 (65)	1.0	0.9	0.8 – 1.0
Mycoses	1	0.9	1 (100)	2	1.2	2 (100)	0.7	0.6	0.0 – 12.4
Septicemia	1	1.6	1 (100)	4	2.2	4 (100)	0.4	0.3	0.0 – 3.5
Tuberculosis	0	0.6	0 (-)	0	0.8	0 (-)	-	-	-
HIV	0	0.3	0 (-)	0	0.3	0 (-)	-	-	-
Viral infections, other	0	1.0	0 (-)	0	1.2	0 (-)	-	-	-
Other infections	313	311.0	225 (72)	431	379.9	284 (66)	1.0	0.9	0.8 – 1.0
2. Cancers and Benign Growths	167	145.9	109 (65)	166	190.5	109 (66)	1.3	1.3	1.1 – 1.6
Neoplasms of the head and neck	1	0.8	1 (100)	0	1.0	0 (-)	-	-	-
Neoplasms of the gastrointestinal tract	30	16.5	21 (70)	29	23.2	26 (90)	1.5	1.5	0.9 – 2.5
Malignant neoplasm of colon	3	1.0	3 (100)	0	1.5	0 (-)	>3.0	3.0	0.6 – 43
Malignant neoplasm of liver	0	0.3	0 (-)	1	0.4	1 (100)	-	-	-
Malignant neoplasm of pancreas	0	0.2	0 (-)	0	0.4	0 (-)	-	-	-
Malignant neoplasm of rectum and anus	3	0.7	3 (100)	1	1.0	1 (100)	4.2	4.1	0.3 – 217
Carcinoma *in situ*, digestive tract	0	0.3	0 (-)	0	0.4	0 (-)	-	-	-

Table 8 (continued)

Benign colonic polyps	24	13.6	20 (83)	27	19.2	24 (89)	1.3	1.3	0.7 – 2.2
Neoplasms of the respiratory tract	0	1.4	0 (-)	0	1.9	0 (-)	-	-	-
Malignant neoplasm of lower respiratory tract	0	1.1	0 (-)	0	1.4	0 (-)	-	-	-
Neoplasms of bones and connective tissue	0	0.3	0 (-)	0	0.4	0 (-)	-	-	-
Malignant neoplasm of bone	0	0.3	0 (-)	0	0.4	0 (-)	-	-	-
Neoplasms of skin	70	52.1	64 (91)	65	69.9	57 (88)	1.4	1.4	1.0 – 2.1
Malignant melanoma of skin	4	1.2	4 (100)	0	1.7	0 (-)	> 3.3	> 3.3	0.9 – 59
Malignant neoplasm of skin other than melanoma	10	13.0	8 (80)	13	18.5	11 (85)	1.1	1.1	0.4 – 2.7
Benign neoplasm of skin	56	37.9	55 (98)	52	49.8	50 (96)	1.4	1.4	1.0 – 2.1
Neoplasms of the breast and female reproductive system	16	22.1	15 (94)	13	23.6	13 (100)	1.4	1.3	0.6 – 3.0
Malignant neoplasm of female breast	2	1.9	2 (100)	0	2.2	0 (-)	-	-	-
Malignant neoplasm of body of uterus	0	0.2	0 (-)	0	0.2	0 (-)	-	-	-
Benign neoplasm of breast	7	9.1	7 (100)	5	10.0	5 (100)	1.7	1.5	0.4 – 6.2
Benign ovarian cyst	3	4.6	3 (100)	2	4.5	2 (100)	1.3	1.5	0.2 – 18
Benign neoplasm of ovary other than cyst	0	0.5	0 (-)	0	0.5	0 (-)	-	-	-
Uterine leiomyoma	4	5.3	4 (100)	6	5.7	6 (100)	0.7	0.7	0.2 – 3.0
Neoplasms of the urinary tract	0	1.0	0 (-)	2	1.4	2 (100)	-	-	-
Malignant neoplasm of bladder	0	0.6	0 (-)	1	0.8	1 (100)	-	-	-
Malignant neoplasm of kidney	0	0.4	0 (-)	1	0.5	1 (100)	-	-	-

Table 8 (continued)

Neoplasms of male reproductive tract	4	2.1	4 (100)	1	3.0	1 (100)	5.4	5.7	0.6 – 276
Malignant neoplasm of prostate	3	1.8	3 (100)	1	2.5	1 (100)	4.2	4.3	0.3 – 224
Malignant neoplasm of testicle	1	0.3	1 (100)	0	0.4	0 (-)	-	-	-
Neoplasms of the nervous system	1	0.9	1 (100)	0	1.1	0 (-)	-	-	-
Malignant neoplasm of CNS, primary	1	0.7	1 (100)	0	0.9	0 (-)	-	-	-
Neoplasms of endocrine organs	0	0.5	0 (-)	0	0.7	0 (-)	-	-	-
Malignant neoplasm of thyroid	0	0.5	0 (-)	0	0.7	0 (-)	-	-	-
Other neoplasms	41	45.9	39 (95)	49	61.1	44 (90)	1.1	1.1	0.7 – 1.7
Malignant neoplasm, other	3	3.0	3 (100)	4	3.9	4 (100)	1.0	1.0	0.2 – 5.9
Malignant neoplasm, unspecified and secondary	0	0.4	0 (-)	0	0.6	0 (-)	-	-	-
Metastatic cancers other than lymph nodes	0	2.4	0 (-)	3	3.2	3 (100)	0.0	0.0	0.0 – 3.2
Carcinoma *in situ,* other than skin, respiratory or gastrointestinal	0	1.6	0 (-)	1	1.9	1 (100)	-	-	-
Other benign or unspecified neoplasm	38	38.4	37 (97)	41	51.5	41 (100)	1.3	1.2	0.8 – 2.0
Neoplasms of the hematologic system	4	2.3	4 (100)	7	3.2	6 (86)	0.8	0.8	0.2 – 3.1
Leukemia, chronic	0	0.4	0 (-)	2	0.6	2 (100)	-	-	-
Lymphoma	3	1.2	3 (100)	2	1.7	2 (100)	2.3	2.1	0.2 – 25.2
Multiple myeloma	1	0.2	1 (100)	1	0.3	1 (100)	-	-	-
Myeloproliferative syndrome	0	0.2	0 (-)	2	0.3	2 (100)	-	-	-
3. Endocrine Disorders	194	197.0	124 (64)	251	263.6	152 (61)	1.1	1.0	0.9 – 1.3
Disorders of the thyroid	18	27.5	13 (72)	18	33.6	16 (89)	1.2	1.2	0.6 – 2.5

Table 8 (continued)

Acquired hypothyroidism with surgery	14	20.9	12 (86)	13	25.5	13 (100)	1.3	1.3	0.6 – 3.0
Hyperthyroidism other than in pregnancy	2	3.6	2 (100)	2	4.4	2 (100)	1.1	1.2	0.1 – 17
Thyroid nodule, benign nontoxic	1	1.7	1 (100)	1	2.1	1 (100)	-	-	-
Thyroiditis	1	1.3	1 (100)	2	1.6	2 (100)	0.7	0.6	0.0 – 11.6
Diabetes	27	36.1	17 (63)	52	50.0	35 (67)	0.8	0.7	0.4 – 1.2
Diabetes Type I with complications	1	1.4	1 (100)	0	1.9	0 (-)	-	-	-
Diabetes Type I without complications	3	5.4	3 (100)	7	7.5	7 (100)	0.7	0.6	0.1 – 2.6
Diabetes Type II with complications	6	8.0	6 (100)	7	11.1	7 (100)	1.3	1.2	0.3 – 4.1
Diabetes Type II without complications	17	21.4	16 (94)	38	29.6	35 (92)	0.6	0.6	0.3 – 1.1
Disorders of lipid metabolism (hyperlipidemia)	93	74.4	83 (89)	104	105	92 (88)	1.3	1.3	0.9 – 1.7
Fluid and electrolyte disorders	8	9.6	4 (50)	17	12.3	15 (88)	0.6	0.6	0.2 – 1.5
Other endocrine or nutritional disorders	48	49.3	43 (90)	60	62.7	48 (80)	1.1	1.0	0.7 – 1.5
Adrenal insufficiency	0	0.3	0 (-)	0	0.3	0 (-)	-	-	-
Hyperparathyroidism	1	0.4	1 (100)	0	0.5	0 (-)	-	-	-
Hypoglycemia	4	3.6	3 (79)	8	4.8	6 (75)	0.7	0.7	0.2 – 2.5
Obesity	20	21.9	20 (100)	27	27.6	24 (89)	1.0	0.9	0.5 – 1.7
Osteoporosis	1	1.6	1 (100)	3	1.9	3 (100)	0.4	0.4	0.0 – 5.0
Other endocrine, nutritional and metabolic disorders	22	21.5	22 (100)	22	27.6	21 (95)	1.4	1.3	0.7 – 2.4
4. Hematologic Disorders	22	24.9	20 (91)	26	31.6	22 (85)	1.2	1.1	0.6 – 2.0
Anemia, acquired	5	4.7	5 (100)	4	5.8	4 (100)	1.6	1.6	0.3 – 7.8

Table 8 (continued)

	Other hematologic disorders	17	19.7	16 (94)	22	25.2	20 (91)	1.1	1.0	0.5 – 1.9
5.	**Psychiatric Disorders**	181	209.5	106 (59)	229	268.1	127 (55)	1.1	1.0	0.8 – 1.2
	Affective disorders	60	78.9	47 (78)	74	100.2	52 (70)	1.1	1.0	0.7 – 1.5
	Depression, major without psychotic behavior	34	31.7	33 (97)	42	40.2	40 (95)	1.1	1.0	0.6 – 1.7
	Depression, minor	22	40.1	21 (95)	25	50.8	24 (96)	1.2	1.1	0.6 – 2.1
	Dissociative and personality disorders	1	2.1	1 (100)	2	2.6	2 (100)	0.5	0.6	0.0 – 12.2
	Neurotic disorders (anxiety disorders)	20	29.0	19 (95)	29	37.4	26 (90)	0.9	0.9	0.5 – 1.6
	Organic mental disorders	1	1.2	1 (100)	1	1.7	1 (100)	-	-	-
	Psychotic disorders	0	1.7	0 (-)	1	2.1	1 (100)	-	-	-
	Substance abuse	98	94.5	79 (81)	120	121.4	87 (73)	1.1	1.1	0.8 – 1.4
6a.	**Neurologic Disorders**	84	112.4	59 (70)	136	144.5	90 (66)	0.8	0.8	0.6 – 1.1
	Congenital or acquired central degenerative disorders	7	7.0	7 (100)	13	9.2	13 (100)	0.7	0.7	0.2 – 1.9
	Benign essential tremor	0	1.0	1 (100)	1	1.4	1 (100)	-	-	-
	Parkinson's disease	7	4.8	7 (100)	12	6.3	12 (100)	0.8	0.8	0.3 – 2.1
	Hemorrhage, cerebrovascular, or other major CNS disorders	7	10.1	7 (100)	19	13.8	13 (68)	0.5	0.5	0.2 – 1.2
	Other diseases of the nervous system	42	50.1	34 (81)	54	62.0	43 (80)	1.0	1.0	0.6 – 1.5
	Migraine	16	19.6	15 (94)	22	23.3	19 (86)	0.8	0.9	0.4 – 1.7
	Tension headache	0	5.0	0 (-)	4	6.0	3 (77)	0.0	0.0	0.0 – 1.8
	Peripheral neuromuscular disorders	28	43.5	25 (89)	50	57.5	43 (86)	0.7	0.7	0.5 – 1.2
	Neuralgia, neuritis, radiculitis	17	31.6	17 (100)	38	41.9	35 (92)	0.6	0.6	0.3 – 1.1

Table 8 (continued)

	Carpel tunnel syndrome	10	9.9	10 (100)	12	12.7	12 (100)	1.1	1.1	0.4 – 2.7
6b.	**Opthamologic Disorders**	91	142.7	64 (70)	120	184.0	95 (79)	1.0	1.0	0.7 – 1.3
	Disorders of the eye	91	142.7	64 (70)	120	184.0	95 (79)	1.0	1.0	0.7 – 1.3
	Cataract	10	8.5	10 (100)	7	11.4	6 (86)	2.0	1.9	0.7 – 5.9
	Conjunctivitis, acute	11	24.6	11 (100)	18	31.0	17 (94)	0.8	0.8	0.3 – 1.7
	Glaucoma	5	9.6	5 (100)	10	13.4	10 (100)	0.7	0.7	0.2 – 2.2
7.	**Cardiovascular Disorders**	216	229.4	122 (56)	326	315.6	165 (51)	0.9	0.9	0.8 – 1.1
	Hypertension	81	80.1	76 (94)	122	111.8	114 (93)	0.9	0.9	0.7 – 1.2
	Atherosclerotic coronary vascular disease	38	41.7	24 (63)	80	60.0	34 (43)	0.7	0.7	0.5 – 1.0
	Carditis and cardiomyopathy/CHF	6	6.6	5 (83)	10	9.1	7 (70)	0.8	0.8	0.3 – 2.5
	Disorders of heart valves	6	6.7	6 (100)	9	8.9	9 (100)	0.9	0.9	0.3 – 2.8
	Dysrhythmia and conduction disorders	7	12.5	6 (86)	8	17.3	8 (100)	1.2	1.2	0.4 – 3.8
	Large arterial and peripheral vascular disorders	2	2.9	2 (100)	1	4.0	1 (100)	2.8	2.8	0.1 – 162
	Large vein thromboembolic disorders	1	4.8	1 (100)	3	6.4	3 (100)	0.5	0.4	0.0 – 5.5
	Minor venous/arterial disorders	2	8.2	2 (100)	0	10.1	0 (-)	-	-	-
	Other cardiovascular disorders	73	65.2	61 (84)	93	87.3	73 (78)	1.1	1.1	0.8 – 1.4
8a.	**Pulmonary Disorders**	430	365.8	202 (47)	524	468.6	240 (46)	1.1	1.1	0.9 – 1.2
	Lower respiratory infections	149	161.3	91 (61)	196	208.5	114 (58)	1.0	1.0	0.8 – 1.2
	Obstructive pulmonary diseases	29	32.1	25 (86)	39	41.7	34 (87)	1.1	1.0	0.6 – 1.6
	Asthma	15	19.4	15 (100)	14	24.6	13 (93)	1.5	1.4	0.6 – 3.0
	Chronic obstructive pulmonary disease	14	12.7	14 (100)	25	17.1	24 (96)	0.8	0.8	0.4 – 1.5

Table 8 (continued)

	Other pulmonary disorders	236	162.3	170 (72)	275	204.1	198 (72)	1.2	1.1	0.9 – 1.3
	Atelectasis	4	1.9	4 (100)	3	2.7	3 (100)	2.2	1.9	0.3 – 12.6
	Painful respiration	13	11.5	9 (69)	18	15.2	16 (89)	1.0	1.0	0.4 – 2.0
	Pleurisy with or without effusion	0	5.5	0 (-)	8	7.3	5 (63)	0.0	0.0	0.0 – 0.8
	Pulmonary eosinophilia	4	1.7	4 (100)	5	2.3	5 (100)	1.2	1.1	0.2 – 5.0
	Other disorders of the respiratory system	215	139.2	163 (76)	240	173.3	190 (79)	1.2	1.1	0.9 – 1.4
	Pulmonary edema	1	4.0	1 (100)	2	5.5	2 (100)	0.7	0.7	0.0 – 13
	Respiratory failure	0	0.2	0 (-)	1	0.3	1 (100)	-	-	-
	Sleep disorders	15	5.9	15 (100)	11	8.4	10 (91)	2.0	2.0	0.8 – 4.7
8b.	**Ear, Nose and Throat Disorders**	699	707.1	221 (32)	941	906.1	256 (27)	1.0	1.0	0.9 – 1.1
	Disorders of the ear and vestibular apparatus	119	140.6	72 (61)	150	184.1	95 (63)	1.1	1.0	0.8 – 1.3
	Upper respiratory infections	490	465.7	175 (36)	649	593.4	198 (31)	1.0	1.0	0.9 – 1.1
	Pharyngitis, acute	113	110.7	64 (57)	124	138.3	71 (57)	1.1	1.1	0.9 – 1.5
	Sinusitis, acute	191	142.8	91 (48)	220	182.1	96 (44)	1.1	1.1	0.9 – 1.4
	Sinusitis, chronic with surgery	44	43.2	43 (98)	63	56.1	61 (97)	0.9	0.9	0.6 – 1.4
	Upper respiratory infection and common cold, acute	136	159.0	62 (46)	232	205.1	93 (40)	0.8	0.8	0.6 – 0.9
	Other upper respiratory disorders	90	100.8	82 (91)	142	128.6	112 (79)	0.8	0.8	0.6 – 1.1
	Allergic rhinitis	81	85.9	77 (95)	116	109.0	102 (88)	0.9	0.9	0.7 – 1.2
9.	**Gastrointestinal Disorders**	320	277.0	139 (43)	467	369.6	187 (40)	1.0	0.9	0.8 – 1.1
	Disorders of esophagus	37	27.5	34 (92)	61	37.5	53 (87)	0.8	0.8	0.5 – 1.3

Table 8 (continued)

Disorders of stomach and duodenum	31	25.5	27 (87)	75	34.0	49 (65)	0.5	0.6	0.4 – 0.9
Disorders of the small intestine	1	2.3	1 (100)	4	3.0	3 (75)	0.4	0.3	0.0 – 3.3
Hernias	15	18.3	13 (87)	34	25.7	29 (85)	0.6	0.6	0.3 – 1.2
Inflammatory bowel disease	3	4.5	3 (100)	5	6.0	5 (100)	0.9	0.8	0.1 – 4.1
Disorders of the large intestine	77	57.8	56 (73)	105	78.6	75 (71)	1.0	1.0	0.7 – 1.4
Disorders of the liver	3	3.1	3 (100)	3	4.4	3 (100)	1.3	1.4	0.2 – 11
Cirrhosis of liver without mention of alcohol	2	0.5	2 (100)	0	0.7	0 (-)	-	-	0.4 – 27.2
Hepatitis, acute alcoholic	0	0.2	0 (-)	1	0.2	1 (100)	-	-	-
Hepatitis, acute without hepatic coma	0	1.3	0 (-)	2	1.8	2 (200)	-	-	-
Hepatitis, chronic without hepatic coma	1	0.9	1 (100)	0	1.2	0 (-)	-	-	-
Disorders of the biliary tract	18	13.9	8 (44)	11	17.8	6 (55)	2.5	2.1	0.9 – 4.9
Cholecystitis without cholelithiasis, acute	0	1.2	0 (-)	1	1.5	1 (100)	-	-	-
Cholecystitis without cholelithiasis, chronic or other	3	2.2	3 (100)	1	2.8	1 (100)	4.6	3.8	0.3 – 198
Cholelithiasis with acute cholecystitis	6	2.3	4 (67)	1	3.0	1 (100)	8.8	7.8	0.9 – 358
Cholelithiasis with chronic or unspecified cholecystitis	5	4.9	5 (100)	3	6.3	3 (100)	2.5	2.13	0.4 – 13.7
Cholelithiasis without cholecystitis	4	3.3	4 (100)	5	4.2	5 (100)	1.3	1.0	0.2 – 4.8
Disorders of the pancreas	7	2.3	1 (14)	3	3.2	2 (67)	3.8	3.3	0.8 – 20
Pancreatitis, acute	6	2.0	1 (17)	3	2.8	2 (67)	3.3	2.8	0.6 – 17.2
Pancreatitis, chronic	1	0.3	1 (100)	0	0.4	0 (-)	-	-	-

Table 8 (continued)

	Other gastrointestinal disorders	128	121.8	98 (77)	166	159.5	131 (79)	1.1	1.0	0.8 – 1.3
10a.	**Urologic Disorders**	273	144	97 (36)	303	192.0	124 (41)	1.2	1.2	1.0 – 1.4
	Disorders of renal function	4	2.1	3 (75)	1	3.0	1 (100)	5.8	5.6	0.6 – 271
	Chronic renal failure	3	1.4	3 (75)	1	1.9	1 (100)	4.2	4.2	0.4 – 104
	Disorders of renal parenchyma	1	0.9	1 (100)	1	1.3	1 (100)	-	-	-
	Renal cyst	1	0.9	1 (100)	1	1.3	1 (100)	-	-	-
	Lower and unspecified urinary tract infections	96	50.7	36 (38)	73	59.0	44 (60)	1.6	1.5	1.1 – 2.1
	Cystitis	47	12.5	13 (28)	27	14.3	20 (74)	1.9	2.0	1.2 – 3.3
	Urinary tract, not specified	49	38.1	29 (59)	46	44.7	32 (70)	1.3	1.3	0.8 – 1.9
	Other disorders of the lower urinary tract	1	2.3	1 (100)	11	3.1	11 (100)	0.1	0.1	0.0 – 0.9
	Urethral stricture	1	2.3	1 (100)	11	3.1	11 (100)	0.1	0.1	0.0 – 0.9
	Other disorders of the upper urinary tract	51	17.0	18 (35)	56	24.3	30 (54)	1.4	1.3	0.9 – 1.9
	Calculus of urinary tract	51	17.0	18 (35)	56	24.3	30 (54)	1.4	1.3	0.9 – 1.9
	Other genitourinary disorders	34	25.9	33 (97)	49	34.6	48 (98)	0.9	0.9	0.6 – 1.5
	Other diseases with surgery	34	25.9	33 (97)	49	34.6	48 (98)	0.9	0.9	0.6 – 1.5
	Upper urinary tract infections	4	2.2	3 (75)	6	2.6	4 (67)	0.9	0.8	0.2 – 3.4
	Acute pyelonephritis	4	2.2	3 (75)	6	2.6	4 (67)	0.9	0.8	0.2 – 3.4
	Disorders of the prostate	82	43.3	48 (59)	106	64.1	63 (59)	1.2	1.1	0.9 – 1.5
	Prostatic hyperplasia	29	22.6	25 (86)	42	33.3	39 (93)	1.0	1.0	0.6 – 1.7
	Prostatitis, acute	53	20.7	29 (55)	64	30.8	38 (59)	1.3	1.2	0.8 – 1.8

Table 8 (continued)

10b.	**Gynecologic and Reproductive Disorders**	187	203.1	99 (53)	192	223.1	122 (64)	1.1	1.1	0.9 – 1.3
	Disorders of the female breast (non-malignant)	18	16.1	16 (89)	13	17.7	11 (85)	1.5	1.5	0.7 – 3.3
	Fibrocystic disease of breast	15	11.6	14 (93)	10	12.5	10 (100)	1.6	1.6	0.7 – 4.1
	Infections of the female genital tract	18	24.2	13 (72)	10	23.5	9 (90)	1.7	1.7	0.8 – 4.2
	Menopausal and menstrual disorders	29	40.1	21 (72)	15	42.6	13 (87)	2.0	2.0	1.1 – 4.0
	Other gynecologic disorders	60	57.3	43 (55)	46	58.5	35 (76)	1.3	1.3	0.9 – 2.0
	Endometriosis	6	3.3	6 (100)	3	3.2	3 (100)	1.9	2.0	0.4 – 12.1
	Fertility and infertility management	62	65.4	53 (85)	108	80.8	86 (80)	0.8	0.7	0.5 – 1.0
	Contraceptive or procreative management	23	27.1	23 (100)	21	26.4	21 (100)	1.1	1.1	0.6 – 2.0
	Infertility female	1	2.3	1 (100)	2	2.0	2 (100)	0.4	0.4	0.0 – 8.5
	Impotence of organic origin	20	14.4	19 (95)	32	21.3	31 (97)	0.9	0.9	0.5 – 1.7
	Other disorders of the male reproductive system	18	21.7	17 (94)	53	31.1	50 (94)	0.5	0.5	0.3 – 0.9
11.	**Pregnancy**	25	24.1	9 (36)	22	18.5	7 (32)	0.8	0.9	0.5 – 1.6
	Complicated pregnancy or delivery	19	16.3	9 (47)	15	12.9	7 (47)	0.9	1.0	0.5 – 2.1
	Diabetes, gestational	1	0.3	1 (100)	0	0.2	0 (-)	-	-	-
	Multiple gestational	1	0.3	1 (100)	0	0.2	0 (-)	-	-	-
	Postpartum hemorrhage	1	1.0	1 (100)	1	0.9	1 (100)	-	-	-
	Pregnancy with abortion	2	1.5	2 (100)	1	1.2	1 (100)	1.4	1.6	0.1 – 94
	Pregnancy, ectopic	1	0.2	1 (100)	0	0.2	0 (-)	-	-	-
	Preterm labor	4	1.7	1 (25)	1	1.3	1 (100)	2.8	3.0	0.3 – 144

Table 8 (continued)

	Other conditions during pregnancy	9	11.0	9 (100)	12	8.7	7 (58)	0.6	0.6	0.2 – 1.5
	Normal or unspecified pregnancy and delivery	6	7.8	5 (83)	7	5.6	5 (71)	0.6	0.6	0.2 – 2.2
	Spontaneous abortion	1	0.7	1 (100)	0	0.5	0 (-)	-	-	-
	Pregnancy	5	7.1	5 (100)	7	5.1	5 (71)	0.5	0.5	0.1 – 1.9
12.	**Dermatologic Disorders**	448	495.4	185 (41)	574	641.7	229 (40)	1.1	1.0	0.9 – 1.2
	Dermatologic infections	148	152.7	84 (57)	177	199.8	98 (55)	1.2	1.1	0.9 – 1.4
	Disorders of the hair and nails	11	17.5	9 (82)	12	22.0	10 (83)	1.4	1.2	0.5 – 2.9
	Immune mediated skin conditions	61	84.5	43 (70)	89	108.7	55 (62)	1.0	0.9	0.6 – 1.2
	Other dermatologic conditions	228	240.8	136 (60)	296	311.2	177 (60)	1.0	1.0	0.8 – 1.2
13.	**Musculoskeletal Disorders**	592	749.9	200 (34)	1099	981.7	260 (24)	0.8	0.7	0.6 – 0.8
	Acute or unspecified arthropathies and minor tendonitis	70	89.5	48 (69)	131	119.8	79 (60)	0.7	0.7	0.5 – 1.0
	Crystalline arthritis	14	8.1	13 (93)	13	11.8	12 (92)	1.5	1.6	0.7 – 3.6
	Degenerative joint disorders, other than spine	39	43.5	31 (79)	63	57.0	54 (86)	0.9	0.8	0.5 – 1.2
	Disorders of the spine	180	184.8	101 (56)	305	244.0	150 (49)	0.8	0.8	0.7 – 0.9
	Vasculitis and connective tissue disorders	5	5.1	5 (100)	11	6.6	10 (91)	0.6	0.6	0.2 – 1.9
	Other	284	418.9	149 (52)	576	542.5	207 (36)	0.7	0.6	0.6 – 0.7
14.	**Congenital Anomalies**	11	15.0	11 (100)	19	19.3	19 (100)	0.8	0.8	0.3 – 1.7
	Congenital Anomalies	11	15.0	11 (100)	19	19.3	19 (100)	0.8	0.8	0.3 – 1.7
	Atrial septal defect	0	0.2	0 (-)	1	0.2	1 (100)	-	-	-

Table 8 (continued)

	Other cardiovascular congenital abnormalities	2	1.6	2 (100)	3	2.3	3 (100)	1.0	0.9	0.1 – 8.0
	Other congenital abnormalities with admittance	9	12.8	9 (100)	15	16.3	15 (100)	0.8	0.8	0.3 – 1.9
	Other respiratory congenital abnormalities	0	0.3	0 (-)	0	0.4	0 (-)	-	-	-
15.	**Perinatal Disorders**	1	1.4	1 (100)	3	1.6	3 (100)	0.3	0.4	0.0 – 4.7
	Disorders originating in the perinatal period	1	1.4	1 (100)	3	1.6	3 (100)	0.3	0.4	0.0 – 4.7
16.	**Miscellaneous**	867	897.0	279 (32)	1066	1151.8	333 (31)	1.1	1.0	1.0 – 1.1
	Other miscellaneous conditions	240	375.5	160 (67)	286	476.4	203 (71)	1.1	1.1	0.9 – 1.3
	Routine health care	138	163.3	130 (94)	160	203.8	149 (93)	1.1	1.1	0.9 – 1.4
	Symptoms or signs	627	521.6	251 (40)	780	675.3	302 (39)	1.1	1.0	0.9 – 1.2
	Abdominal pain	106	76.1	72 (72)	113	98.0	78 (69)	1.3	1.2	0.9 – 1.6
	Chest pain, unspecified	106	71.1	67 (63)	130	98.5	81 (62)	1.2	1.1	0.9 – 1.5
	Fever	10	8.7	10 (100)	15	11.4	15 (100)	1.0	0.9	0.4 – 2.1
	Headache with radiology	65	60.2	38 (58)	80	74.2	46 (58)	1.1	1.0	0.7 – 1.4
	Malaise and fatigue	35	35.4	28 (80)	35	44.8	33 (94)	1.3	1.3	0.8 – 2.1
	Syncope and collapse	8	10.0	6 (75)	10	13.3	8 (80)	1.0	1.1	0.4 – 3.0
	Symptoms, signs and ill-defined conditions	297	259.2	221 (74)	397	333.9	269 (68)	1.0	1.0	0.8 – 1.1
17.	**Injury and Poisoning**	263	411.3	126 (48)	381	536.4	176 (46)	1.0	0.9	0.8 – 1.1
	Major traumatic injury	62	117.1	38 (61)	85	153.2	64 (75)	1.0	1.0	0.7 – 1.3
	Minor traumatic injury	140	232.1	86 (61)	226	301.9	136 (60)	0.9	0.8	0.7 – 1.0

Table 8 (continued)

Other injury	61	62.1	52 (85)	70	81.4	57 (81)	1.2	1.1	0.8 – 1.6

Table 9

Observed, Expected and Unique Number of Individuals by Plant with Risk Ratios of Episode of Care (with and without correction factor) and 95% Confidence Interval of Risk Ratio (not corrected) for CCG Specialty Category, Category, and Class Descriptions

Study Comparison Group C (High Exposure Employees)

CCG Specialty Category, Category and Class Description	Chemical Obs	Chemical Exp	Chemical Unique Number of Individuals (%)	Film Obs	Film Exp	Film Unique Number of Individuals (%)	RRE_pC_{ci}	RRE_p	95% CI
1. Infectious Diseases	445	425.5	304 (68)	492	432.5	317 (64)	1.0	0.9	0.8 – 1.1
Mycosis	3	1.2	3 (100)	3	1.4	3 (100)	1.4	1.2	0.2 – 9.2
Septicemia	1	2.1	1 (100)	3	2.8	3 (100)	0.4	0.4	0.0 – 5.5
Tuberculosis	1	0.8	1 (100)	0	1.0	0 (-)	-	-	-
HIV	0	0.4	0 (-)	0	0.5	0 (-)	-	-	-
Viral infections, other	0	1.4	0 (-)	0	1.3	0 (-)	-	-	-
Other Infections	439	417.1	303 (69)	482	423.2	316 (65)	1.0	0.9	0.8 – 1.1
2. Cancers and Benign Growths	201	181.9	134 (67)	193	230.3	122 (63)	1.4	1.3	1.1 – 1.6
Neoplasms of the head and neck	3	0.9	3 (100)	0	1.3	0 (-)		> 3.3	0.6 – > 150
Neoplasms of the gastrointestinal tract	42	20.3	29 (69)	34	30.2	26 (76)	2.0	1.8	1.2 – 3.0
Malignant neoplasm of colon	3	1.2	3 (100)	1	1.9	1 (100)	5.5	4.5	0.4 – 238.4
Malignant neoplasm of liver	0	0.3	0 (-)	1	0.4	1 (100)	-	-	-
Malignant neoplasm of pancreas	1	0.3	1 (100)	0	0.5	0 (-)	-	-	-
Malignant neoplasm of rectum and anus	3	0.9	3 (100)	3	1.3	3 (100)	1.8	1.5	0.2 – 11.4
Carcinoma *in situ,* digestive tract	0	0.3	0 (-)	1	0.5	1 (100)	-	-	-

Table 9 (continued)

Benign colonic polyps	35	16.8	27 (77)	28	25.0	23 (82)	2.0	1.9	1.1 – 3.2
Neoplasms of the respiratory tract	1	1.6	1 (100)	1	2.4	1 (100)	-	-	-
Malignant neoplasm of lower respiratory tract	1	1.2	1 (100)	1	1.9	1 (100)	-	-	-
Neoplasms of bones and connective tissue	0	0.4	0 (-)	0	0.6	0 (-)	-	-	-
Malignant neoplasm of bone	0	0.4	0 (-)	0	0.6	0 (-)	-	-	-
Neoplasms of skin	75	68.8	68 (91)	81	82.8	67 (83)	1.1	1.1	0.8 – 1.5
Malignant melanoma of skin	4	1.6	4 (100)	0	1.9	0 (-)	> 2.5	> 2.5	0.8 – 51
Malignant neoplasm of skin other than melanoma	11	16.6	9 (82)	22	23.4	18 (82)	0.8	0.7	0.3 – 1.5
Benign neoplasm of skin	60	50.6	59 (98)	59	57.4	56 (95)	1.1	1.2	0.8 – 1.7
Neoplasms of the breast and female reproductive system	21	22.9	20 (95)	18	27.4	16 (89)	1.3	1.4	0.7 – 2.74
Malignant neoplasm of female breast	1	1.9	1 (100)	0	2.7	0 (-)	-	-	-
Malignant neoplasm of body of uterus	1	0.2	1 (100)	0	0.3	0 (-)	-	-	-
Benign neoplasm of breast	7	9.4	7 (100)	8	11.7	8 (100)	1.0	1.1	0.3 – 1.5
Benign ovarian cyst	8	5.1	8 (100)	3	4.9	3 (100)	3.1	2.6	0.6 – 15.1
Benign neoplasm of ovary other than cyst	0	0.5	0 (-)	0	-	0 (-)	-	-	-
Uterine leiomyoma	4	5.3	4 (100)	7	6.6	7 (100)	0.7	0.7	0.2 – 2.8
Neoplasms of the urinary tract	0	1.2	0 (-)	1	1.8	1 (100)	-	-	-
Malignant neoplasm of bladder	0	0.7	0 (-)	0	1.1	0 (-)	-	-	-
Malignant neoplasm of kidney	0	0.5	0 (-)	1	0.7	1 (100)	-	-	-
Neoplasms of male reproductive tract	5	2.6	5 (100)	1	4.0	1 (100)	8.6	7.6	0.9 – 359

Table 9 (continued)

Malignant neoplasm of prostate	4	2.1	4 (100)	1	3.5	1 (100)	7.3	6.7	0.7 – 325
Malignant neoplasm of testicle	1	0.5	1 (100)	0	0.4	0 (-)	-	-	-
Neoplasms of the nervous system	1	1.0	1 (100)	1	1.4	1 (100)	-	-	-
Malignant neoplasm of CNS, primary	1	0.8	1 (100)	1	1.1	1 (100)	-	-	-
Neoplasms of endocrine organs	1	0.7	1 (100)	0	0.8	0 (-)	-	-	-
Malignant neoplasm of thyroid	1	0.7	1 (100)	0	0.8	0 (-)	-	-	-
Other neoplasms	50	58.4	47 (94)	49	73.8	44 (90)	1.3	1.3	0.9 – 2.0
Malignant neoplasm, other	2	3.7	2 (100)	3	4.8	3 (100)	0.9	0.9	0.1 – 7.7
Malignant neoplasm, unspecified and secondary	0	0.5	0 (-)	1	0.7	1 (100)	-	-	-
Metastatic cancers other than lymph nodes	5	2.8	5 (100)	3	4.1	3 (100)	2.4	2.4	0.5 – 15.5
Carcinoma *in situ,* other than skin, respiratory or gastrointestinal	0	1.9	0 (-)	0	2.2	0 (-)	-	-	-
Other benign or unspecified neoplasms	43	49.5	41 (95)	42	61.9	42 (100)	1.3	1.3	0.8 – 2.0
Neoplasms of the hematologic system	2	3.1	2 (100)	7	3.8	6 (86)	0.4	0.4	0.0 – 1.9
Leukemia, chronic	0	0.6	0 (-)	2	0.8	2 (100)	-	-	-
Lymphoma	2	1.7	2 (100)	3	2.0	3 (100)	1.0	0.8	0.1 – 6.9
Multiple myeloma	0	0.3	0 (-)	1	0.4	1 (100)	-	-	-
Myeloproliferative syndrome	0	0.3	0 (-)	1	0.3	1 (100)	-	-	-
3. Endocrine Disorders	256	249.2	164 (64)	344	317.1	196 (57)	1.0	1.0	0.8 – 1.1
Disorders of the thyroid	17	32.0	13 (76)	25	39.8	21 (84)	0.8	0.8	0.4 – 1.6
Acquired hypothyroidism with surgery	15	24.2	13 (87)	17	30.2	17 (100)	1.1	1.1	0.5 – 2.3

Table 9 (continued)

Hyperthyroidism other than in pregnancy	1	4.3	1 (100)	3	5.2	3 (100)	0.4	0.4	0.0 – 5.1
Thyroid nodule, benign nontoxic	0	2.0	0 (-)	3	2.4	3 (100)	0.0	0.0	0.0 – 3.0
Thyroiditis	1	1.6	1 (100)	2	1.9	2 (100)	0.4	0.6	0.0 – 11.5
Diabetes	57	46.2	36 (63)	78	62.0	54 (69)	1.0	1.0	0.7 – 1.4
Diabetes Type I with complications	2	1.7	2 (100)	0	2.3	0 (-)	-	-	-
Diabetes Type I without complications	8	7.1	8 (100)	8	9.0	8 (100)	1.3	1.3	0.4 – 3.9
Diabetes Type II with complication	8	10.1	8 (100)	14	14.1	14 (100)	0.8	0.8	0.3 – 2.0
Diabetes Type II without complications	39	27.3	35 (90)	56	36.5	53 (95)	1.0	0.9	0.6 – 1.4
Disorders of lipid metabolism (hyperlipidemia)	109	97.7	99 (91)	144	126.9	127 (88)	1.0	1.0	0.8 – 1.3
Fluid and electrolyte disorders	14	11.8	12 (86)	25	14.9	20 (80)	0.7	0.7	0.4 – 1.4
Other endocrine or nutritional disorders	59	61.4	51 (86)	72	73.5	58 (81)	1.0	1.0	0.7 – 1.4
Adrenal insufficiency	0	0.3	0 (-)	1	0.4	1 (100)	-	-	-
Hyperparathyroidism	0	0.4	0 (-)	2	0.6	2 (100)	-	-	-
Hypoglycemia	4	4.8	4 (100)	7	5.5	6 (86)	0.7	0.7	0.1 – 2.5
Obesity	29	27.7	28 (97)	30	31.8	28 (93)	1.2	1.1	0.7 – 1.9
Osteoporosis	1	1.6	1 (100)	3	2.4	3 (100)	0.5	0.5	0.0 – 6.1
Other endocrine, nutritional and metabolic disorders	25	26.5	24 (96)	29	32.8	27 (93)	1.0	1.1	0.6 – 1.9
4. Hematologic Disorders	30	30.7	23 (77)	35	37.6	32 (91)	1.1	1.1	0.6 – 1.8
Anemia, acquired	6	5.5	6 (100)	5	6.9	5 (100)	1.2	1.5	0.4 – 6.3
Disorders of hemostatic function	2	0.6	1 (50)	0	0.8	0 (-)	-	-	-
Other hematologic disorders	22	24.5	19 (86)	30	30.0	29 (97)	1.0	0.9	0.5 – 1.6

Table 9 (continued)

5.	**Psychiatric Disorders**	297	277.1	168 (57)	280	304.4	154 (55)	1.2	1.2	1.0 – 1.4
	Affective disorders	104	105.3	81 (78)	78	112.0	57 (73)	1.5	1.4	1.1 – 1.9
	Depression, major without psychotic behavior	60	41.7	57 (95)	44	45.4	42 (95)	1.5	1.5	1.0 – 2.2
	Depression, minor	36	54.1	34 (94)	28	56.3	26 (93)	1.6	1.3	0.8 – 2.3
	Dissociative and personality disorders	3	2.9	3 (100)	2	2.8	2 (100)	1.6	1.5	0.2 – 17.3
	Neurotic disorders (anxiety disorders)	33	38.8	31 (94)	35	42.1	32 (91)	1.1	1.0	0.6 – 1.7
	Organic mental disorders	1	1.5	1 (100)	0	2.2	0 (-)	-	-	-
	Psychotic disorders	0	2.2	0 (-)	2	2.4	2 (100)	-	-	-
	Substance abuse	155	123.4	118 (76)	160	140.0	114 (71)	1.2	1.1	0.9 – 1.4
6a.	**Neurologic Disorders**	128	143.8	93 (73)	180	169.0	119 (66)	0.8	0.8	0.7 – 1.1
	Congenital or acquired central degenerative disorders	10	9.2	10 (100)	15	10.7	14 (93)	0.7	0.8	0.3 – 1.8
	Benign essential tremor	0	1.3	0 (-)	1	1.7	1 (100)	-	-	-
	Parkinson's disease	10	6.4	10 (100)	14	7.3	14 (100)	0.8	0.8	0.3 – 2.0
	Hemorrhage, cerebrovascular, or other major CNS disorders	13	12.1	10 (77)	24	17.7	17 (71)	0.8	0.8	0.4 – 1.6
	Other diseases of the nervous system	61	63.3	49 (80)	73	71.4	60 (82)	0.9	0.9	0.7 – 1.3
	Migraine	27	24.7	23 (85)	21	26.2	18 (86)	1.3	1.4	0.8 – 2.5
	Tension headache	6	6.9	4 (67)	1	7.5	1 (100)	5.6	6.6	0.8 – 304
	Peripheral neuromuscular disorders	44	56.9	41 (93)	68	66.7	62 (91)	0.8	0.8	0.5 – 1.1
	Neuralgia, neuritis, radiculitis	29	41.7	29 (90)	50	48.8	47 (94)	0.7	0.7	0.4 – 1.1
	Carpel Tunnel Syndrome	13	12.4	13 (100)	17	14.8	17 (100)	0.9	0.9	0.4 – 2.0

Table 9 (continued)

6b.	**Opthamologic Disorders**	118	185.3	80 (68)	153	216.8	108 (71)	0.9	0.9	0.7 – 1.2
	Disorders of the eye	118	185.3	80 (68)	153	216.8	108 (71)	0.9	0.9	0.7 – 1.2
	Cataract	9	9.8	9 (100)	13	15.1	12 (92)	1.0	1.1	0.4 – 2.7
	Conjunctivitis, acute	19	32.3	19 (100)	19	35.6	18 (95)	1.1	1.1	0.6 – 2.2
	Glaucoma	7	12.3	7 (100)	12	16.4	12 (100)	0.8	0.8	0.3 – 2.1
7.	**Cardiovascular Disorders**	322	290.2	175 (54)	443	390.5	222 (50)	1.0	1.0	0.9 – 1.1
	Hypertension	123	103.8	111 (90)	162	135.9	146 (90)	1.0	1.0	0.8 – 1.3
	Atherosclerotic coronary vascular disease	67	53.3	39 (58)	106	76.3	50 (47)	1.0	0.9	0.7 – 1.2
	Carditis and cardiomyopathy/CHF	7	8.0	6 (86)	9	11.9	8 (89)	1.1	1.2	0.4 – 3.5
	Disorders of heart valves	13	8.2	13 (100)	16	11.1	16 (100)	1.0	1.1	0.5 – 2.4
	Dysrhythmia and conduction disorders	9	15.7	8 (89)	15	21.9	14 (93)	1.0	0.8	0.3 – 2.0
	Large arterial and peripheral vascular disorders	2	3.5	2 (100)	3	5.3	3 (100)	1.2	1.0	0.1 – 9.0
	Large vein thromboembolic disorders	3	6.0	2 (67)	6	7.8	6 (100)	0.7	0.7	0.1 – 3.1
	Minor venous/arterial disorders	0	9.6	0 (-)	0	12.1	0 (-)	-	-	-
	Other cardiovascular disorders	98	81.3	81 (83)	126	107.2	100 (79)	1.1	1.0	0.8 – 1.4
8a.	**Pulmonary Disorders**	643	481.3	287 (45)	681	540.9	293 (43)	1.1	1.1	1.0 – 1.2
	Lower respiratory infections	246	211.3	138 (56)	262	241.6	140 (53)	1.1	1.1	0.9 – 1.3
	Obstructive pulmonary diseases	42	41.3	35 (83)	47	49.3	44 (94)	1.2	1.1	0.7 – 1.7
	Asthma	18	25.6	17 (94)	21	28.0	20 (95)	1.1	1.0	0.5 – 1.8
	Chronic obstructive pulmonary disease	24	15.7	24 (100)	26	21.2	26 (100)	1.3	1.3	0.7 – 2.3
	Other pulmonary disorders	340	215.4	247 (73)	353	232.7	254 (72)	1.1	1.0	0.9 – 1.2

Table 9 (continued)

	Atelectasis	4	2.4	4 (100)	3	3.4	3 (100)	1.5	1.9	0.3 – 12.9
	Painful respiration	20	15.1	15 (75)	27	17.7	26 (96)	1.0	0.9	0.5 – 1.6
	Pleurisy with or without effusion	2	7.1	2 (100)	8	8.7	7 (88)	0.2	0.3	0.0 – 1.5
	Pulmonary eosinophilia	7	2.1	7 (100)	8	2.8	8 (100)	1.2	1.2	0.4 – 3.7
	Other disorders of the respiratory system	304	185.6	231 (76)	302	196.0	240 (79)	1.2	1.1	0.9 – 1.3
	Pulmonary edema	2	5.0	2 (100)	2	6.9	2 (100)	1.1	1.4	0.1 – 19.1
	Respiratory failure	0	0.3	0 (-)	1	0.3	1 (100)	-	-	-
	Sleep disorders	13	8.1	13 (100)	16	10.1	15 (94)	1.1	1.0	0.5 – 2.2
8b.	**Ear, Nose and Throat Disorders**	1048	952.0	293 (28)	1134	1025.9	306 (27)	1.1	1.0	0.9 – 1.1
	Disorders of the ear and vestibular apparatus	167	190.3	98 (59)	183	211.0	116 (63)	1.1	1.0	0.8 – 1.3
	Upper respiratory infections	747	625.7	249 (33)	789	669.1	245 (31)	1.1	1.0	0.9 – 1.1
	Pharyngitis, acute	164	151.9	89 (54)	139	152.9	80 (57)	1.3	1.2	0.9 – 1.5
	Sinusitis, acute	287	189.6	129 (45)	313	206.3	124 (40)	1.0	1.0	0.9 – 1.2
	Sinusitis, chronic with surgery	69	58.2	68 (99)	79	63.8	77 (97)	1.1	1.0	0.7 – 1.3
	Upper respiratory infection and common cold, acute	215	212.1	96 (45)	249	233.3	113 (45)	1.1	1.0	0.8 – 1.1
	Other upper respiratory disorders	134	136.0	113 (84)	162	145.9	129 (80)	0.9	0.9	0.7 – 1.1
	Allergic rhinitis	110	115.4	102 (93)	128	123.4	117 (91)	0.9	0.9	0.7 – 1.2
9.	**Gastrointestinal Disorders**	455	363.1	192 (42)	541	437.3	231 (43)	1.1	1.0	0.9 – 1.2
	Disorders of esophagus	54	36.1	44 (81)	75	44.5	63 (84)	0.9	0.9	0.6 – 1.3
	Disorders of stomach and duodenum	47	33.2	37 (79)	75	40.2	51 (68)	0.8	0.8	0.5 – 1.1
	Disorders of the small intestine	2	3.2	2 (100)	2	3.3	2 (100)	1.2	1.0	0.1 – 14

Table 9 (continued)

	Hernias	19	24.5	17 (89)	42	31.0	38 (90)	0.6	0.6	0.3 – 1.0
	Inflammatory bowel disease	8	6.0	8 (100)	7	7.0	7 (100)	1.3	1.3	0.4 – 4.2
	Disorders of the large intestine	106	75.5	79 (75)	122	94.7	85 (70)	1.2	1.1	0.8 – 1.4
	Disorders of the liver	3	4.3	3 (100)	2	5.0	2 (100)	2.0	1.8	0.2 – 21
	Cirrhosis of the liver without mention of alcohol	2	0.6	2 (100)	0	0.8	0 (-)	-	-	-
	Hepatitis, acute alcoholic	0	0.3	0 (-)	1	0.3	1 (100)	-	-	-
	Hepatitis, acute without hepatic coma	0	1.8	0 (-)	1	2.0	1 (100)	-	-	-
	Hepatitis, chronic without hepatic coma	1	1.2	1 (100)	0	1.3	0 (-)	-	-	-
	Disorders of the biliary tract	22	16.7	11 (50)	17	21.8	10 (59)	1.8	1.7	0.9 – 3.3
	Cholecystitis without cholelithiasis, acute	1	1.4	1 (100)	2	1.9	2 (100)	0.8	0.7	0.0 – 13.1
	Cholecystitis without cholelithiasis, chronic or other	5	2.6	5 (100)	4	3.3	4 (100)	1.8	1.6	0.3 – 8.0
	Cholelithiasis with acute cholecystitis	7	2.8	5 (71)	1	3.7	1 (100)	10.9	9.3	1.2 – 415
	Cholelithiasis with chronic or unspecified cholecystitis	6	5.9	6 (100)	4	7.6	4 (100)	2.1	1.9	0.5 – 9.3
	Cholelithiasis without cholecystitis	3	3.9	3 (100)	6	5.2	6 (100)	0.7	0.7	0.1 – 3.1
	Disorders of the pancreas	7	3.0	1 (14)	2	4.0	1 (50)	3.3	4.7	0.9 – 46
	Pancreatitis, acute	6	2.6	1 (17)	2	3.4	1 (50)	2.9	4.0	0.7 – 41
	Pancreatitis, chronic	1	0.4	1 (100)	0	0.5	0 (-)	-	-	-
	Other gastrointestinal disorders	187	160.5	145 (78)	197	185.9	157 (80)	1.2	1.1	0.9 – 1.4
10a.	**Urologic Disorders**	288	185.6	114 (40)	331	230.4	155 (47)	1.1	1.1	0.9 – 1.3
	Disorders of renal function	4	2.8	3 (75)	2	3.6	2 (100)	2.6	2.6	0.4 – 29

Table 9 (continued)

Chronic renal failure	3	1.8	3 (100)	1	2.3	1 (100)	4.0	3.8	0.3 – 200
Disorders of renal parenchyma	3	1.2	3 (100)	1	1.5	1 (100)	3.6	3.9	0.3 – 202
Renal cyst	3	1.2	3 (100)	1	1.5	1 (100)	3.6	3.8	0.3 – 202
Lower and unspecified urinary tract infections	83	59.3	38 (46)	73	68.1	48 (66)	1.4	1.3	0.9 – 1.8
Cystitis	29	14.4	15 (52)	25	16.5	18 (72)	1.4	1.3	0.8 – 2.4
Urinary tract, not specified	54	44.9	31 (57)	48	51.6	35 (73)	1.3	1.3	0.9 – 1.9
Other disorders of the lower urinary tract	2	3.0	2 (100)	13	3.6	12 (92)	0.2	0.2	0.0 – 0.8
Urethral stricture	2	3.0	2 (100)	13	3.6	12 (92)	0.2	0.2	0.0 – 0.8
Other disorders of the upper urinary tract	58	23.8	24 (41)	60	28.8	31 (52)	1.3	1.2	0.8 – 1.7
Calculus of urinary tract	58	23.8	24 (41)	60	28.8	31 (52)	1.3	1.2	0.8 – 1.7
Other genitourinary disorders	39	33.8	38 (97)	61	41.4	60 (98)	0.8	0.8	0.5 – 1.2
Other diseases with surgery	39	33.8	38 (97)	61	41.4	60 (98)	0.8	0.8	0.5 – 1.2
Upper urinary tract infections	7	2.7	6 (86)	6	3.0	4 (67)	1.3	1.3	0.4 – 4.6
Acute pyelonephritis	7	2.7	6 (86)	6	3.0	4 (67)	1.3	1.3	0.4 – 4.6
Disorders of the prostate	92	59.1	61 (66)	115	80.4	84 (73)	1.1	1.1	0.8 – 1.4
Prostatic hyperplasia	43	29.2	38 (88)	60	43.8	57 (95)	1.1	1.1	0.7 – 1.6
Prostatitis, acute	49	29.9	35 (71)	55	36.6	40 (73)	1.2	1.1	0.7 – 1.6
10b. Gynecologic and Reproductive Disorders	225	236.4	117 (52)	232	251.2	137 (59)	1.1	1.0	0.9 – 1.2
Disorders of the female breast (non-malignant)	22	16.7	19 (86)	15	20.8	14 (93)	1.8	1.8	0.9 – 3.7
Fibrocystic disease of breast	18	11.7	17 (94)	11	14.7	11 (100)	2.0	2.1	0.9 – 4.8
Fertility and infertility management	88	91.6	71 (81)	109	89.8	88 (81)	0.9	0.8	0.6 – 1.1

Table 9 (continued)

Contraceptive or procreative management	23	37.4	22 (96)	19	24.8	19 (100)	0.8	0.8	0.4 – 1.5
Infertility female	2	2.9	2 (100)	1	1.8	1 (100)	1.7	1.2	0.1 – 73
Impotence of organic origin	36	19.3	34 (94)	38	27.1	37 (97)	1.3	1.3	0.8 – 2.2
Other disorders of the male reproductive system	27	32.0	26 (96)	51	36.1	50 (98)	0.7	0.6	0.4 – 1.0
Infections of the female genital tract	19	26.6	14 (74)	19	25.2	13 (68)	1.1	1.0	0.5 – 1.9
Menopausal and menstrual disorders	27	40.4	19 (70)	29	49.7	20 (69)	1.1	1.1	0.7 – 2.0
Other gynecologic disorders	69	61.1	46 (67)	60	65.6	45 (75)	1.2	1.2	0.9 – 1.8
Endometriosis	8	3.6	8 (100)	3	3.5	3 (100)	3.4	2.6	0.6 – 15.2
11. Pregnancy	19	31.4	6 (32)	6	14.7	4 (67)	1.9	1.5	0.6 – 4.5
Complicated pregnancy or delivery	14	21.1	5 (36)	4	10.6	4 (100)	2.2	1.8	0.6 – 7.4
Diabetes, gestational	1	0.4	1 (100)	0	0.2	0 (-)	-	-	-
Multiple gestational	1	0.3	1 (100)	0	0.2	0 (-)	-	-	-
Postpartum hemorrhage	0	1.2	0 (-)	0	0.8	0 (-)	-	-	-
Pregnancy with abortion	0	1.9	0 (-)	0	1.0	0 (-)	-	-	-
Pregnancy, ectopic	0	0.3	0 (-)	0	0.2	0 (-)	-	-	-
Preterm labor	6	2.2	2 (33)	0	0.9	0 (-)	> 2.7	> 2.7	0.5 – 27
Other conditions during pregnancy	6	14.3	5 (83)	4	7.1	4 (100)	0.9	0.8	0.2 – 3.6
Normal or unspecified pregnancy and delivery	5	10.4	5 (100)	2	4.1	2 (100)	1.5	1.0	0.2 – 10.4
Spontaneous abortion	0	0.9	0 (-)	0	0.4	0 (-)	-	-	-
Pregnancy	5	9.5	5 (100)	2	3.7	2 (100)	1.5	1.0	0.2 – 10

Table 9 (continued)

12.	**Dermatologic Disorders**	605	658.4	252 (42)	682	743.0	265 (39)	1.1	1.0	0.9 – 1.1
	Dermatologic infections	204	205.4	115 (56)	215	230.8	125 (58)	1.2	1.1	0.9 – 1.3
	Disorders of the hair and nails	9	21.9	8 (89)	19	26.0	16 (84)	0.6	0.6	0.2 – 1.3
	Immune mediated skin conditions	94	111.4	60 (64)	108	125.1	63 (58)	1.0	1.0	0.7 – 1.3
	Other dermatologic conditions	298	319.7	194 (65)	340	361.1	200 (59)	1.1	1.0	0.8 – 1.2
13.	**Musculoskeletal Disorders**	1081	980.8	274 (25)	1357	1137.3	316 (23)	1.0	0.9	0.9 – 1.0
	Acute or unspecified arthropathies and minor tendonitis	105	118.2	70 (67)	157	139.5	91 (58)	0.9	0.8	0.6 – 1.0
	Crystalline arthritis	10	11.1	9 (90)	15	14.2	15 (100)	0.8	0.9	0.3 – 2.0
	Degenerative joint disorders, other than spine	44	53.0	33 (75)	90	69.2	74 (82)	0.7	0.6	0.4 – 0.9
	Disorders of the spine	300	246.9	166 (55)	389	279.8	178 (46)	0.9	0.9	0.8 – 1.0
	Vasculitis and connective tissue disorders	10	6.1	10 (100)	12	7.9	11 (92)	1.2	1.1	0.4 – 2.7
	Other	612	545.4	222 (36)	694	626.5	252 (36)	1.1	1.0	0.9 – 1.1
14.	**Congenital Anomalies**	19	19.6	19 (100)	17	22.3	16 (94)	1.2	1.3	0.6 – 2.6
	Congenital Anomalies	19	19.6	19 (100)	17	22.3	16 (94)	1.2	1.3	0.6 – 2.6
	Atrial septal defect	0	0.2	0 (-)	0	0.3	0 (-)	-	-	-
	Other cardiovascular congenital abnormalities	1	2.1	1 (100)	4	2.8	4 (100)	0.4	0.4	0.0 – 3.4
	Other congenital abnormalities with admittance	17	16.8	17 (100)	12	18.6	12 (100)	1.5	1.6	0.7 – 3.6
	Other respiratory congenital abnormalities	1	0.4	1 (100)	1	0.5	1 (100)	-	-	-

Table 9 (continued)

15.	**Perinantal Disorders**	1	1.9	1 (100)	3	1.7	3 (100)	0.2	0.3	0.0 – 3.8
	Conditions originating in the perinatal period	1	1.5	1 (100)	3	1.4	3 (100)	0.2	0.3	0.0 – 3.9
16.	**Miscellaneous**	1196	1169.0	379 (32)	1234	1332.7	387 (31)	1.2	1.1	1.0 – 1.2
	Other miscellaneous conditions	273	486.6	195 (71)	297	549.5	214 (72)	1.1	1.0	0.9 – 1.2
	Routine health care	152	212.2	144 (95)	161	232.1	149 (93)	1.1	1.0	0.8 – 1.3
	Symptoms or signs	923	682.3	351 (38)	937	783.2	358 (38)	1.2	1.1	1.0 – 1.2
	Abdominal pain	146	98.1	109 (75)	133	114.2	93 (70)	1.4	1.3	1.0 – 1.6
	Chest pain, unspecified	146	93.0	100 (68)	169	118.7	102 (59)	1.2	1.1	0.9 – 1.4
	Fever	17	11.8	17 (100)	18	13.1	18 (100)	1.0	1.1	0.5 – 2.1
	Headache with radiology	104	76.1	58 (56)	84	84.1	48 (57)	1.4	1.4	1.0 – 1.8
	Malaise and fatigue	44	44.7	35 (80)	57	52.0	49 (86)	0.9	0.9	0.6 – 1.4
	Syncope and collapse	19	13.0	15 (88)	15	16.0	11 (61)	1.6	1.6	0.8 – 3.2
	Symptoms, signs and ill-defined conditions	447	344.6	312 (70)	461	383.7	321 (70)	1.2	1.1	1.0 – 1.2
17.	**Injury and Poisoning**	416	561.0	210 (50)	464	605.4	223 (48)	1.1	1.0	0.9 – 1.1
	Major traumatic injury	96	159.7	70 (73)	109	172.8	82 (75)	1.0	1.0	0.7 – 1.3
	Minor traumatic injury	227	317.7	143 (63)	271	339.0	167 (62)	1.0	0.9	0.8 – 1.1
	Other injury	93	83.6	81 (87)	84	93.5	70 (83)	1.4	1.2	0.9 – 1.7

Table 10

Observed, Expected and Unique Number of Individuals by Plant with Risk Ratios of Episode of Care (with and without correction factor) and 95% Confidence Interval of Risk Ratio (not corrected) for CCG Specialty Category, Category, and Class Descriptions

Study Comparison Group D (Long-Term High Exposure Employees)

CCG Specialty Category, Category and Class Description	Chemical			Film					
	Obs	Exp	Unique Number of Individuals (%)	Obs	Exp	Unique Number of Individuals (%)	RRE_pC_{cr}	RRE_pC	95% CI
1. Infectious Diseases	217	190.2	149 (70)	380	332.3	235 (62)	1.0	1.0	0.8 - 1.2
Mycoses	2	0.6	2 (100)	2	1.2	2 (100)	1.6	1.9	0.1 – 26.5
Septicemia	1	1.3	1 (100)	1	2.3	1 (100)	-	-	-
Tuberculosis	0	0.4	0 (-)	0	0.8	0 (-)	-	-	-
HIV	0	0.2	0 (-)	0	0.4	0 (-)	-	-	-
Viral infections, other	0	0.5	0 (-)	0	0.9	0 (-)	-	-	-
Other infections	214	187.2	148 (69)	377	326.7	235 (62)	1.0	1.0	0.8 - 1.2
2. Cancers and Benign Growths	113	98.1	76 (67)	137	189.1	89 (65)	1.6	1.6	1.2 - 2.1
Neoplasms of the head and neck	0	0.6	0 (-)	0	1.1	0 (-)	-	-	-
Neoplasms of the gastrointestinal tract	33	13.2	22 (67)	22	25.9	19 (86)	3.2	2.9	1.7 - 5 .2
Malignant neoplasm of colon	3	0.8	3 (100)	0	1.6	0 (-)	> 3.8	> 3.8	0.9 - 60
Malignant neoplasm of liver	0	0.2	0 (-)	1	0.4	1 (100)	-	-	-
Malignant neoplasm of pancreas	1	0.2	1 (100)	0	0.4	0 (-)	-	-	-
Malignant neoplasm of rectum and anus	3	0.6	3 (100)	0	1.1	0 (-)	> 5.0	> 5.0	0.9 – 62
Carcinoma *in situ,* digestive tract	0	0.2	0 (-)	0	0.4	0 (-)	-	-	-

Table 10 (continued)

Benign colonic polyps	26	11.0	20 (77)	21	21.4	18 (86)	2.7	2.4	1.3 - 4.5
Neoplasms of the respiratory tract	1	1.0	1 (100)	0	2.0	0 (-)	-	-	-
Malignant neoplasm of lower respiratory tract	1	0.8	1 (100)	0	1.6	0 (-)	-	-	-
Neoplasms of bones and connective tissue	0	0.2	0 (-)	0	0.5	0 (-)	-	-	-
Malignant neoplasm of bone	0	0.2	0 (-)	0	0.5	0 (-)	-	-	-
Neoplasms of skin	41	38.1	38 (93)	60	68.1	49 (82)	1.3	1.2	0.8 - 1.9
Malignant melanoma of skin	3	1.0	3 (100)	0	1.6	0 (-)	> 3.0	> 3.0	0.8 - 52
Malignant neoplasm of skin other than melanoma	7	10.7	5 (71)	16	20.1	14 (88)	1.0	0.8	0.3 - 2.1
Benign neoplasm of skin	31	26.5	31 (100)	44	46.4	42 (95)	1.3	1.2	0.8 - 2.0
Neoplasms of the breast and female reproductive system	4	7.3	3 (75)	11	20.7	10 (91)	1.0	1.0	0.2 - 3.5
Malignant neoplasm of female breast	1	0.7	1 (100)	0	2.1	0 (-)	-	-	-
Malignant neoplasm of body of uterus	0	0.1	0 (-)	0	0.2	0 (-)	-	-	-
Benign neoplasm of breast	2	3.3	2 (100)	4	8.9	4 (100)	1.1	1.4	0.1 - 9.6
Benign ovarian cyst	0	1.2	0 (-)	2	3.5	2 (100)	0.0	0.0	0.0 – 15
Benign neoplasm of ovary other than cyst	0	0.1	0 (-)	0	0.4	0 (-)	-	-	-
Uterine leiomyoma	1	1.7	1 (100)	5	5.0	5 (100)	0.6	0.6	0.0 - 5.3
Neoplasms of the urinary tract	0	0.8	0 (-)	1	1.5	1 (100)	-	-	-
Malignant neoplasm of bladder	0	0.5	0 (-)	0	0.9	0 (-)	-	-	-
Malignant neoplasm of kidney	0	0.3	0 (-)	1	0.6	1 (100)	-	-	-
Neoplasms of male reproductive tract	5	1.8	5 (100)	1	3.4	1 (100)	10.3	9.7	1.1 - 458

Table 10 (continued)

Malignant neoplasm of prostate	4	1.5	4 (100)	1	3.1	1 (100)	8.8	8.2	0.8 - 399
Malignant neoplasm of testicle	1	0.3	1 (100)	0	0.3	0 (-)	-	-	-
Neoplasms of the nervous system	1	0.5	1 (100)	0	1.1	0 (-)	-	-	-
Malignant neoplasm of CNS, primary	1	0.4	1 (100)	0	0.9	0 (-)	-	-	-
Neoplasms of endocrine organs	0	0.3	0 (-)	0	0.6	0 (-)	-	-	-
Malignant neoplasm of thyroid	0	0.3	0 (-)	0	0.6	0 (-)	-	-	-
Other neoplasms	26	32.5	24 (92)	36	60.9	32 (89)	1.4	1.4	0.8 - 2.3
Malignant neoplasm, other	1	2.1	1 (100)	3	4.0	3 (100)	0.6	0.7	0.0 - 8.1
Malignant neoplasm, unspecified and secondary	0	0.3	0 (-)	1	0.6	1 (100)	-	-	-
Metastatic cancers other than lymph nodes	2	1.7	2 (100)	1	3.4	1 (100)	3.7	4.1	0.2 - 242
Carcinoma *in situ,* other than skin, respiratory or gastrointestinal	0	0.8	0 (-)	0	1.7	0 (-)	-	-	-
Other benign or unspecified neoplasms	23	27.7	21 (91)	31	51.1	31 (100)	1.4	1.4	0.8 - 2.4
Neoplasms of the hematologic system	2	1.8	2 (100)	6	3.2	5 (83)	0.7	0.6	0.1 - 3.2
Leukemia, chronic	0	0.4	0 (-)	2	0.7	2 (100)	0.0	0.0	0.0 - 9.9
Lymphoma	2	1.0	2 (100)	2	1.7	2 (100)	2.0	1.7	0.1 – 23
Multiple myeloma	0	0.2	0 (-)	1	0.3	1 (100)	-	-	-
Myeloproliferative syndrome	0	0.2	0 (-)	1	0.3	1 (100)	-	-	-
3. Endocrine Disorders	148	139.8	96 (65)	277	262.5	154 (56)	1.0	1.0	0.8 - 1.2
Disorders of the thyroid	4	14.9	4 (100)	20	31.7	16 (80)	0.4	0.4	0.1 - 1.3
Acquired hypothyroidism with surgery	4	11.2	4 (100)	14	24.1	14 (100)	0.6	0.6	0.2 - 2.0

Table 10 (continued)

Hyperthyroidism other than in pregnancy	0	2.0	0 (-)	3	4.2	3 (100)	0.0	0.0	0.0 - 5.0
Thyroid nodule, benign nontoxic	0	0.9	0 (-)	2	2.0	2 (100)	-	-	-
Thyroiditis	0	0.7	0 (-)	1	1.5	1 (100)	-	-	-
Diabetes	42	28.1	25 (60)	60	52.2	41 (68)	1.3	1.3	0.9 - 2.0
Diabetes Type I with complications	1	1.1	1 (100)	0	2.0	0 (-)	-	-	-
Diabetes Type I without complications	8	4.2	8 (100)	7	7.5	7 (100)	2.0	2.0	0.7 - 6.6
Diabetes Type II with complications	6	6.3	6 (100)	10	11.9	10 (100)	1.2	1.1	0.3 - 3.5
Diabetes Type II without complications	27	16.5	25 (93)	43	30.8	40 (93)	1.1	1.2	0.7 - 1.9
Disorders of lipid metabolism (hyperlipidemia)	65	59.9	60 (92)	125	107.2	110 (88)	1.0	0.9	0.7 - 1.3
Fluid and electrolyte disorders	6	6.1	5 (83)	16	12.1	12 (75)	0.7	0.7	0.2 - 2.0
Other endocrine or nutritional disorders	31	30.8	28 (90)	56	59.3	45 (80)	1.1	1.1	0.7 - 1.7
Adrenal insufficiency	0	0.1	0 (-)	1	0.3	1 (100)	-	-	-
Hyperparathyroidism	0	0.2	0 (-)	1	0.5	1 (100)	-	-	-
Hypoglycemia	3	2.6	3 (100)	7	4.5	6 (86)	0.6	0.7	0.1 - 3.3
Obesity	13	13.4	13 (100)	25	25.3	23 (92)	1.0	1.0	0.5 - 2.0
Osteoporosis	0	0.8	0 (-)	2	1.9	2 (100)	-	-	-
Other endocrine, nutritional and metabolic disorders	15	13.7	15 (100)	20	26.8	18 (90)	1.4	1.5	0.7 - 3.0
4. Hematologic Disorders	18	15.5	12 (67)	28	30.4	25 (89)	1.1	1.3	0.7 - 2.4
Anemia, acquired	2	2.7	2 (100)	4	5.6	4 (100)	0.8	1.0	0.1 - 7.3
Disorders of hemostatic function	2	0.3	1 (50)	0	0.6	0 (-)	-	-	-

Table 10 (continued)

	Other hematologic disorders	14	12.5	11 (79)	24	24.2	23 (96)	1.1	1.1	0.6 - 2.3
5.	**Psychiatric Disorders**	144	136.5	79 (55)	206	242.2	116 (56)	1.3	1.2	1.0 - 1.5
	Affective disorders	40	50.6	28 (70)	56	88.4	38 (68)	1.4	1.3	0.8 - 1.9
	Depression, major without psychotic behavior	24	20.2	22 (92)	28	36.0	29 (100)	1.6	1.5	0.9 – 2.7
	Depression, minor	12	25.8	11 (92)	23	44.3	21 (91)	1.1	0.9	0.4 – 1.9
	Dissociative and personality disorders	0	1.4	0 (-)	0	2.2	0 (-)	-	-	-
	Neurotic disorders (anxiety disorders)	16	19.3	15 (94)	30	33.5	27 (90)	1.0	0.9	0.5 - 1.8
	Organic mental disorders	1	1.0	1 (100)	0	1.9	0 (-)	-	-	-
	Psychotic disorders	0	1.1	0 (-)	2	1.9	2 (100)	-	-	-
	Substance abuse	87	61.9	64 (74)	117	112.0	87 (74)	1.3	1.4	1.0 - 1.8
6a.	**Neurologic Disorders**	60	73.2	45 (75)	130	136.2	90 (69)	0.8	0.9	0.6 - 1.2
	Congenital or acquired central degenerative disorders	6	4.9	6 (100)	11	8.7	10 (100)	0.9	1.0	0.3 - 2.9
	Benign essential tremor	0	0.8	0 (-)	1	1.4	1 (100)	-	-	-
	Parkinson's disease	6	3.3	6 (100)	10	5.9	10 (100)	1.0	1.1	0.3 - 3.2
	Hemorrhage, cerebrovascular, or other major CNS disorders	9	7.4	7 (78)	17	15.0	13 (76)	1.0	1.1	0.4 - 2.5
	Other diseases of the nervous system	25	29.7	20 (80)	48	56.5	41 (85)	0.9	1.0	0.6 - 1.6
	Migraine	9	10.5	9 (100)	14	20.2	12 (86)	1.1	1.2	0.5 - 3.1
	Tension headache	4	3.0	3 (75)	1	5.9	1 (100)	5.5	7.9	0.8 – 384
	Peripheral neuromuscular disorders	20	30.2	20 (100)	54	54.2	49 (91)	0.7	0.7	0.4 - 1.1
	Neuralgia, neuritis, radiculitis	15	22.3	15 (100)	41	39.7	39 (95)	0.7	0.7	0.3 - 1.2

Table 10 (continued)

	Carpel Tunnel Syndrome	4	6.3	4 (100)	12	11.9	12 (100)	0.6	0.6	0.2 - 2.1
	Seizure disorders	0	0.9	0 (-)	0	1.5	0 (-)	-	-	-
6b.	**Opthamologic Disorders**	72	94.9	46 (64)	124	174.3	84 (68)	1.1	1.1	0.8 - 1.4
	Disorders of the eye	72	94.9	46 (64)	124	174.3	84 (68)	1.1	1.1	0.8 - 1.4
	Cataract	7	6.0	7 (100)	9	12.7	8 (89)	1.5	1.7	0.5 - 5.0
	Conjunctivitis, acute	12	15.5	12 (100)	14	28.0	13 (93)	1.6	1.6	0.7 - 3.6
	Glaucoma	6	7.4	6 (100)	10	13.8	10 (100)	1.1	1.1	0.3 - 3.4
7.	**Cardiovascular Disorders**	205	174.5	105 (51)	355	328.3	182 (51)	1.1	1.1	0.9 - 1.3
	Hypertension	73	62.9	66 (90)	134	114.3	122 (91)	1.0	1.0	0.7 - 1.3
	Atherosclerotic coronary vascular disease	50	35.3	28 (56)	84	65.7	40 (48)	1.1	1.1	0.8 - 1.6
	Carditis and cardiomyopathy/CHF	2	5.0	1 (50)	2	10.1	2 (100)	2.0	2.0	0.2 - 28
	Disorders of heart valves	5	4.6	5 (100)	16	9.2	16 (100)	0.6	0.6	0.2 - 1.8
	Dysrhythmia and conduction disorders	7	9.7	6 (86)	12	18.5	11 (92)	1.2	1.1	0.4 - 3.1
	Large arterial and peripheral vascular disorders	2	2.2	2 (100)	2	4.6	2 (100)	2.3	2.0	0.2 – 28
	Large vein thromboembolic disorders	1	3.3	1 (100)	4	6.4	4 (100)	0.5	0.5	0.0 - 4.9
	Minor venous/arterial disorders	0	4.7	0 (-)	0	9.7	0 (-)	-	-	-
	Other cardiovascular disorders	65	46.3	53 (82)	101	89.0	81 (80)	1.2	1.2	0.9 - 1.7
8a.	**Pulmonary Disorders**	314	239.8	144 (46)	515	431.0	224 (43)	1.1	1.1	1.0 - 1.3
	Lower respiratory infections	110	107.4	61 (55)	191	193.7	114 (60)	1.0	1.0	0.8 - 1.3
	Obstructive pulmonary diseases	20	21.6	17 (85)	37	39.9	34 (92)	1.0	1.0	0.6 - 1.8
	Asthma	6	12.4	6 (100)	17	22.1	16 (94)	0.7	0.6	0.2 – 1.7

Table 10 (continued)

	Chronic obstructive pulmonary disease	14	9.1	14 (100)	20	17.7	20 (100)	1.3	1.4	0.7 – 2.8
	Other pulmonary disorders	175	102.8	125 (71)	275	182.9	195 (71)	1.1	1.1	0.9 - 1.4
	Atelectasis	2	1.5	2 (100)	2	2.9	2 (100)	1.7	1.9	0.1 – 26.6
	Painful respiration	12	8.0	8 (67)	23	14.3	22 (96)	1.0	0.9	0.4 – 2.0
	Pleurisy with or without effusion	0	3.8	0 (-)	5	7.1	4 (80)	0.0	0.0	0.0 – 2.0
	Pulmonary eosinophilia	5	1.2	5 (100)	6	2.4	6 (100)	1.4	1.6	0.4 – 6.3
	Other disorders of the respiratory system	154	86.4	116	235	152.8	184 (78)	1.2	1.2	0.9 – 1.4
	Pulmonary edema	1	3.0	1 (100)	0	5.8	0 (-)	-	-	-
	Respiratory failure	0	0.2	0 (-)	0	0.3	0 (-)	-	-	-
	Sleep disorders	8	5.0	8 (100)	12	8.5	11 (92)	1.4	1.1	0.4 – 3.0
8b.	**Ear, Nose and Throat Disorders**	499	468.0	130 (26)	891	811.9	230 (26)	1.0	1.0	0.9 - 1.1
	Disorders of the ear and vestibular apparatus	94	98.1	52 (55)	133	169.2	86 (65)	1.3	1.2	0.9 - 1.6
	Upper respiratory infections	339	303.6	111 (33)	640	527.7	189 (30)	1.0	0.9	0.8 - 1.1
	Pharyngitis	63	69.9	38 (60)	112	118.0	67 (60)	1.1	1.0	0.7 – 1.3
	Sinusitis, acute	137	92.5	62 (45)	262	163.3	95 (36)	0.9	0.9	0.8 – 1.1
	Sinusitis, chronic with surgery	33	29.4	32 (97)	60	50.9	56 (93)	1.0	1.0	0.6 – 1.5
	Upper respiratory infection and Common cold, acute	106	106.0	43 (41)	200	186.0	88 (44)	0.9	0.9	0.7 – 1.2
	Other upper respiratory disorders	66	66.3	53 (80)	118	115.0	94 (80)	0.9	1.0	0.7 - 1.3
	Allergic rhinitis	54	55.6	49 (91)	95	97.0	86 (91)	0.9	1.0	0.7 – 1.4
9.	**Gastrointestinal Disorders**	254	198.8	94 (37)	426	358.2	181 (42)	1.1	1.1	0.9 - 1.3
	Disorders of esophagus	27	20.6	23 (85)	63	36.9	53 (84)	0.8	0.8	0.5 - 1.2

Table 10 (continued)

Disorders of stomach and duodenum	25	18.1	19 (76)	64	33.0	41 (64)	0.7	0.7	0.4 - 1.2
Disorders of the small intestine	1	1.6	1 (100)	1	2.6	1 (100)	-	-	-
Hernias	6	14.9	6 (100)	33	26.0	30 (91)	0.3	0.3	0.1 - 0.8
Inflammatory bowel disease	3	3.1	3 (100)	4	5.6	4 (100)	1.3	1.3	0.2 - 7.9
Disorders of the large intestine	66	43.4	47 (71)	94	78.6	63 (67)	1.3	1.3	0.9 - 1.8
Disorders of the liver	2	2.5	2 (100)	2	4.2	2 (100)	2.0	1.7	0.1 – 23
Cirrhosis of liver without mention of alcohol	2	0.4	2 (100)	0	0.7	0 (-)	-	-	-
Hepatitis, acute alcoholic	0	0.1	0 (-)	1	0.2	1 (100)	-	-	-
Hepatitis, acute without hepatic coma	0	1.0	0 (-)	1	1.6	1 (100)	-	-	-
Hepatitis, chronic without hepatic coma	0	0.7	0 (-)	0	1.1	0 (-)	-	-	-
Disorders of the biliary tract	18	8.8	8 (44)	14	17.8	9 (64)	2.4	2.6	1.2 - 5.5
Cholecystitis without cholelithiasis, acute	1	0.7	1 (100)	1	1.6	1 (100)	-	-	-
Cholecystitis without cholelithiasis, chronic or other	3	1.3	3 (100)	4	2.7	4 (100)	1.4	1.5	0.2 - 9.0
Cholelithiasis with acute cholecystitis	6	1.5	4 (67)	0	3.1	0 (-)	> 4.0	> 4.0	2.1 – 128
Cholelithiasis with chronic or unspecified cholecystitis	5	3.1	5 (100)	4	6.2	4 (100)	2.3	2.5	0.5 - 12.7
Cholelithiasis without cholecystitis	3	2.1	3 (100)	5	4.3	5 (100)	1.0	1.2	0.2 - 6.2
Disorders of the pancreas	7	1.8	1 (14)	2	3.4	1 (50)	4.3	6.4	1.2 - 63
Pancreatitis, acute	6	1.6	1 (17)	2	2.9	1 (50)	3.7	5.5	1.0 - 56
Pancreatitis, chronic	1	0.3	1 (100)	0	0.5	0 (-)	-	-	-
Other gastrointestinal disorders	99	83.9	75 (76)	149	150.2	119 (80)	1.2	1.2	0.9 - 1.5

Table 10 (continued)

10a.	**Urologic Disorders**	175	102.8	71 (41)	268	190.3	123 (46)	1.2	1.2	1.0 - 1.5
	Disorders of the renal function	3	1.7	2 (67)	1	3.0	1 (100)	5.3	5.5	0.4 - 287
	Chronic renal failure	2	1.1	2 (100)	0	1.9	1 (100)	-	-	-
	Disorders of renal parenchyma	2	0.7	2 (100)	1	1.3	1 (100)	3.0	3.6	0.2 - 213
	Renal cyst	2	0.7	2 (100)	1	1.3	1 (100)	3.0	3.6	0.2 – 211
	Lower and unspecified urinary tract infections	49	24.5	20 (41)	49	53.1	34 (69)	2.2	2.2	1.4 - 3.3
	Cystitis	18	5.7	7 (39)	17	12.8	13 (76)	2.6	2.4	1.2 – 4.8
	Urinary tract, not specified	31	18.8	16 (52)	32	40.4	25 (78)	2.0	2.1	1.2 – 3.5
	Other disorders of the lower urinary tract	1	1.7	1 (100)	13	2.9	12 (92)	0.2	0.1	0.0 - 0.9
	Urethral stricture	1	1.7	1 (100)	13	2.9	12 (92)	0.2	0.1	0.0 - 0.9
	Other disorders of the upper urinary tract	30	14.5	15 (50)	50	24.2	24 (48)	1.0	1.0	0.6 - 1.6
	Calculus of urinary tract	30	14.5	15 (50)	50	24.2	24 (48)	1.0	1.0	0.6 - 1.6
	Other genitourinary disorders	21	18.7	20 (95)	49	34.0	48 (98)	0.8	0.8	0.5 - 1.3
	Other diseases with surgery	21	18.7	20 (95)	49	34.0	48 (98)	0.8	0.8	0.5 - 1.3
	Upper urinary tract infections	3	1.2	2 (67)	5	2.3	3 (60)	1.1	1.2	0.2 - 6.0
	Acute pyelonephritis	3	1.2	2 (67)	5	2.3	3 (60)	1.1	1.2	0.2 - 6.0
	Disorders of the prostate	66	39.9	42 (64)	100	69.4	73 (73)	1.2	1.2	0.8 - 1.6
	Prostatic hyperplasia	28	20.6	24 (86)	55	38.2	52 (95)	1.0	1.0	0.6 - 1.5
	Prostatitis, acute	38	19.3	26 (68)	45	31.2	33 (73)	1.5	1.4	0.9 - 2.2
10b.	**Gynecologic and Reproductive Disorders**	72	83.8	50 (69)	173	190.0	100 (58)	0.9	0.9	0.7 - 1.3
	Disorders of the female breast (non-malignant)	4	5.8	4 (100)	11	15.9	10 (91)	0.9	1.0	0.2 - 3.4

Table 10 (continued)

Fibrocystic disease of breast	2	3.9	2 (100)	8	11.2	8 (100)	0.8	0.7	0.1 – 3.6
Infections of the female genital tract	4	6.3	3 (75)	16	18.0	10 (63)	0.8	0.7	0.2 - 2.2
Menopausal and menstrual disorders	8	12.5	6 (75)	23	37.4	16 (70)	0.9	1.0	0.4 - 2.5
Other gynecologic disorders	13	16.9	11 (85)	40	48.3	30 (75)	0.9	0.9	0.5 - 1.8
Endometriosis	0	0.9	0 (-)	1	2.5	1 (100)	-	-	-
Fertility and infertility management	43	42.4	36 (84)	83	70.5	66 (80)	0.9	0.9	0.6 - 1.3
Contraceptive or procreative management	4	9.6	4 (100)	10	16.0	10 (100)	0.7	0.7	0.2 – 2.3
Infertility female	0	0.5	0 (-)	1	1.1	1 (100)	-	-	-
Impotence of organic origin	24	13.3	23 (96)	31	23.5	31 (100)	1.4	1.4	0.8 - 2.4
Other disorders of the male reproductive system	15	19.0	14 (93)	41	29.8	40 (98)	0.6	0.6	0.3 - 1.1
11. Pregnancy	0	3.5	0 (-)	2	7.9	2 (100)	-	-	-
Complicated pregnancy or delivery	0	2.6	0 (-)	2	6.0	2 (100)	-	-	-
Diabetes, gestational	0	0.0	0 (-)	0	0.1	0 (-)	-	-	-
Multiple gestational	0	0.0	0 (-)	0	0.1	0 (-)	-	-	-
Postpartum hemorrhage	0	0.3	0 (-)	0	0.5	0 (-)	-	-	-
Pregnancy with abortion	0	0.2	0 (-)	0	0.6	0 (-)	-	-	-
Pregnancy, ectopic	0	0.0	0 (-)	0	0.1	0 (-)	-	-	-
Preterm labor	0	0.2	0 (-)	0	0.5	0 (-)	-	-	-
Other conditions during pregnancy	0	1.8	0 (-)	2	4.0	2 (100)	-	-	-
Normal or unspecified pregnancy and delivery	0	0.9	0 (-)	0	1.9	0 (-)	-	-	-
Spontaneous abortion	0	0.1	0 (-)	0	0.2	0 (-)	-	-	-

Table 10 (continued)

	Pregnancy	0	0.8	0 (-)	0	1.7	0 (-)	-	-	-
12.	**Dermatologic Disorders**	296	335.7	123 (42)	535	595.3	208 (39)	1.0	1.0	0.9 - 1.1
	Dermatologic infections	105	106.3	59 (56)	179	185.3	103 (58)	1.0	1.0	0.8 - 1.3
	Disorders of the hair and nails	6	10.7	5 (83)	16	20.6	13 (81)	0.7	0.7	0.2 - 1.9
	Immune mediated skin conditions	43	55.9	28 (65)	85	99.9	46 (54)	0.9	0.9	0.6 - 1.3
	Other dermatologic conditions	142	162.8	89 (63)	255	289.5	152 (60)	1.1	1.0	0.8 - 1.2
13.	**Musculoskeletal Disorders**	489	510.6	135 (28)	1047	918.4	245 (23)	0.8	0.8	0.8 - 0.9
	Acute or unspecified arthropathies and minor tendonitis	47	64.2	37 (79)	136	113.8	76 (56)	0.7	0.6	0.4 - 0.9
	Crystalline arthritis	8	7.1	7 (88)	10	12.1	10 (100)	1.5	1.4	0.5 - 3.8
	Degenerative joint disorders, other than spine	27	28.9	22 (81)	73	57.0	60 (82)	0.7	0.7	0.5 - 1.2
	Disorders of the spine	161	129.4	83 (52)	293	226.0	140 (48)	1.0	1.0	0.8 - 1.2
	Vasculitis and connective tissue disorders	4	3.3	4 (100)	7	6.5	7 (100)	1.3	1.1	0.2 - 4.4
	Other	242	277.7	112 (46)	528	503.0	197 (37)	0.8	0.8	0.7 - 1.0
14.	**Congenital Anomalies**	9	9.9	9 (100)	12	17.9	11 (92)	1.4	1.4	0.5 - 3.5
	Congenital Anomalies	9	9.9	9 (100)	12	17.9	11 (92)	1.4	1.4	0.5 - 3.5
	Atrial septal defect	0	0.1	0 (-)	0	0.3	0 (-)	-	-	-
	Other cardiovascular congenital abnormalities	0	1.3	0 (-)	3	2.4	3 (100)	0.0	0.0	0.0 - 4.5
	Other congenital abnormalities with admittance	9	8.3	9 (100)	8	14.8	8 (100)	2.0	2.0	0.7 - 6.0
	Other respiratory congenital abnormalities	0	0.2	0 (-)	1	0.4	1 (100)	-	-	-

Table 10 (continued)

15.	**Perinatal Disorders**	0	0.7	0 (-)	1	1.3	1 (100)	-	-	-
	Conditions originating in the perinatal period	0	0.6	0 (-)	1	1.0	1 (100)	-	-	-
16.	**Miscellaneous**	644	589.3	189 (29)	952	1070.6	294 (31)	1.2	1.2	1.1 - 1.4
	Other miscellaneous conditions	147	239.9	98 (67)	221	439.7	156 (71)	1.3	1.2	1.0 - 1.5
	Routine health care	84	100.8	77 (92)	120	184.2	112 (93)	1.3	1.3	1.0 - 1.7
	Symptoms or signs	497	349.4	181 (36)	731	630.9	275 (38)	1.2	1.2	1.1 - 1.4
	Abdominal pain	93	50.0	64 (69)	110	92.0	75 (68)	1.6	1.6	1.2 - 2.1
	Chest pain, unspecified	93	55.2	61 (66)	142	99.4	85 (60)	1.2	1.2	0.9 - 1.6
	Fever	8	6.2	8 (100)	11	10.6	11 (100)	1.2	1.3	0.4 – 3.4
	Headache with radiology	48	35.0	25 (52)	59	66.2	37 (63)	1.5	1.5	1.0 – 2.3
	Malaise and fatigue	22	22.1	16 (73)	40	41.6	37 (93)	1.0	1.0	0.6 - 1.8
	Syncope and collapse	7	7.2	6 (86)	8	13.1	7 (88)	1.7	1.6	0.5 – 5.0
	Symptoms, signs and ill-defined conditions	226	173.3	160 (71)	361	306.8	247 (68)	1.1	1.1	0.9 - 1.3
17.	**Injury and Poisoning**	191	283.1	102 (53)	358	481.0	170 (45)	1.0	1.0	0.8 - 1.1
	Major traumatic injury	39	81.1	30 (77)	80	137.6	61 (17)	0.9	0.8	0.6 – 1.2
	Minor traumatic injury	108	158.9	70 (65)	218	268.4	128 (59)	0.9	0.8	0.7 - 1.1
	Other injury	44	43.2	40 (91)	60	75.0	54 (90)	1.4	1.3	0.9 - 1.9

Table 11

Specialty Categories, Categories and Classes Which Had an RRE_pC that Excluded the Null Hypothesis in the 95% Confidence Interval for at Least One of the Four Comparison Groups A – D

CCG Description	Comparison Group A		Comparison Group B		Comparison Group C		Comparison Group D	
	RRE_pC	95% CI	RRE_pC	95% CI	RRE_pC	95% CI	RRE_pC	95% CI
Specialty Categories								
Cancers and Benign Growths	1.3	1.1 – 1.6	1.3	1.1 – 1.6	1.3	1.1 – 1.6	1.6	1.2 – 2.1
Miscellaneous	1.0	1.0 – 1.1	1.0	1.0 – 1.1	1.1	1.0 – 1.2	1.2	1.1 – 1.4
Categories								
Neoplasm of gastrointestinal tract	1.5	1.0 – 2.2	1.5	0.9 – 2.5	1.8	1.2 – 3.0	2.9	1.7 – 5.2
Neoplasm of male reproductive tract	10.0	1.3 – 447	5.7	0.6 – 276	7.6	0.9 – 359	9.7	1.1 – 458
Affective disorders	1.3	1.0 – 1.7	1.0	0.7 – 1.5	1.4	1.1 – 1.9	1.3	0.8 – 1.9
Disorders of the biliary tract	1.6	0.8 – 2.9	2.1	0.9 – 4.9	1.7	0.9 – 3.3	2.6	1.2 – 55
Disorders of the pancreas	3.0	0.7 – 18	3.3	0.8 – 20	4.7	0.9 – 46	6.4	1.2 – 63
Lower and unspecified urinary tract infections	1.3	1.0 – 1.6	1.5	1.1 – 2.1	1.3	0.9 – 1.8	2.2	1.4 – 3.3
Menopausal and menstrual disorders	1.1	0.7 – 1.7	2.0	1.1 – 4.0	1.1	0.7 – 2.0	1.0	0.4 – 2.5
Symptoms or signs	1.1	1.0 – 1.2	1.0	0.9 – 1.2	1.1	1.0 – 1.2	1.2	1.1 – 1.4
Classes								
Benign colon polyps	1.4	0.9 – 2.1	1.3	0.7 – 2.2	1.9	1.1 – 3.2	2.4	1.3 – 4.5

Table 11 (continued)

Cholelithiasis with acute cholecystitis	8.6	1.1 – 381	7.8	0.9 – 358	9.2	1.2 – 415	> 4.0	2.1 – 128
Cystitis	1.5	1.0 – 2.2	2.0	1.2 – 3.3	1.3	0.8 – 2.4	2.4	1.2 – 4.8
Urinary tract infections not specified	1.1	0.8 – 1.6	1.3	0.8 – 1.9	1.3	0.9 – 1.9	2.1	1.2 – 3.5
Abdominal pain	1.2	1.0 – 1.5	1.2	0.9 – 1.6	1.3	1.0 – 1.6	1.6	1.2 – 2.1

Table 12

Number of Episodes of Care for Benign Colonic Polyps, By Plant
and by Year (Percent in Parentheses)

	1993	1994	1995	1996	1997	1998	Total
Chemical Plant	15 (31)	9 (19)	6 (13)	1 (2)	8 (17)	9 (19)	48 (100)
Film Plant	12 (26)	8 (17)	6 (13)	5 (11)	7(15)	9 (19)	47 (100)

Appendix A

Appendix A
Table 1

Employment Status by Gender and Plant of the Four Study Comparison Groups per Beginning of Each Study Year and End of Study

	Study Group A		Study Group B		Study Group C		Study Group D	
	Chemical	Film	Chemical	Film	Chemical	Film	Chemical	Film
January 1, 1993								
Active	427 (65)	502 (26)	202 (52)	296 (70)	308 (62)	370 (76)	210 (100)	345 (100)
Inactive	20 (3)	26 (4)	11 (3)	12 (3)	18 (4)	22 (4)	1 (8)	0 (0)
Not yet hired	205 (31)	131 (20)	175 (45)	116 (27)	172 (35)	98 (20)	0 (0)	0 (0)
Retired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Terminated	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deceased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transferred	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100)	490 (100)	211 (100)	345 (100)
January 1, 1994								
Active	420 (64)	499 (76)	197 (51)	299 (71)	305 (61)	366 (75)	202 (96)	336 (97)
Inactive	21 (3)	26 (4)	11 (3)	13 (3)	19 (4)	23 (5)	4 (2)	2 (1)
Not yet hired	190 (29)	116 (18)	167 (43)	107 (25)	163 (33)	87 (18)	0 (0)	0 (0)
Retired	8 (1)	8 (1)	5 (1)	2 (1)	5 (1)	7 (1)	4 (2)	5 (1)
Terminated	10 (2)	6 (1)	5 (1)	1 (0)	4 (1)	5 (1)	1 (0)	2 (1)
Deceased	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transferred	3 (0)	4 (1)	3 (1)	2 (1)	2 (0)	2 (0)	0 (0)	0 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100)	490 (100)	211 (100)	345 (100)
January 1, 1995								
Active	422 (65)	469 (71)	202 (52)	295 (70)	306 (61)	343 (70)	194 (92)	311 (90)
Inactive	26 (4)	32 (5)	15 (4)	14 (3)	23 (5)	29 (6)	8 (4)	9 (3)
Not yet hired	174 (27)	111 (17)	155 (40)	103 (24)	150 (30)	86 (18)	0 (0)	0 (0)
Retired	14 (2)	33 (5)	8 (2)	5 (1)	10 (2)	24 (5)	8 (4)	21 (6)
Terminated	13 (2)	5 (1)	5 (1)	1 (0)	7 (1)	4 (1)	1 (0)	2 (1)
Deceased	0 (0)	2 (0)	0 (0)	1 (0)	0 (0)	2 (0)	0 (0)	1 (0)
Transferred	3 (0)	6 (1)	3 (1)	5 (1)	2 (0)	2 (0)	0 (0)	1 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100)	490 (100)	211 (100)	345 (100)

January 1, 1996								
Active	428 (66)	467 (71)	207 (53)	298 (70)	314 (63)	339 (69)	190 (90)	298 (86)
Inactive	20 (3)	33 (5)	11 (3)	16 (4)	17 (3)	27 (6)	4 (2)	9 (3)
Not yet hired	159 (24)	98 (15)	143 (37)	91 (21)	136 (27)	77 (16)	0 (0)	0 (0)
Retired	25 (4)	44 (7)	17 (4)	9 (2)	19 (4)	35 (7)	15 (7)	32 (9)
Terminated	15 (2)	10 (2)	6 (2)	4 (1)	9 (2)	9 (2)	2 (1)	4 (1)
Deceased	1 (0)	2 (0)	0 (0)	1 (0)	1 (0)	2 (0)	0 (0)	1 (0)
Transferred	4 (1)	5 (1)	4 (1)	5 (1)	2 (0)	1 (0)	0 (0)	1 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100)	490 (100)	211 (100)	345 (100)
January 1, 1997								
Active	435 (67)	458 (69)	221 (57)	304 (72)	326 (65)	337 (69)	173 (82)	275 (80)
Inactive	26 (4)	39 (6)	15 (4)	18 (4)	21 (4)	33 (7)	6 (3)	17 (5)
Not yet hired	118 (18)	75 (11)	108 (28)	71 (17)	101 (20)	57 (12)	0 (0)	0 (0)
Retired	45 (7)	63 (10)	29 (7)	15 (4)	33 (7)	49 (10)	27 (13)	45 (13)
Terminated	18 (3)	12 (2)	8 (2)	5 (1)	12 (2)	9 (2)	3 (1)	5 (1)
Deceased	4 (1)	4 (1)	1 (0)	3 (1)	3 (1)	4 (1)	2 (1)	2 (1)
Transferred	6 (1)	8 (1)	6 (2)	8 (2)	2 (0)	1 (0)	0 (0)	1 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100)	490 (100)	211 (100)	345 (100)
January 1, 1998								
Active	518 (79)	484 (73)	300 (77)	335 (79)	403 (81)	363 (74)	163 (77)	260 (75)
Inactive	26 (4)	39 (6)	18 (5)	21 (5)	20 (4)	33 (7)	7 (3)	17 (5)
Not yet hired	15 (2)	21 (3)	15 (4)	21 (5)	12 (2)	10 (2)	0 (0)	0 (0)
Retired	57 (9)	84 (13)	35 (9)	24 (6)	41 (8)	64 (13)	34 (16)	59 (17)
Terminated	20 (3)	18 (3)	10 (3)	12 (3)	15 (3)	15 (3)	4 (2)	6 (2)
Deceased	6 (1)	5 (1)	2 (1)	3 (1)	5 (1)	5 (1)	3 (1)	3 (1)
Transferred	10 (2)	8 (1)	8 (2)	8 (2)	2 (0)	0 (0)	0 (0)	0 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100)	490 (100)	211 (100)	345 (100)

December 31, 1998								
Active	511 (78)	470 (71)	301 (78)	338 (80)	400 (80)	346 (71)	156 (74)	237 (69)
Inactive	29 (4)	39 (6)	19 (5)	24 (6)	22 (4)	33 (7)	7 (3)	20 (6)
Not yet hired	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retired	72 (11)	112 (17)	45 (12)	35 (8)	48 (10)	84 (17)	39 (18)	77 (22)
Terminated	23 (4)	22 (3)	13 (3)	15 (4)	20 (4)	19 (4)	5 (2)	7 (2)
Deceased	7 (1)	8 (1)	2 (1)	4 (1)	6 (1)	8 (2)	4 (2)	4 (1)
Transferred	10 (2)	8 (1)	8 (2)	8 (2)	2 (0)	0 (0)	0 (0)	0 (0)
TOTAL	652 (100)	659 (100)	388 (100)	424 (100)	498 (100	490 (100)	211 (100)	345 (100)