Healthcare Workers and Antineoplastic Drugs: Evaluating the Risks and Identifying Determinants of Exposure

Presented by:

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Agenda

- Background
- Methods and results for each objective (x4)
- Summary
- Strengths and limitations
- Future studies

Antineoplastic drugs

- Also known as chemotherapeutic or cytoxoxic drugs
- Primarily used for the treatment of cancer
- Inherently toxic agents; however, to patients, benefits > risks
- Occupational exposure concerns initially surfaced in the 1970's
  - Non-selective mode of action – normal cells may also be affected

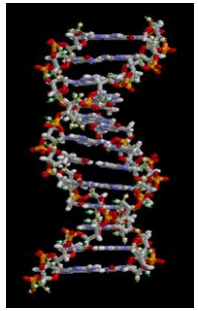
Exposure limits?

- No exposure limits listed in Ontario OHS Regulation
- No ACGIH threshold limit values (TLVs®)
- No OSHA permissible exposure limits (PELs)

The ALARA Principle applies (As Low As Reasonably Achievable)

Occupational exposure to antineoplastic drugs

- Documented health effects of exposed workers:
  - Mutagenicity *(damage to genetic material)*
  - Reproductive toxicity *(e.g. miscarriages)*
  - Carcinogenicity



- Pilot study at hospital pharmacies in BC found:
  - Surface contamination on work surfaces
  - Certain personnel had dermal contamination

Gaps in literature

- Unknown dermal contact frequency
- Only select departments/job categories assessed
- Exposure underestimate
  - Number of workers at risk
  - Urinary drug contamination levels
- Determinants of contamination and/or exposure

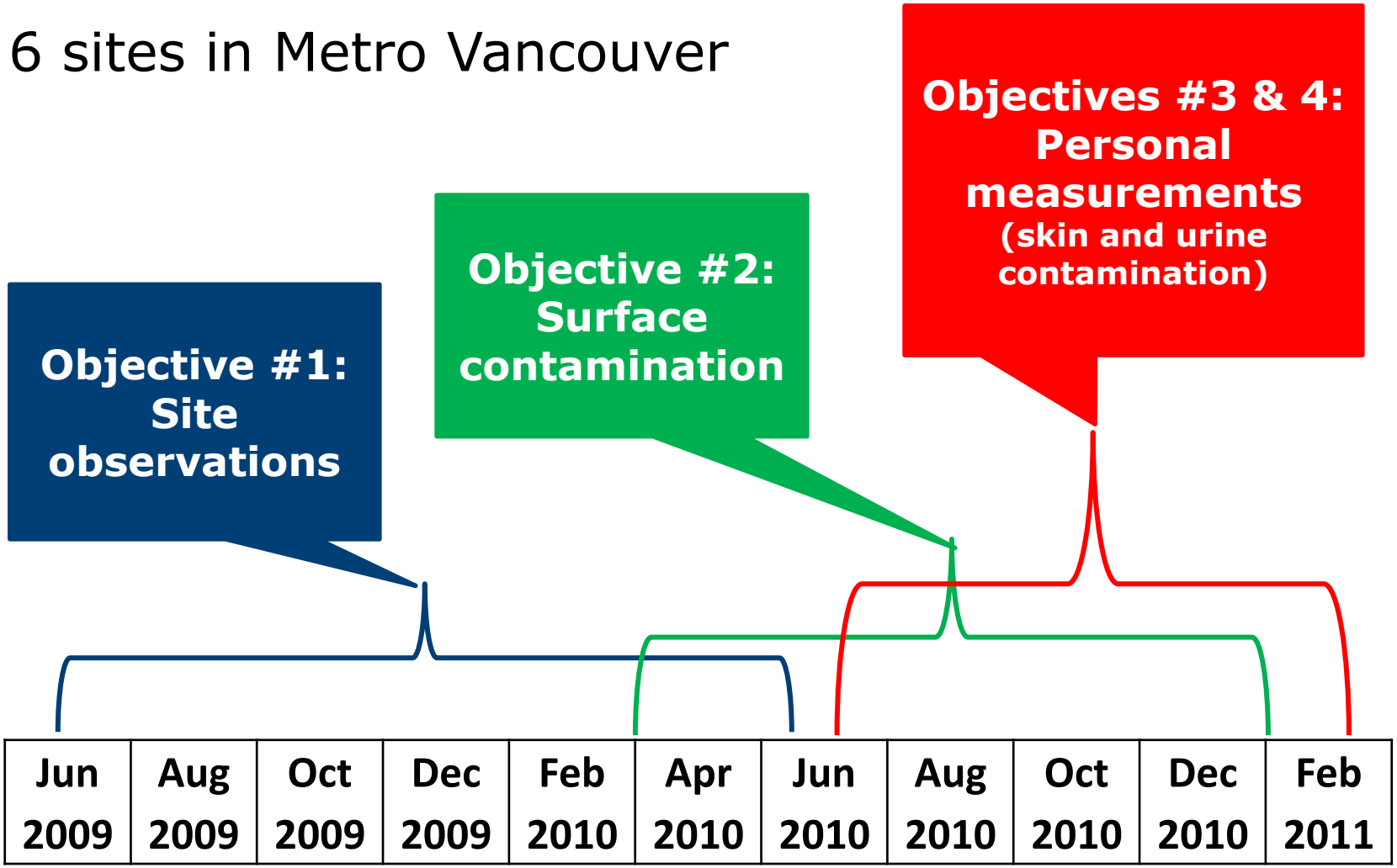
Pursue current study building upon pilot study findings and gaps in the literature

Research questions

1. Is antineoplastic drug contamination found on surfaces located throughout the hospital medication system?
2. Are healthcare workers throughout the hospital medication system occupationally exposed to antineoplastic drugs?
3. What are the factors associated with surface contamination and occupational exposure (skin and urine contamination)?

Four study objectives

6 sites in Metro Vancouver



Notes pertaining to entire study

- Ethics approval received prior to start
- Used cyclophosphamide (CP) as marker drug of exposure
- Included six facilities in GVRD – 5 acute care hospitals + 1 cancer treatment hospital
  - All drugs prepared in biological safety cabinet
  - Closed drug system transfer devices NOT employed
- Housekeepers declined to participate
- Laboratory analyses of samples using HPLC MS/MS
- Generated mathematical models to identify determinants of surface, skin and urine contamination

Objective 1

Identify

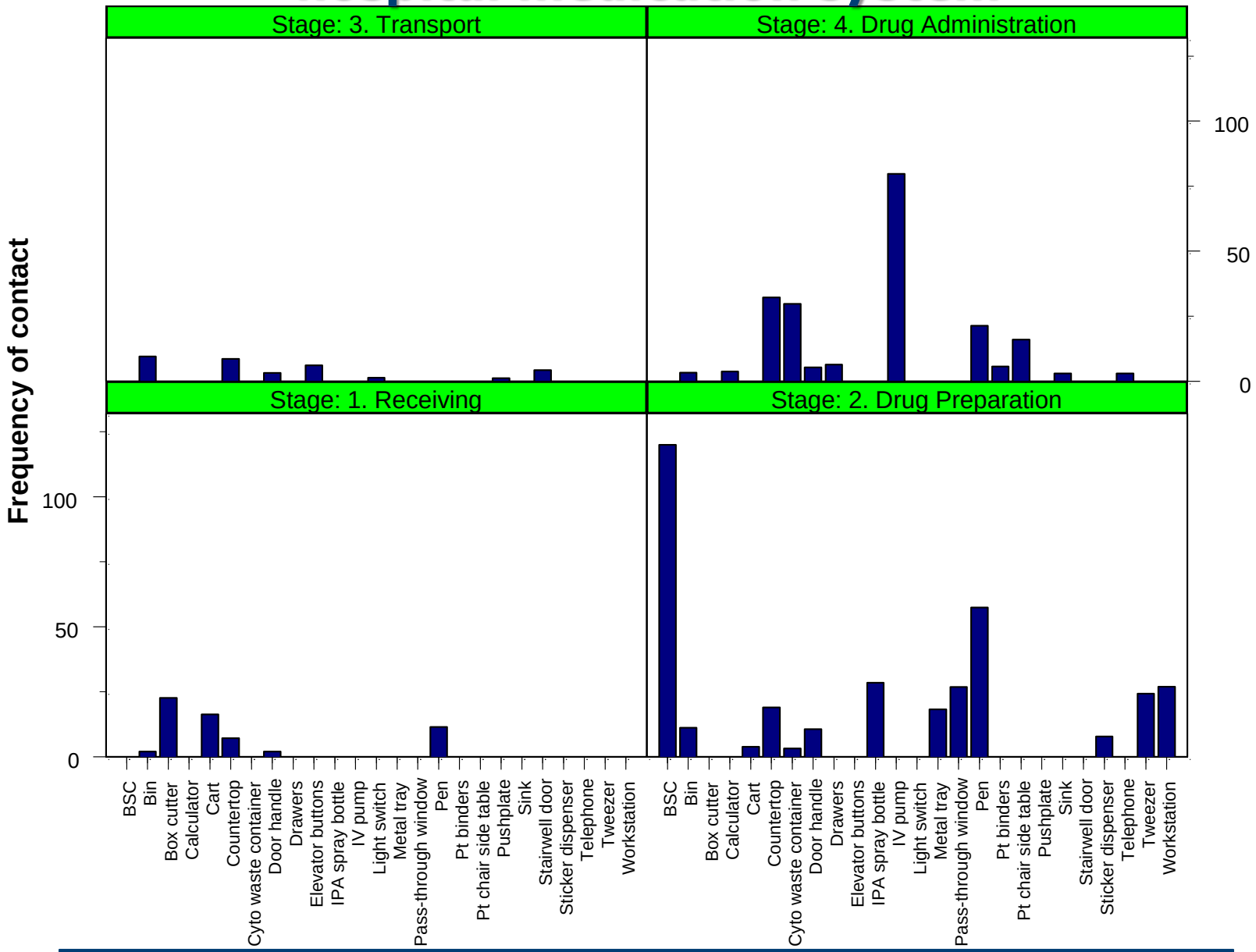
- surfaces most likely contaminated
- job categories potentially at risk of exposure

to antineoplastic drugs throughout the hospital medication system

Objective 1 – Methods

- Key informant interviews
  - Ascertain depts/job categories
- Repeated site observations
  - Establish hospital medication system
  - Identify potentially-contaminated surfaces
  - Identify job categories which may contact drugs/surfaces (directly or indirectly)
- Contact frequency graphs and tallied job categories

Surface contact frequency by stage of hospital medication system



SITE OBSERVATIONS

Objective 1 – Results

Observed job categories at risk of exposure stratified by stage of hospital medication system

Stage	Job Category
1. Delivery	Shipper/Receiver; Pharmacy Receiver
2. Drug Preparation	Pharmacy Technician; Pharmacist
3. Transport to Ward	Porter; Nurse; Pharmacist; Unit Clerk; Ward Aide
4. Drug Administration	Nurse; Volunteer; Unit Clerk; Dietician; Oncologist; Clinic Pharmacist
5. Waste Disposal	Nurse; Pharmacist; Pharmacy Technician; Biopacker

Up to 11 job categories per site at risk

SITE OBSERVATIONS

Objective 2

Quantify drug contamination levels on surfaces from Objective #1 and identify determinants

Objective 2 – Methods

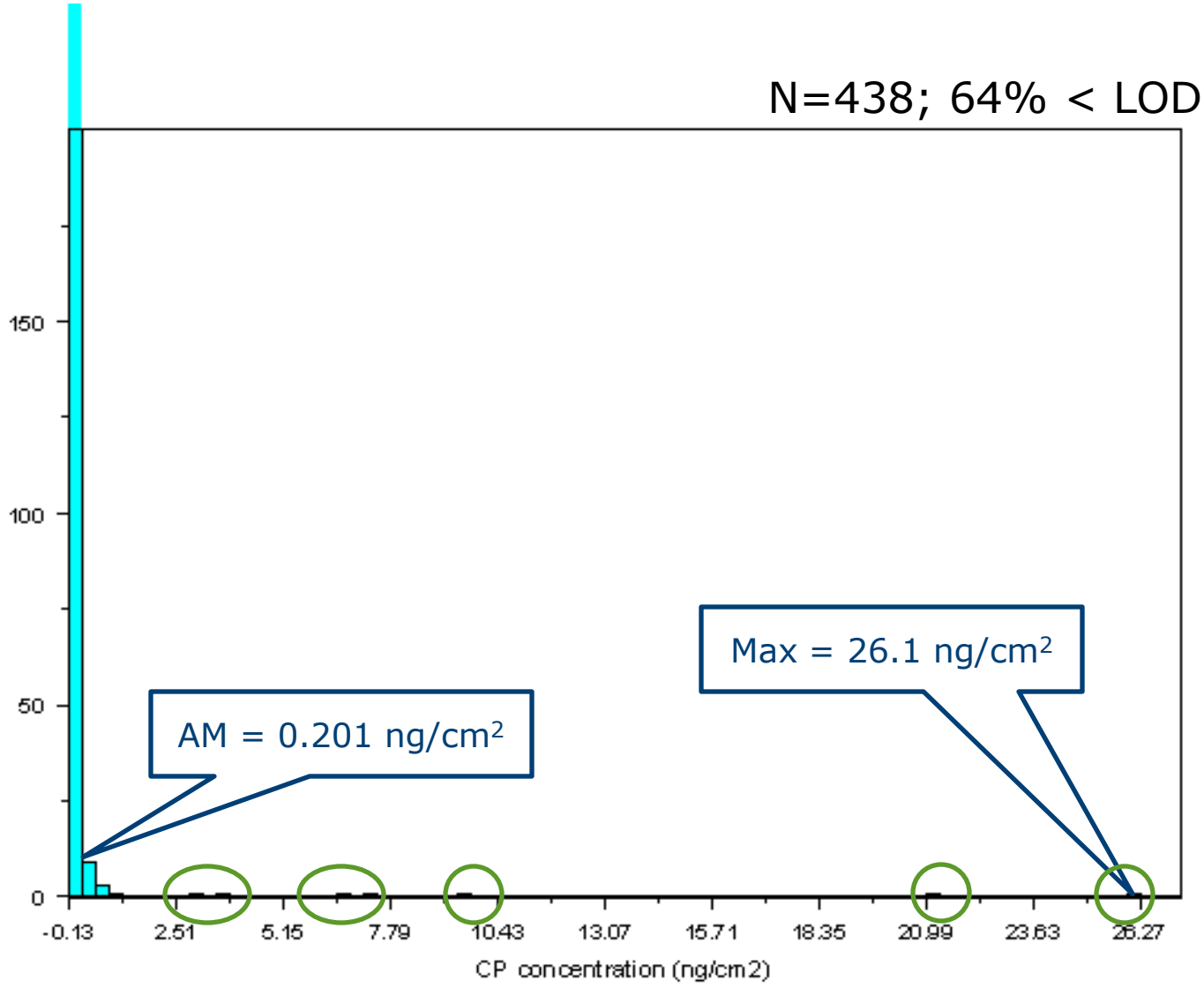
- Used a pre-moistened Kimwipe
- 100 cm^2 template used where possible
- For other surfaces, area most likely contacted was sampled
  - Dimensions taken and surface area calculated
- LOD 0.356 ng/wipe

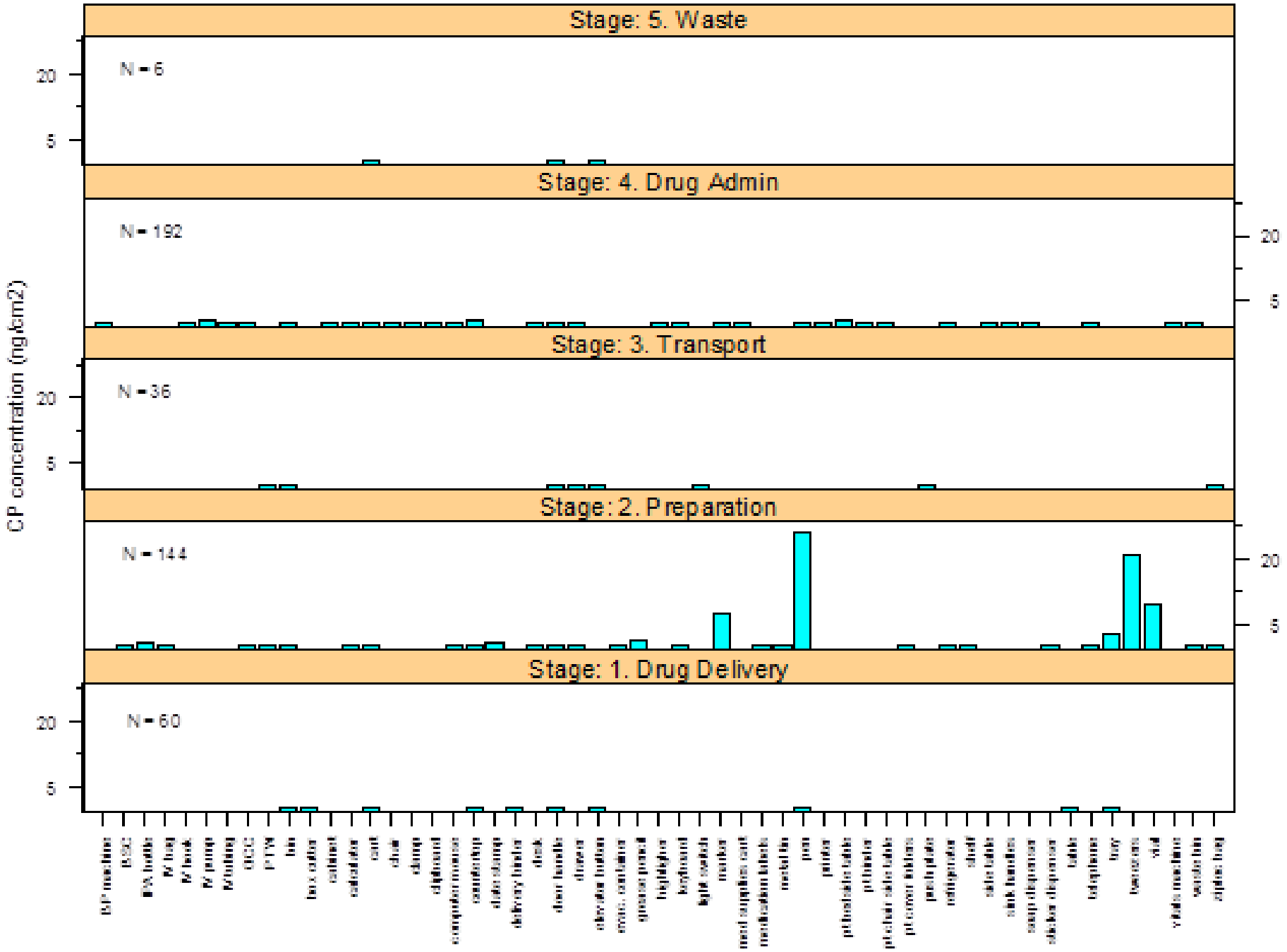
Objective 2 – Methods

Independent Variables:

- CP handled prior?
- Spill or leak of CP prior?
- Surface cleaned prior?
- Hospital characteristics
  - E.g. # job categories responsible for drug transport
- Attributes of the wipe sample
  - E.g. stage of hospital medication system

Histogram of surface contamination levels



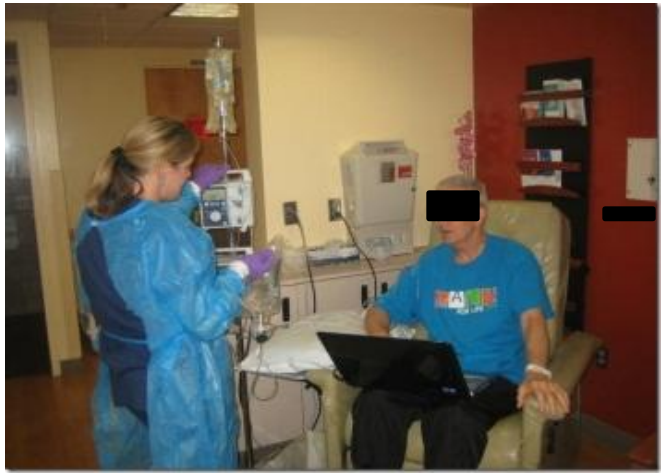


SURFACE CONTAMINATION

Objective 2 – Results

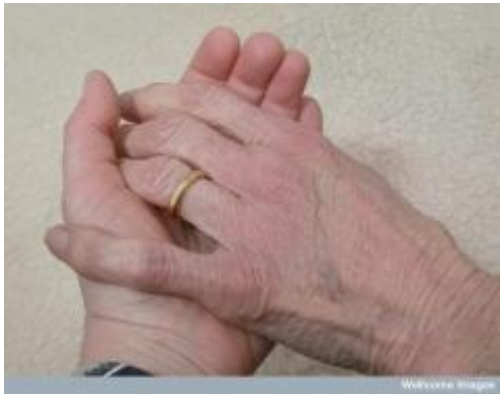
Factors associated with increased surface contamination:

1. Stage of hospital medication system
   - Drug preparation
   - Drug administration
2. Having more job categories responsible for drug transport (positive association)



Personal samples

Objective #3: Assess contamination levels on hands of at-risk job categories and identify determinants



Objective #4: Determine urinary drug contamination levels in at-risk job categories and identify determinants

Objectives 3&4 – Methods

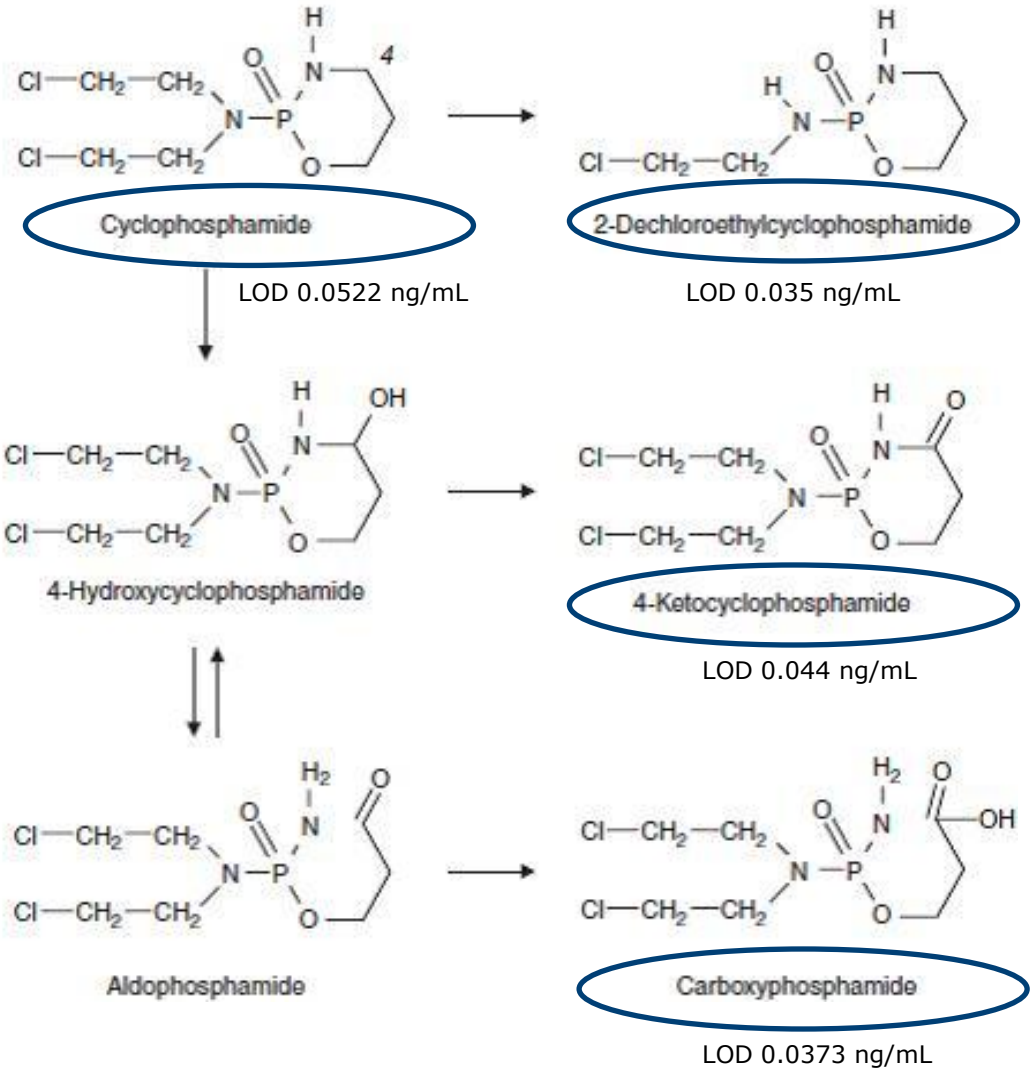
Recruitment:

- Job categories identified in Objective #1 invited to participate
  - 3 representatives/job category/site
- Based on convenience sampling
  - i.e. not worst-case

Dermal samples - Methods

- Similar to surface wipe sampling
  - Front and back of both workers' hands were wiped
- LOD of 0.356 ng/wipe

Urine samples – Methods



- 24-hr urine samples collected
- CP and 3 stable urinary metabolites analyzed
- Tallied; results reported in nmol/L

URINE SAMPLES

Objective 3&4 – Methods

Independent Variables:

1) On-site survey

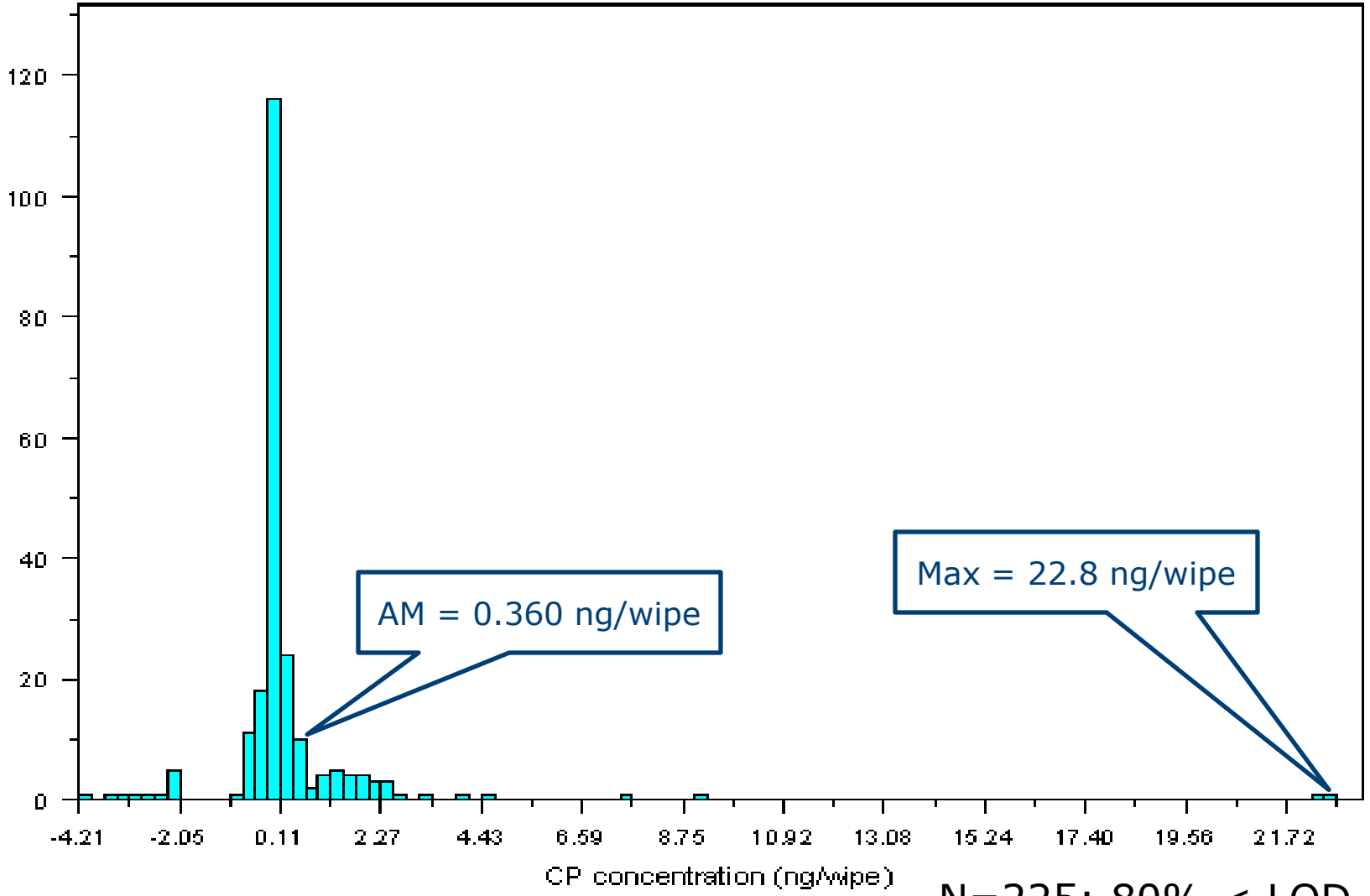
- CP contact methods
- Hand washing practices
- Glove use prior to sample collection

2) Self-administered questionnaire

- Demographic data
- Duty to handle antineoplastic drugs
- Education/training
- Usual personal protective equipment practices

PERSONAL SAMPLES

Histogram of dermal contamination levels



N=225; 80% < LOD

DERMAL WIPES

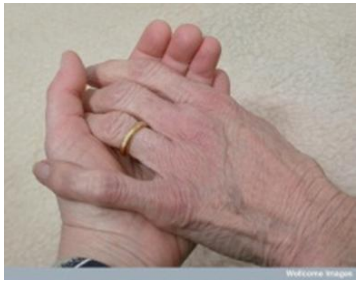
Objective 3 - Dermal results

Job Title	N	% > LOD	AM (ng/wipe)	SD (ng/wipe)	GM (ng/wipe)	GSD	Max
Pharmacist	40	10.0	< LOD	1.08	< LOD	4.15	1.49
Pharmacy Receiver	12	25.0	< LOD	0.39	< LOD	1.09	1.27
Pharmacy Technician	45	17.8	< LOD	1.63	< LOD	1.42	9.29
Porter	11	9.1	0.404	1.37	< LOD	1.25	4.55
RN (includes LPN)	64	26.6	0.767	3.11	0.363	1.46	22.8
Transport (includes biopacker, transporter, and shipper/receiver)	8	12.5	< LOD	0.21	< LOD	1.05	0.56
Unit clerk	24	16.7	< LOD	0.98	< LOD	1.31	2.03
Others in drug admin unit (volunteer, oncologist, dietitian, ward aide)	21	28.6	1.321	4.93	0.504	1.64	22.4

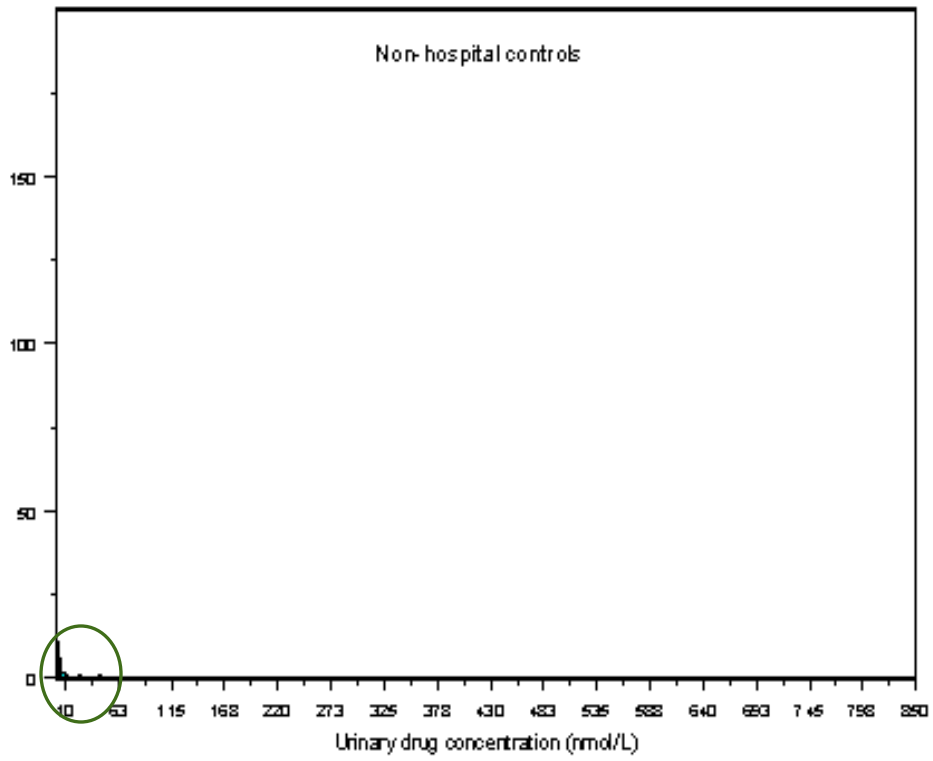
Objective 3 – Dermal results

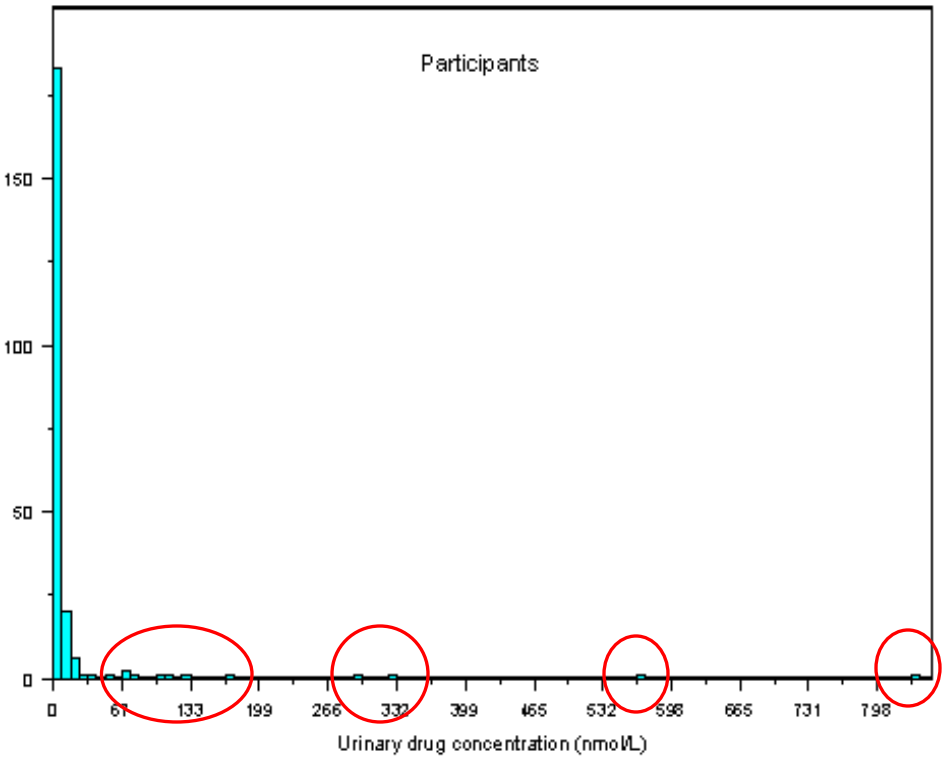
Factors associated with increased dermal contamination:

1. Working in acute care hospital
2. Employed as porter, nurse, transport staff or in the drug administration unit
3. Female
4. Having a duty to handle antineoplastic drugs



Histogram of urinary drug contamination levels





Suggests that participants have opportunities for higher exposure

URINE SAMPLES

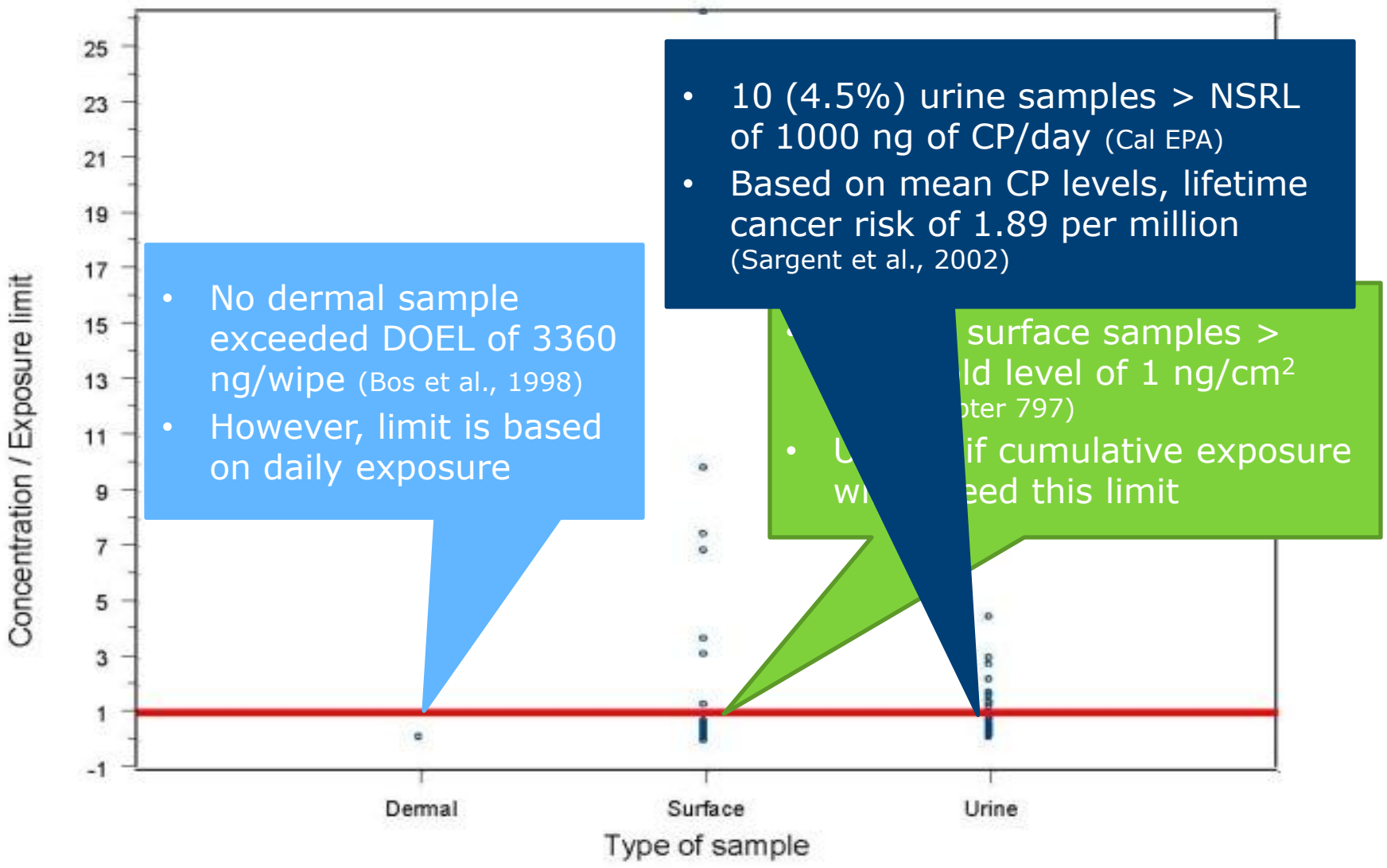
Objective 4 – Urine results

Factors associated with increased urinary contamination:

1. Employed as pharmacy receiver, pharmacy technician, porter, nurse, or unit clerk
2. Having more job categories responsible for drug transport (positive association)

URINE SAMPLES

Summary of results



- No dermal sample exceeded DOEL of 3360 ng/wipe (Bos et al., 1998)
- However, limit is based on daily exposure

- 10 (4.5%) urine samples > NSRL of 1000 ng of CP/day (Cal EPA)
- Based on mean CP levels, lifetime cancer risk of 1.89 per million (Sargent et al., 2002)

- surface samples > ld level of 1 ng/cm^2 pter 797)
- U if cumulative exposure wi eed this limit

SUMMARY

"Take home" messages

- Surface contamination found throughout the hospital medication system
- Occupational exposure potential
  - More job categories than previously believed are at risk of exposure
- Overall, contamination and occupational exposure levels are low
  - Controls working; unable to eliminate contamination/exposure
- Adds to the list of occupational hazards in hospital settings

SUMMARY

Policy implications

- Indicate potential exposure risk throughout the hospital medication system
- All job categories at-risk should be trained
- Implement control measures at every stage of the hospital medication system
  - Examples:
    a) Reduce number of transport job categories
    b) Clean surfaces including vials
    c) Use closed system drug transfer devices

Study strengths

- Looked at entire hospital medication system
- Sampled surfaces where contact is known to occur
- Large sample size
- Sensitive analytical method
- Looked at CP and metabolites in urine samples
- Duplicate samples collected

Study limitations

- Cross-sectional design
- Only examined one analyte
- Unequal representation of job categories and one cohort not included
- Two sites did not have random selection of potential subjects
- Unknown wipe recovery from surfaces/hands
- Unable to accurately assess amount of CP handled
- Most independent variables collected via self-report

Future studies

- Surface cleaning
- Evaluate health risks
- Determine mechanism of spread
- Identify determinants for each stage/job category separately

Associated publications

Hon C-Y, Teschke K, Chu W, Demers P, Venners S. (2013) "Antineoplastic drug contamination of surfaces throughout the hospital medication system in Canadian Hospitals." *J Occup Environ Hygiene*. 10(7); 374-383.

Hon C-Y (2012). "Healthcare workers and antineoplastic drugs: evaluating the risks and identifying determinants of exposure". UBC cIRcle available at https://circle.ubc.ca/handle/2429/42505.

Hon C-Y, Teschke K, Chua PPS, Venners S and Nakashima L. (2011) "Occupational Exposure to Antineoplastic Drugs: A Qualitative Assessment of Healthcare Workers at Risk throughout the Hospital Medication System". *Saf Health Work* 2:273-281

Associated conference presentations

May 2013	American Industrial Hygiene Conference and Exposition (Montreal, QC) ▪ Urinary Contamination of Healthcare Workers to Antineoplastic Drugs Throughout the Entire Hospital Medication Circuit
May 2012	CARWH-RRSSTQ 2012 Conference (Vancouver, BC) ▪ Urinary Contamination Levels of Healthcare Workers Exposed to Antineoplastic Drugs at British Columbian Hospital Pharmacies ▪ Nurses' exposures to antineoplastic drugs in Canada and risk assessment of lifetime cancer incidence
Mar 2012	30th Congress of the International Commission on Occupational Health (Cancun, Mexico) ▪ Occupational dermal exposure to antineoplastic drugs throughout the hospital medication system at Canadian hospital
Sep 2011	Association of Occupational Health Professionals in Healthcare 2011 AGM (Minneapolis, MN) ▪ Antineoplastic Drugs in Hospitals – Toxicology, Exposure Potential and Recommendations for Reducing Exposure
May 2011	American Industrial Hygiene Conference and Exposition (Portland, OR) ▪ Antineoplastic drug contamination levels throughout the medication circuit in British Columbian hospitals
Sep 2010	International Occupational Hygiene Association 8th International Scientific Conference (Rome, Italy) ▪ Identifying healthcare workers at risk of exposure to antineoplastic drugs: More than just pharmacists and nurses

Acknowledgements

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Questions

Laboratory analyses

- Analyzed for cyclophosphamide (CP) (surface and dermal) and its metabolites (urine)
- HPLC MS/MS
  - Very sensitive – detection limit (LOD) in nanogram (ng) range
- QC: field, travel, and lab blanks
- QA: freeze-thaw experiments; storage stability testing