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Analysis of a Standardized Approach to Healthcare Worker Hazardous Medication Surveillance: Lessons learned and future enhancements.

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Running Head Title: Standardized Surveillance for Hazardous Medications

Abstract:

Objective: To evaluate the effectiveness of a standardized hazardous medication surveillance program and identify occupational factors associated with adverse health outcomes among healthcare workers (HCWs).

Methods: We analyzed data from 2,625 HCWs enrolled in a multi-site surveillance program (2020–2022). Participants completed a standardized questionnaire and underwent complete blood count testing. Exposure was categorized by weekly time handling hazardous medications. Associations were evaluated using univariate and multivariable analyses.

Results: Higher exposure (>8 hours/week) was associated with increased symptom reporting, hazardous medication spills, and adverse reproductive outcomes. Female sex, older age, and spill exposure independently predicted symptom reporting and reproductive outcomes. No significant association was observed between exposure intensity and abnormal blood counts.

Conclusion: Questionnaire-based surveillance effectively identified exposure-related health risks, whereas routine complete blood count testing showed limited utility.

Keywords: Hazardous Medications, Adverse Events, Reproductive Outcome.

Learning Outcomes:

At the end of this manuscript, readers should be able to:

- Identify key occupational exposure factors linked to reproductive outcomes and symptom reporting among healthcare workers handling hazardous medications.
- Assess the role of standardized surveillance questionnaires in capturing exposure-related health risks in clinical practice.
- Compare questionnaire-based surveillance with routine complete blood count testing to guide evidence-based occupational health monitoring strategies.

Introduction

Hazardous drug exposure, particularly to antineoplastic agents, poses substantial health risks to healthcare workers (HCWs), including risks of reproductive toxicity, cancers, and organ damage [1-3]. Although preventive measures have advanced, including the use of closed-system transfer devices (CSTDs) and improved personal protective equipment (PPE), hazardous drug spills continue to be a source of occupational exposure for healthcare workers including oncology nurses, underscoring persistent gaps in exposure prevention practices [1]. This risk is compounded by the cumulative nature of low-dose occupational exposure. Biomonitoring studies have shown that HCWs handling antineoplastic agents may have detectable levels of these medications, although the concentrations are typically very low (often in pg/mL range). These levels are substantially lower than therapeutic concentrations observed in treated patients; however, repeated low-level exposures may still represent a relevant occupational health concern[4-6]. Prior studies have evaluated trends in medical center surveillance programs for HCWs handling hazardous medications[7,8]. Hazardous Medication Surveillance Programs (HMSPs) aim to reduce workplace exposure to hazardous medications and support early identification of adverse health outcomes, including increased rates of cancer and reproductive complications among HCWs [7,8]. Despite hazardous medication handling among healthcare staff, many institutions lack standardized monitoring programs, emphasizing the need for consistent surveillance protocols [7]. Further qualitative research among occupational health leaders identified challenges in establishing effective surveillance, with many institutions citing a lack of clear outcome correlations and standardized practices as significant barriers [8]. To address these challenges, current programs have increasingly emphasized preventive strategies, such as enhanced PPE use and routine health monitoring[9,10].

Since 2020, the adoption of USP <800> standards have further driven safety improvements, mandating CSTDs and environmental wipe sampling as part of comprehensive exposure control protocols [11-13]. Despite these initiatives, recent evidence suggests that drug spills remain a common exposure route, and environmental testing alone may not be sufficient as a surveillance measure [14,15]. Additionally, logistical and financial constraints continue to hinder the implementation of systematic, cost-effective surveillance programs, leaving many institutions questioning the feasibility of routine monitoring [7,16,17].

The objective of this analysis is to evaluate the effectiveness and feasibility of a standardized approach to hazardous medication surveillance, aiming to identify best practices for enhancing healthcare worker safety and minimizing occupational exposure risks.

Methods

Study setting:

Data collected from HCWs at a large multi-site medical institution between January 12, 2020, and May 27, 2022, were included in the analysis. A summary of the design of the HMSP at our institution has previously been published including the questionnaire used for the surveillance cycle presented here[9]. The institution includes three major sites and several community hospitals within a single healthcare system, each with inpatient and outpatient oncology services and centralized pharmacy compounding units responsible for antineoplastic agents' preparations.

Participant Eligibility and Enrolment:

HCWs identified at increased risk of exposure were enrolled in the HMSP and given the option to decline participation (opt out') if they desired. A multidisciplinary team consisting of Occupational Medicine physicians, Occupational Health nurses, Pharmacy staff, and Occupational Safety personnel including Industrial Hygienists identified a threshold for routine

contact with hazardous medications (and therefore increased risk of inadvertent exposure) as: "health care workers who prepare, handle, administer, transport, or dispose of hazardous medications or waste at least 2 times per week for at least 26 weeks annually as part of their job assignment"[9]. Supervisors and leaders identified work units and roles within those units that would meet these criteria to be considered at *elevated risk* of hazardous medication exposure. Examples include pharmacists who compound hazardous medications, staff who work regularly on oncology units, and nurses who routinely administer hazardous medications to patients. HCWs who experience a spill of hazardous medications are required to complete an incident report; their risk of exposure, either from the single exposure event or from ongoing handling/administration, is evaluated, and they may be added to the HMSP after review by an employee occupational health professional. In addition, newly hired HCWs who are within one of the pre-identified groups at increased risk are enrolled in the program at the time of their post offer pre-placement evaluation in Employee Occupational Health Services (EOHS) and sent a HMSP questionnaire invitation immediately after their start date (once their business email is active).

Study and Questionnaire design:

This is a cross-sectional analysis of a prospective occupational surveillance program that uses a primarily structured electronic questionnaire composed of close-ended questions with categorical or binary response options. Beginning on January 6, 2020, all HCWs enrolled in the HMSP across all institutional sites received a standardized electronic questionnaire by email to complete. Standard questions inquire about health symptoms and adverse reproductive outcomes for those regularly handling hazardous medications, including antineoplastic agents. We removed a question about menstrual irregularity which was present prior to 2020 while retaining

questions about adverse reproductive outcomes. The historic HMSP prior to 2020 demonstrated that the majority of reproductive age HCWs who menstruate endorsed irregularity in cycles and it was determined that additional workup of this symptom in isolation could cause inadvertent harm such as increased anxiety or unnecessary testing in HCWs. Specific questions regarding frequency of use of personal protective equipment were replaced with a question seeking feedback on adequacy of safety controls and protection from hazardous medications in the work area. The list of symptoms was adjusted based on our experience with hazardous medication exposure risks and occupational health subject matter expert input. We also added a question similar to one in the Occupational Safety and Health Administration's respirator medical clearance questionnaire, which asks whether the employee would like to speak with a health care professional in Occupational Health about their responses. A copy of the Hazardous Medication Surveillance Program questionnaire, which was used for baseline surveillance during the period of 2020-2022, is included as SDC#1, http://links.lww.com/JOM/C493.

Data collection:

Healthcare workers (HCWs) received an initial email invitation to participate in the HMSP including a questionnaire and, subsequently, laboratory testing with a complete blood count (CBC). Two reminder emails were sent with the third notification including a declination form if the HCW chose not to participate. It was communicated to HCWs that participation was voluntary but strongly encouraged. Those that did not complete the questionnaire or who indicated they desired to decline participation were not escalated to the supervisor as the program is voluntary. The declination form and process were modeled after declination for Hepatitis B vaccination in healthcare institutions where the HCW was advised that if they opted out and chose later to enroll in the program, the institution would support their later enrollment. All

evaluations, including laboratory testing, were provided free of charge to the HCWs. All sites aimed to launch the first cycle of the standardized HMSP in January 2020, however one site representing approximately 15% of HCWs enrolled in the program launched in June 2020 due to site specific constraints. HCWs completed one surveillance questionnaire between January 1, 2020, and Dec 31, 2021. The cohort included existing HCWs who were identified as meeting criteria for enrollment in the program as of January 1, 2020, as well as new HCWss hired into roles that involved handling or administering hazardous medications.

After the HCWs completed and submitted the electronic questionnaire, they received a lab requisition to complete a CBC with differentialFor the largest site participating, an automated process for sending the lab requisitions was developed with software that allowed test results to be imported directly into the EOHS confidential occupational health database for HCWss. Other sites manually emailed lab requisitions and transcribed results into the EOHS database once received. Quality assurance of the data was performed to ensure that all results were within physiological ranges. Reference ranges for CBC parameters used in the surveillance program are shown in SDC#2, http://links.lww.com/JOM/C494.

Outcomes assessed included any poor reproductive outcome reported on the questionnaire among female HCWs ages 18-44, any reported symptom associated with handling hazardous medications, any abnormal lab value, development of a new malignancy, and report of any safety concerns. A poor reproductive outcome was defined as the HCW reporting having difficulty conceiving (ever or while in their current job) or conceiving a child resulting in miscarriage, stillbirth, or birth defect in the last 2 years. Among the 1691 females ages 18-44, analysis for the reproductive outcome questions was limited to the 1688 who responded to the reproductive outcome questions. Reported symptoms associated with handling hazardous medications

included bruising; burning, tearing, or redness of the eye; coughing; dizziness/lightheadedness; difficulty remembering or concentrating; facial flushing; hair loss; headache; nausea; nasal sores; skin rash; vomiting; and involuntary weight loss. CBC labs included basophil count, eosinophil count, erythrocyte count, hematocrit, hemoglobin, leukocyte count, lymphocyte count, mean corpuscular volume monocyte count, neutrophil count, platelet count, and red cell distribution width. HCWs who completed the questionnaire but were missing CBC results (N=109) were included in the overall program evaluation but excluded from analysis of CBC results. Results were collated for trends and at the end of the surveillance cycle, emails were sent to supervisors which included the anonymous concern(s) reported in their area as well as a summary of concerns across other work units with the request that they work with their teams and occupational safety to mitigate any remaining safety concerns.

Statistical analysis:

Demographics, questionnaire data, and complete blood count results were compared by HCW self-reported amount of time per week working with hazardous medications (grouped as None yet, up to 8 hours/week, >8 hours/week), and associations of demographics and questionnaire data with outcomes were evaluated. Demographics included sex, age at questionnaire, occupational grouping, and time from hiring to questionnaire; questionnaire data included past exposures to medication spills, diagnosed conditions, symptoms, HCW safety concerns, and reproductive health. Discrete factors were described as N (%), and continuous factors were described as median (interquartile range [IQR], range). All bivariate associations were assessed using Chi-Square and Fisher Exact tests for discrete factors and Kruskal-Wallis tests for continuous measures. Multivariable logistic regression evaluated factors associated with each outcome accounting for amount of time per week working with hazardous medications, sex, age,

site, occupation type, exposure status to hazardous medication spill in the past 2 years. The model of poor reproductive outcome did not include sex as it was limited to female HCWs only, and the model of new malignancy only included amount of time per week working with hazardous medications and age due to a low event rate. Model results were reported as odds ratio (OR) and 95% confidence interval (CI). Statistical analyses were performed using SAS version 9.4, and a $p<0.05$ was considered statistically significant.

Ethical approval:

This surveillance program was conducted as a part of the institution occupational health monitor initiative. Data were analyzed in a de-identified form in accordance with the participant institution policies.

Results:

A total of 2625 HCWs completed the HMSP questionnaire between January 1, 2020, and December 31, 2021, across all enterprise sites. An additional 18 HCWs started but did not complete the questionnaire, and their information was excluded from the analysis. Fewer than ten HCWs who were enrolled in the program did not complete the questionnaire but reported results of a CBC obtained outside of the HMSP to EOHS. These individuals were also excluded from the analysis.

Demographic data by time per week working with hazardous medications for the 2625 HCWss who completed the questionnaire are included in Table 1. As the first cycle of the standardized questionnaire between 2020-2022 included many new hires, an internal control group for those who had not yet had exposure to hazardous medications emerged with 618 respondents out of 2625 indicating they had not yet worked with hazardous medications. The majority of HCWs included in the analysis (78.9%) were between 18-44 years old, and the most prevalent

occupational group undergoing surveillance were Registered Nurses (RNs) or Licensed Practical Nurses (LPNs) (76.2%). Physicians and advanced practice providers (APPs) represented 1.4% of all respondents with only 8 physicians or APPs reporting >8 hours/week working with hazardous medications in the cohort. Female HCWs made up 81.4% of the cohort. HCWss who were exposed to hazardous medications >8 hours/week were more likely to be older and be in a Technician or Healthcare Professional role (both $p<0.001$),

Table 2 summarizes responses to the questionnaire and complete blood count results stratified by self-reported amount of time per week spent working with hazardous medications. On univariate analysis, exposure to hazardous medication spills, number of reported symptoms, HCWs with safety concerns, and difficulty conceiving among female HCWs ages 18-44 were all higher among HCWs who spent >8 hours/week working with hazardous medications (all $p<0.001$). Any newly diagnosed condition (cancer, liver, or neurologic disease) in the last two years was greater for HCWs who handled hazardous medications > 8hrs/week ($p<0.004$) (Table 2). Type and amount of spill among HCWs who were exposed to a spill, evaluation and diagnoses by a medical provider for difficulty conceiving and fathering a child resulting in a poor birth outcome among male HCWs did not differ significantly by amount of time per week spent working with hazardous medications (all $p>0.05$). An abnormal result on the complete blood count labs was also not significantly associated with hours per week spent working with hazardous medications ($p=0.14$).

Adverse Reproductive Outcomes

Among females age 18-44 who responded to the reproductive outcomes questions, 9.5% (160/1688) reported a negative fertility or pregnancy outcome. On univariate analysis, negative reproductive outcomes were more likely among HCWs with increased exposure to hazardous medications per week (14.6% among those exposed >8 hours/week vs, 8.3% among those up to 8

hours/week vs. 4.8% among those with no exposure; p<0.001) and among those who reported exposure to a hazardous medication spill within the past 2 years (20.5% vs. 9.0%; p<0.001). HCWs with a negative reproductive outcome were also older than those without such outcome (median [IQR] 33 [29-37] vs. 27 [24-33]; p<0.001). On multivariable analysis, odds of poor reproductive outcomes were higher among HCWs handling hazardous medications more than 8 hours/week compared to those with no exposure (OR 2.49, 95% CI 1.47, 4.22). Higher odds were also observed among physicians and APPs compared with RN/LPN (OR 2.93, 95% CI 1.09, 7.86), as well as with increasing age (OR 1.10 per year of increasing age, 95% CI 1.07, 1.13). However, the physician and APP group represented a substantially smaller proportion of the HCW population compared with RN/LPNs, which may limit the precision and stability of this measurement. After controlling for other factors, exposure to a hazardous medication spill in the past 2 years was no longer significantly associated with a adverse reproductive outcome. (Table 3*).*

Report of Symptoms

One tenth of HCWs (257/2625, 9.8%) reported one or more symptom on the surveillance questionnaire. On univariate analysis, rates of HCWs reporting any symptom were higher among females (10.9% vs 4.7%; p<0.001), HCWs with higher amount of time per week working with hazardous medications (15.9% >8 hours/week vs. 7.9% up to 8 hours/week vs. 3.9% none; p<0.001), and those reporting exposure to a spill in the last 2 years (28.8% vs. 9.0%, p<0.001). Those reporting at least one symptom were older (median [IQR] 37 [29-50] vs. 30 [25-40]). On multivariable analysis, increased odds of endorsement of any symptom were associated with handling hazardous medications up to 8 hours/week (OR 1.74, 95% CI 1.08, 2.79) or more than 8 hours/week (OR 3.29, 95% CI 2.07, 5.24), compared to no exposure. Higher odds of symptom endorsement were also observed among females (OR 2.42, 95% CI 1.53, 3.83), for older age (OR

1.03 per year of increasing age, 95% CI 1.02, 1.04), and among those reporting exposure to a hazardous medication spill (OR 2.67, 95% CI 1.67, 4.26). (Table 3).

Lab Abnormality

Among HCWs with CBC results, 57.0% (1433/2516) had one or more abnormal lab value. On univariate analysis, having an abnormality on CBC was more likely among females (59.1% vs. 47.6%; $p<0.001$) but was not significantly associated with amount of time per week working with hazardous medications or exposure to a hazardous medication spill in the past 2 years. On multivariable analysis, increased odds of an abnormality on CBC were observed with female sex (OR 1.70, 95% CI 1.38, 2.10) and the occupational group Healthcare Professional (OR 1.46, 95% CI 1.04, 2.04) compared to RN/LPN. CBC abnormalities were inversely associated with older age (OR 0.98 per year of increasing age, 95% CI 0.98, 0.99). Additionally,on multivariable analysis, CBC abnormalities were not associated with amount of time working with hazardous medications or with exposure to a spill. (Table 3)

New Malignancy

A small number of HCWs reported a new malignancy diagnosis within the past 2 years (N=21, 0.8%). On univariate analysis, higher rates of a new malignancy diagnosis were associated with increased hours of exposure to hazardous medications per week (1.5% among >8 hours/week vs. 0.6% up to 8 hours/week vs. 0.2% no exposure; $p=0.007$) and exposure to a hazardous medication spill in the past 2 years (3.8% vs 0.7%; $p=0.008$). In a multivariable model including weekly exposure and age, development of any cancer was associated with older age (OR 1.07 per year of increasing age, 95% CI 1.04, 1.11). New cancers were not associated with amount of time working with hazardous medications after adjusting for age (Table 3). The incidence of new cancers was low overall (21 out of 2625 total respondents).

Safety Concerns

The questionnaire included an item asking HCWs if they had safety concerns related to hazardous medication handling in their work area. Seventy-five total HCWs reported safety concerns and of those, 46 (61.3%) did not discuss the concern with their supervisor. Among HCWs reporting safety concerns, some had discussed these concerns with their supervisor, while others had not. While a small number of HCWs who reported safety concerns indicated wanting to speak to an EOHS professional about a safety related question, follow-up was conducted with every HCW reporting a safety concern. **?**

'Discussion

Principal Findings

In this large, multisite medical institution, a comprehensive medical surveillance program was implemented for all workers at risk of handing antineoplastic and other hazardous medications. From this surveillance, several important findings emerged. First, frequent handling of hazardous medications was significantly associated with higher odds of adverse reproductive outcomes among female HCWs of reproductive age on univariate and multivariate analysis, consistent with prior epidemiologic reports[18]. Second, HCWs with greater exposure frequency or recent hazardous medication spills were more likely to report symptoms. In contrast, CBC-based laboratory surveillance frequently identified abnormalities that were not associated with hazardous medication exposure, indicating that routine CBC monitoring is not a clinically effective method for detecting occupational toxicity. Finally, the inclusion of questions related to workplace safety concerns provided a practical mechanism for identifying and addressing unreported hazards.

Reproductive Outcomes and Reported Symptoms

The observed association on univariate analysis between frequency of hazardous medication handling and adverse reproductive outcomes aligns with existing literature, demonstrating increased risks of adverse pregnancy outcomes among HCWs exposed to antineoplastic drugs[3,18,19]. The association remained statistically significant on multivariate analysis for staff handling hazardous medications more than 8hrs per week. However, we were not able to do detailed analysis of individual adverse pregnancy outcomes (miscarriage, stillbirth, or birth defect) due to the way the question was asked. While our results identified this outcome among HCWs exposed to hazardous medications, adverse reproductive outcomes are also known to increase with age in the general population with those age over 35 years often referred to as 'advanced maternal age'[20,21] due to poor pregnancy outcome risk. Although the questionnaire did not ask about pregnancy incidence and therefore did not allow calculation of adverse pregnancy outcome rates, spontaneous miscarriage or pregnancy loss is approximately 15-20% in the general population with rates increasing with age[22].

Similarly, HCWs with higher exposure frequency or recent spill events were more likely to report symptoms. While these symptoms may reflect a combination of occupational and non-occupational factors, the trend was not statistically significant. However, the trend supports the value of symptom surveillance as a potential early signal of potential exposure-related effects.

Laboratory Testing

A key finding in this analysis was the limited clinical value of CBC testing as a surveillance tool. More than half of the participants had at least one abnormal CBC value, yet these abnormalities were not associated with exposure frequency, spill events, or other exposure-related measurements. Many CBC abnormalities were related to anemia in female HCWs of

reproductive age. None of the CBC abnormalities identified in this analysis resulted in meaningful interventions. Such testing may add cost and complexity without providing actionable guidance. In this context, routine CBC surveillance appears to have limited value as a consistent screening tool for occupational exposure to hazardous medication.

Cancer Outcomes

The surveillance incidence of newly diagnosed cancer was low, and while univariate analyses initially suggested an increased risk among HCWs with greater exposure, this association was no longer present after adjustment for age. We did observe an association between increasing age and cancer diagnosis, which is consistent with population-level cancer incidence and likely reflects underlying background risk rather than occupational exposure[23]. Cancer latency periods often exceed the surveillance window, and the program may detect rare, long-latency cancer outcomes that are not correlated with occupational exposure.

Safety Concerns

The inclusion of questions regarding workplace safety concerns was one of the most actionable components of the surveillance program. A majority of HCWs reporting concerns had not previously raised them with their supervisor or leadership teams, highlighting the value of providing an alternative and confidential pathway for HCW reporting. The ability to share aggregate anonymous concerns with leadership facilitated targeted interventions and reinforced a culture of safety, representing a meaningful benefit of this program beyond basic health outcome surveillance. HCWs expressed appreciation for this mechanism of feedback.

Strengths

Strengths of the analysis include a large sample size, multisite implementation with geographic diversity, standardized data collection, and high participation rates for both the questionnaire and

laboratory testing. The predominance of female HCWs of reproductive age enhanced the ability to evaluate reproductive outcomes, a key concern in hazardous medication exposure.

Limitations

Several limitations should be acknowledged. As the first year of the standardized medical surveillance program, these data represent a true baseline only for newly hired HCWs without prior exposure. The cross-sectional design limits causal inference and the ability to evaluate changes over time. However, future evaluation addressing these limitations is planned. Although the program was implemented across multiple sites, all sites were part of the same healthcare institution and operated under similar occupational safety policies, pharmacy procedures, and hazardous drug handling protocols. Consequently, the findings may not be fully generalizable to institutions with different organizational structures or safety practices, and additional multi-institutional studies would help determine whether similar patterns are observed across diverse healthcare systems. Also,this work relies on self-reported symptoms that are subject to reporting and recall bias, as well as symptoms related to preexisting medical conditions. Finally, the questionnaire did not include pregnancy incidence; therefore, denominator data was not available to calculate adverse reproductive outcome rates. This limited the ability to compare the hazard exposure risk with population data.

Implications for Future Surveillance

Our findings support the feasibility, scalability, and value of a standardized medical surveillance questionnaire for HCWs handling hazardous medications. Questions about workplace safety concerns identified opportunities to intervene and enhance training, procedures, and hazard controls. Incidence data on pregnancies conceived will be added to future questionnaires, allowing calculation of adverse reproductive outcome rates to compare to the general population.

Further refinements planned for future HMSP cycles include strategies to reduce reporting of unrelated chronic symptoms from preexisting medical conditions to help isolate symptoms that are occurring due to hazardous medication exposure. Using the initial year as a baseline, at least one more cycle of laboratory testing will be offered to determine whether changes from an individual's baseline are associated with measures of exposure frequency or intensity, or result in actionable findings.

Conclusion:

HCWs who handle hazardous medication are at risk of adverse health effects related to occupational exposure. Healthcare facilities should implement comprehensive occupational safety programs incorporating environmental controls, training, optimal work practices, environmental monitoring, and personal protective equipment. A standardized medical surveillance questionnaire offers a practical and informative approach to monitoring the occupational health and safety concerns of HCW who handle hazardous medications. Routine laboratory testing using a CBC does not appear to be advantageous in identifying abnormalities attributable to occupational exposure.

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Table 1: Demographics by Amount of Time per Week Working with Hazardous Medications[1]

	None yet (N=618)	Up to 8 hours/week (N=1085)	>8 hours/week (N=922)	Total (N=2625)	P-value
Female sex	491 (79.4%)	878 (80.9%)	769 (83.4%)	2138 (81.4%)	0.12[2]
Age at questionnaire					<0.001[3]
Median (IQR)	26 (22, 34)	32 (26, 43)	34 (27, 450)	31 (25, 42)	
Range	18, 72	19, 76	19, 72	18, 76	
Age category					<0.001[2]
18-24	274 (44.3%)	195 (18.0%)	110 (11.9%)	579 (22.1%)	
25-29	121 (19.6%)	268 (24.7%)	210 (22.8%)	599 (22.8%)	
30-34	79 (12.8%)	171 (15.8%)	163 (17.7%)	413 (15.7%)	
35-39	47 (7.6%)	126 (11.6%)	118 (12.8%)	291 (11.1%)	
40-44	28 (4.5%)	81 (7.5%)	81 (8.8%)	190 (7.2%)	
45-54	31 (5.0%)	121 (11.2%)	128 (13.9%)	280 (10.7%)	
55+	38 (6.1%)	123 (11.3%)	112 (12.1%)	273 (10.4%)	
Site					<0.001[2]
A	107 (17.3%)	291 (26.8%)	270 (29.3%)	668 (25.4%)	
B	2 (0.3%)	47 (4.3%)	88 (9.5%)	137 (5.2%)	
C	464 (75.1%)	593 (54.7%)	447 (48.5%)	1504 (57.3%)	
D	45 (7.3%)	154 (14.2%)	117 (12.7%)	316 (12.0%)	
Occupational grouping					<0.001[2]
RN/LPN	493 (79.8%)	848 (78.2%)	659 (71.5%)	2000 (76.2%)	
Technician	66 (10.7%)	83 (7.6%)	136 (14.8%)	285 (10.9%)	
Healthcare Professional	17 (2.8%)	75 (6.9%)	88 (9.5%)	180 (6.9%)	

Services/Support Personnel	27 (4.4%)	52 (4.8%)	12 (1.3%)	91 (3.5%)	
Physician/Advanced Practice Provider	11 (1.8%)	17 (1.6%)	8 (0.9%)	36 (1.4%)	
Other	4 (0.6%)	10 (0.9%)	19 (2.1%)	33 (1.3%)	
Time to questionnaire[4]					<0.001[2]
>6 months prior to hire	8 (1.3%)	19 (1.8%)	10 (1.1%)	37 (1.4%)	
>1 to 6 months prior to hire	136 (22.0%)	25 (2.3%)	12 (1.3%)	173 (6.6%)	
≤1 month prior to hire	360 (58.3%)	242 (22.3%)	190 (20.6%)	792 (30.2%)	
0 to <6 months after hire	16 (2.6%)	65 (6.0%)	49 (5.3%)	130 (5.0%)	
6 to <12 months after hire	1 (0.2%)	53 (4.9%)	44 (4.8%)	98 (3.7%)	
1 to <2 years after hire	10 (1.6%)	127 (11.7%)	92 (10.0%)	229 (8.7%)	
2 to <3 years after hire	7 (1.1%)	70 (6.5%)	49 (5.3%)	126 (4.8%)	
3 to <5 years after hire	16 (2.6%)	130 (12.0%)	113 (12.3%)	259 (9.9%)	
5 to <10 years after hire	21 (3.4%)	141 (13.0%)	139 (15.1%)	301 (11.5%)	
10 to <20 years after hire	20 (3.2%)	110 (10.1%)	133 (14.4%)	263 (10.0%)	
20+ years after hire	23 (3.7%)	103 (9.5%)	91 (9.9%)	217 (8.3%)	

[1]Results are reported as N (%) unless otherwise noted

[2]Chi-Square p-value

[3]Kruskal-Wallis p-value

[4]Longest duration prior to hire was 34 months, longest duration after hire was 50 years

Table 2: Questionnaire Data and Complete Blood Count Results by Amount of Time per Week Working with Hazardous Medications[1]

	None yet (N=618)	Up to 8 hours/week (N=1085)	>8 hours/week (N=922)	Total (N=2625)	P-value
Exposed to hazardous medication spill in past 2 years	3/618 (0.5%)	21/1085 (1.9%)	80/922 (8.7%)	104/2625 (4.0%)	<0.001[2]
Type and amount of spill[3]					0.204[4]
Chemo >5mL	1/3 (33.3%)	8/21 (38.1%)	43/80 (53.8%)	52/104 (50.0%)	
Chemo <5mL	2/3 (66.7%)	6/21 (28.6%)	28/80 (35.0%)	36/104 (34.6%)	
Other >5mL	0/3 (0.0%)	4/21 (19.0%)	5/80 (6.3%)	9/104 (8.7%)	
Other <5mL	0/3 (0.0%)	3/21 (14.3%)	4/80 (5.0%)	7/104 (6.7%)	
Diagnosed condition in last 2 years[5]					0.004[4]
None	617/618 (99.8%)	1076/1085 (99.2%)	900/922 (97.6%)	2593/2625 (98.8%)	
Any cancer	1/618 (0.2%)	6/108 (0.6%)	14/922 (1.5%)	21/2625 (0.8%)	
Liver disease	0/618 (0.0%)	2/1085 (0.2%)	3/922 (0.3%)	5/2625 (0.2%)	
Neurological disorder	0/618 (0.0%)	1/1085 (0.1%)	5/922 (0.5%)	6/2625 (0.2%)	
Number of symptoms reported					<0.001[2]
0	594/618 (96.1%)	999/1085 (92.1%)	775/922 (84.1%)	2368/2625 (90.2%)	
1	20/618 (3.2%)	54/1085 (5.0%)	63/922 (6.8%)	137/2625 (5.2%)	

2+	4/618 (0.6%)	32/1085 (2.9%)	84/922 (9.1%)	120/2625 (4.6%)	
Employee has safety concerns	2/618 (0.3%)	16/1085 (1.5%)	57/922 (6.2%)	75/2625 (2.9%)	<0.001[2]
Employee has discussed concerns with supervisor[6]	2/2 (100.0%)	8/16 (50.0%)	19/57 (33.3%)	29/75 (38.7%)	0.087[4]
Employee would like to speak with EOHS	0/618 (0.0%)	4/1085 (0.4%)	9/922 (1.0%)	13/2625 (0.5%)	0.017[4]
Reproductive Outcomes					
Ever had difficulty conceiving[7,8]	16/437 (3.7%)	39/689 (5.7%)	66/562 (11.7%)	121/1688 (7.2%)	<0.001[2]
Had difficulty conceiving in current job[7,8]	5/437 (1.1%)	16/689 (2.3%)	40/562 (7.1%)	61/1688 (3.6%)	<0.001[2]
Evaluated by medical provider[7,9]	4/5 (80.0%)	13/16 (81.3%)	36/40 (90.0%)	53/61 (86.9%)	0.379[4]
Received diagnosis of infertility[7,9]	4/5 (80.0%)	6/16 (37.5%)	18/40 (45.0%)	28/61 (45.9%)	0.255[4]
Received another diagnosis[7,9]	2/5 (40.0%)	3/16 (18.8%)	15/40 (37.5%)	20/61 (32.8%)	0.426[4]
Conceived a child resulting in miscarriage, stillbirth, or birth defect in last 2 years[7,8]	8/437 (1.8%)	27/689 (3.9%)	29/562 (5.2%)	64/1688 (3.8%)	0.023[2]
Fathered a child resulting in miscarriage, stillbirth, or birth defect in last 2 years[10]	1/127 (0.8%)	3/207 (1.4%)	4/153 (2.6%)	8/487 (1.6%)	0.547[4]
Lab Complete Blood Count (CBC) Results					

Normal vs abnormal results[11]					0.140[2]
All values in normal range	233/542 (43.0%)	436/1063 (41.0%)	414/911 (45.4%)	1083/2516 (43.0%)	
One or more values abnormal	309/542 (57.0%)	627/1063 (59.0%)	497/911 (54.6%)	1433/2516 (57.0%)	

[1]Results are reported as N (%) unless otherwise noted

[2]Chi-Square p-value

[3]Only HCWs who reported exposure to hazardous medication spill are included in the denominator for percentages

[4]Fisher Exact p-value

[5]N=1 respondent reported both liver disease and neurological disorder is included here in the liver disease category

[6]Only respondents who reported a safety concern are included in the denominator for percentages

[7]Among N=1688 female and age 18-44 respondents

[8]Responses missing for N=3, not included in the denominator for percentages

[9]Among N=61 respondents who reported difficulty conceiving in current job

[10]Among N=487 male respondents (all ages)

[11]N=109 with no CBC data not included in the denominator

Table 3: Multivariable Logistic Regression Models of Adverse Reproductive Outcomes, Symptoms, and Abnormal Lab Values

		Outcome: Adverse Reproductive Outcome[1]		Outcome: Any Symptom		Outcome: Any Abnormal Lab Value	
		OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Amount of time per week working with hazardous medications (reference: None yet)	Up to 8 hours/week	1.41 (0.83, 2.39)	0.208	1.74 (1.08, 2.79)	0.022	1.15 (0.92, 1.43)	0.213
	>8 hours/week	2.49 (1.47, 4.22)	<0.001	3.29 (2.07, 5.24)	<0.001	0.91 (0.72, 1.14)	0.404
Sex (reference: Male)	Female	N/A	N/A	2.42 (1.53, 3.83)	<0.001	1.70 (1.38, 2.10)	<0.001
Age at questionnaire[2]		1.10 (1.07, 1.13)	<0.001	1.03 (1.02, 1.04)	<0.001	0.98 (0.98, 0.99)	<0.001
Site (reference: A)	B	0.95 (0.64, 1.41)	0.789	1.13 (0.83, 1.56)	0.441	1.07 (0.88, 1.30)	0.478
	C	0.54 (0.23, 1.28)	0.163	1.20 (0.72, 1.99)	0.483	2.64 (1.74, 3.99)	<0.001
	D	0.87 (0.51, 1.47)	0.594	0.78 (0.50, 1.22)	0.271	0.76 (0.58, 1.00)	0.053
Occupational grouping (reference: RN/LPN)	Technician	0.70 (0.36, 1.39)	0.312	0.96 (0.62, 1.49)	0.850	1.22 (0.93, 1.60)	0.160
	Healthcare Professional	0.68 (0.29, 1.55)	0.353	1.29 (0.79, 2.12)	0.315	1.46 (1.04, 2.04)	0.029

	Services/Support Personnel	0.78 (0.29, 2.10)	0.616	1.43 (0.68, 3.05)	0.349	1.42 (0.89, 2.26)	0.140
	Physician/Advanced Practice Provider	2.93 (1.09, 7.86)	0.033	1.22 (0.36, 4.08)	0.753	1.28 (0.64, 2.56)	0.485
	Other	1.06 (0.34, 3.32)	0.926	1.63 (0.64, 4.16)	0.310	0.69 (0.34, 1.39)	0.299
Exposed to hazardous medication spill in past 2 years (reference: No)	Yes	1.66 (0.88, 3.14)	0.119	2.67 (1.67, 4.26)	<0.001	1.07 (0.70, 1.62)	0.763

Abbreviations: OR: odds ratio; CI: confidence interval; RN: registered nurse; LPN: licensed practical nurse

[1]Adverse Reproductive Outcome was assessed in the subset of employees who were female and age 18-44

[2]Odds ratio for age is per 1 year increase in age

Graphical abstract