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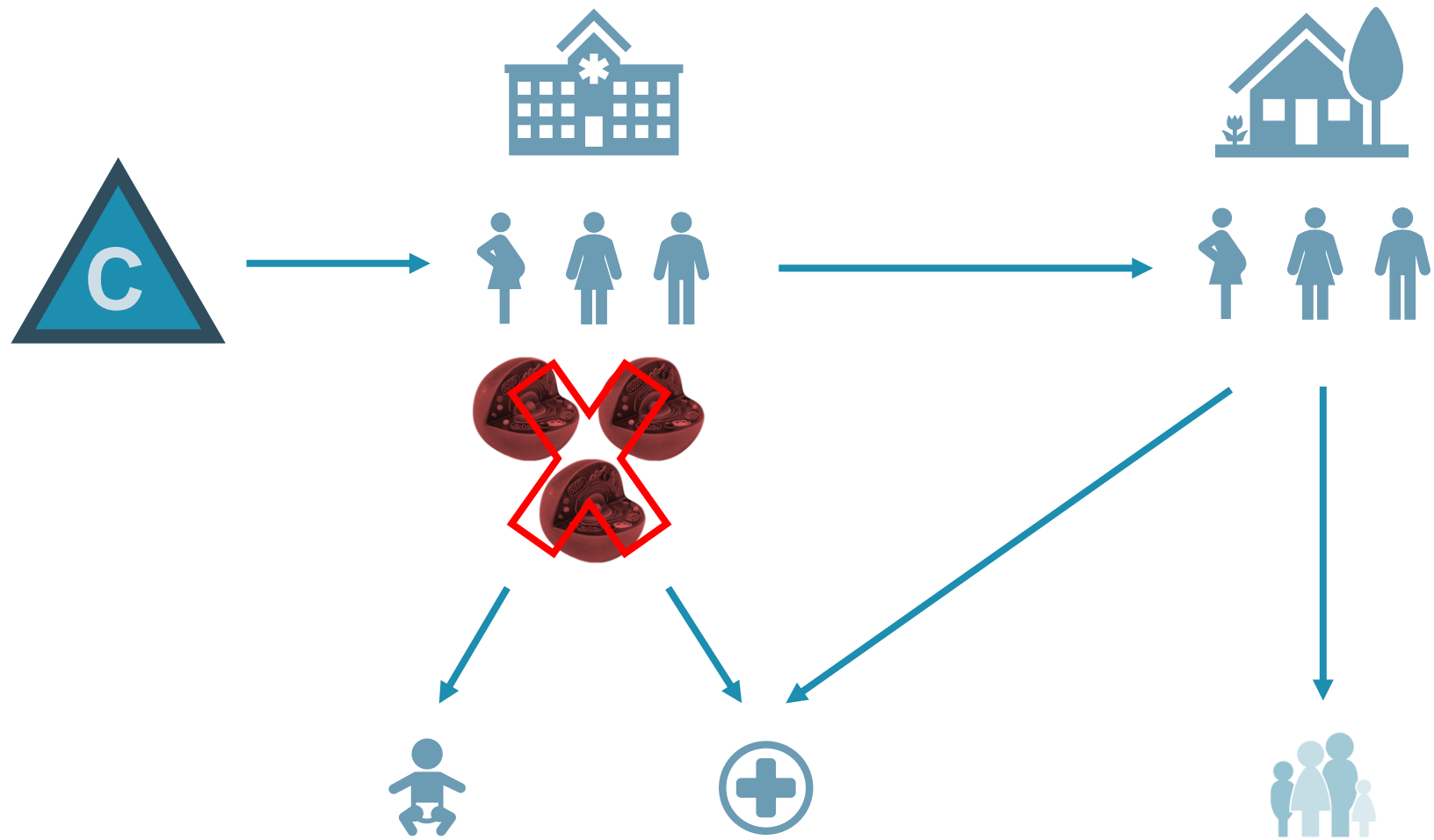
# The unintended exposure to cytostatic drugs in health care



*Prof. Lode Godderis*

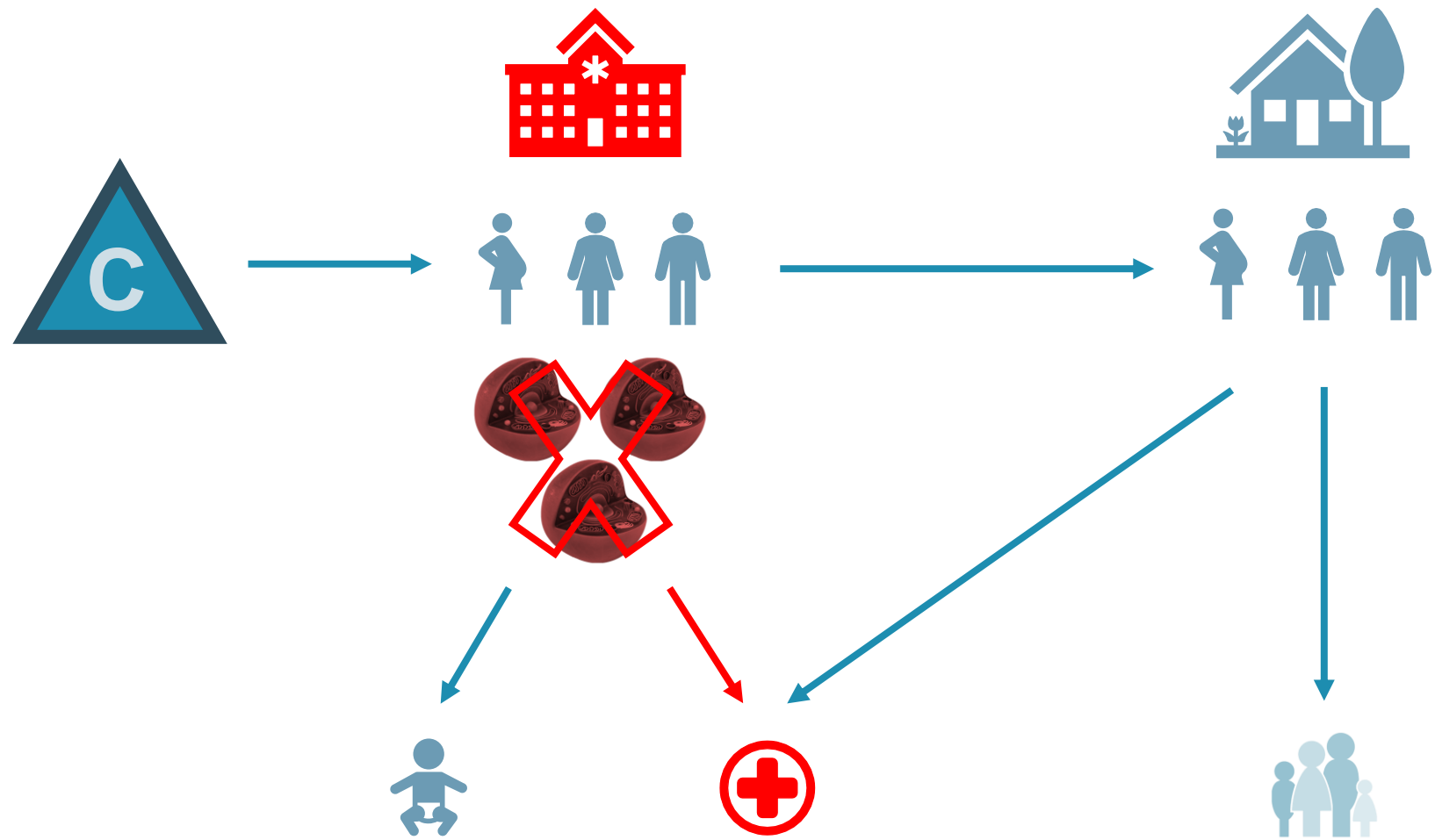
*Webinar Protection of Hospital Workers from the  
Occupational Risks Related to Carcinogens,*

*Friday, 3 September 2021*

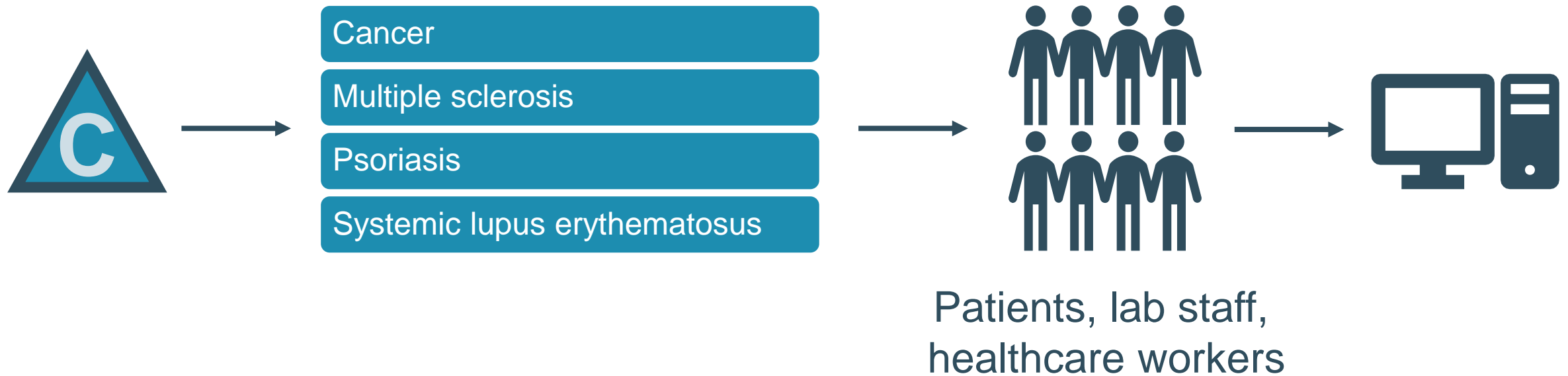


# Occupational exposure





# Necessity of exposure monitoring



# Two examples

University hospital Leuven, Belgium



University hospital Tlemcen, Algeria



## ORIGINAL RESEARCH article

Front. Public Health, 05 August 2020 | <https://doi.org/10.3389/fpubh.2020.00374>



## Environmental Contamination and Occupational Exposure of Algerian Hospital Workers

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Guidelines are in place to assure limited occupational exposure to cytostatic drugs. Even though this has led to a reduction in exposure, several studies reported quantifiable concentrations of these compounds in healthcare workers. In this study, we evaluated occupational exposure to cytostatic drugs in hospital workers from the University Hospital in Tlemcen, Algeria. Monitoring was performed by collecting wipe samples from surfaces, objects, personal protective equipment (gloves and masks) and from the skin of employees at an Algerian university hospital. Wipe samples were analyzed with ultra-performance liquid chromatography coupled to a mass spectrometer. Concentrations ranged from below the limit of quantification up to 208.85, 23.45, 10.49, and 22.22 ng/cm<sup>2</sup> for cyclophosphamide, ifosfamide, methotrexate and 5-fluorouracil, respectively. The highest values were observed in the oncology department. Nowadays, there are still no safe threshold limit values for occupational exposure to cytostatic agents. Therefore, contamination levels should be kept as low as reasonably achievable. Yet, healthcare workers in this hospital are still exposed to cytostatic agents, despite the numerous guidelines, and recommendations. Consequently, actions should be taken to reduce the presence of harmful agents in the work environment.

# Algeria



# 3 types of samples from 6 departments



39



13



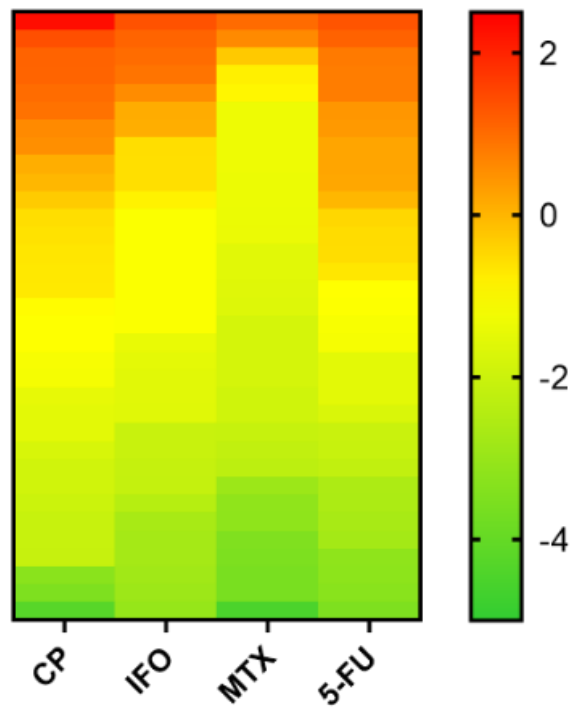
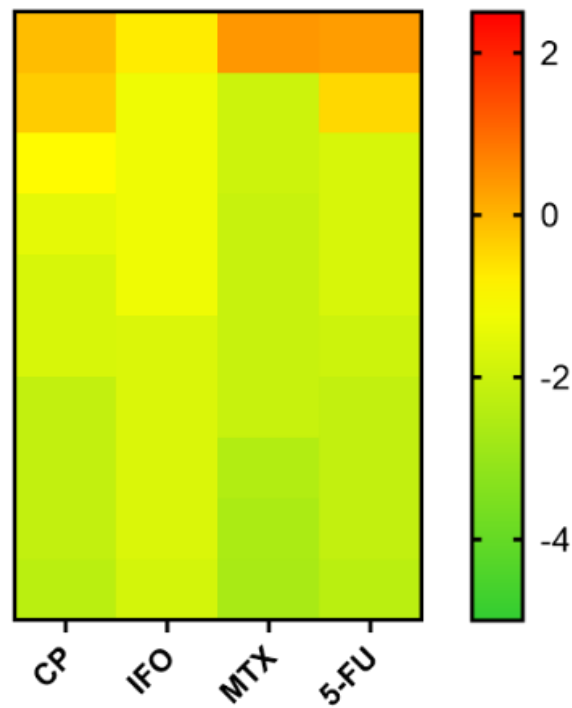
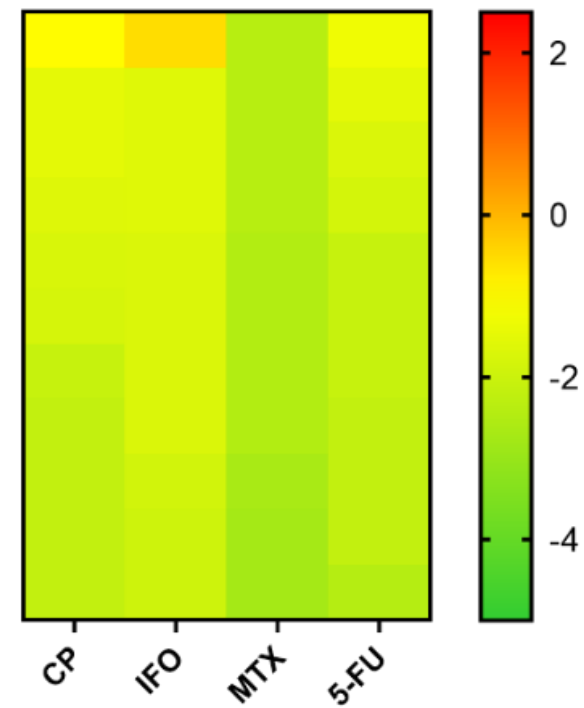
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Dermatology  
Maternity oncology  
Haematology

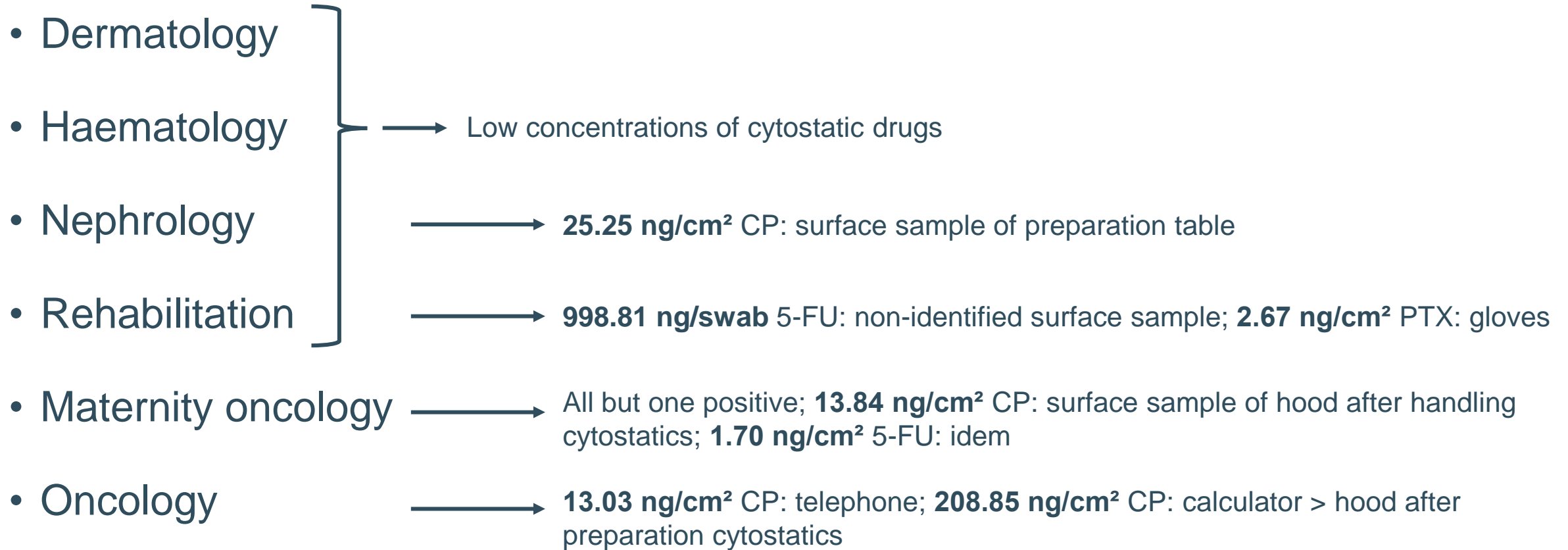
Oncology  
Nephrology  
Rehabilitation



CP  
IFO  
PTX  
MTX  
5-FU

**A****Surface****B****Personal protective  
equipment****C****Dermal**

# Comparison within departments



# Explanation?

8/33 samples:

High concentrations ( $>10 \text{ ng/cm}^2$ )

→ inadequate cleaning

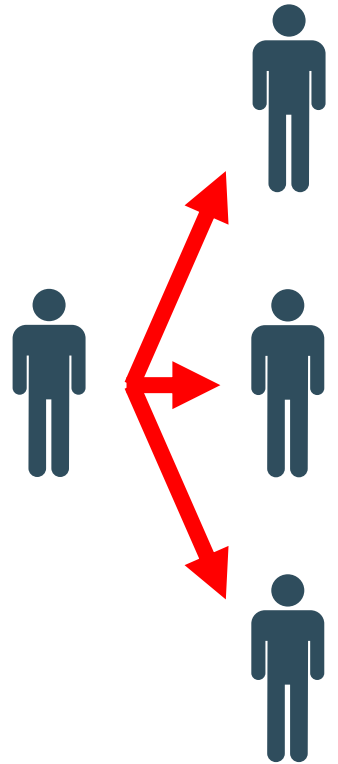
→ spilling

14/33 samples:

Lower concentrations ( $0.1\text{-}10 \text{ ng/cm}^2$ )

→ careless working

Dermal contamination



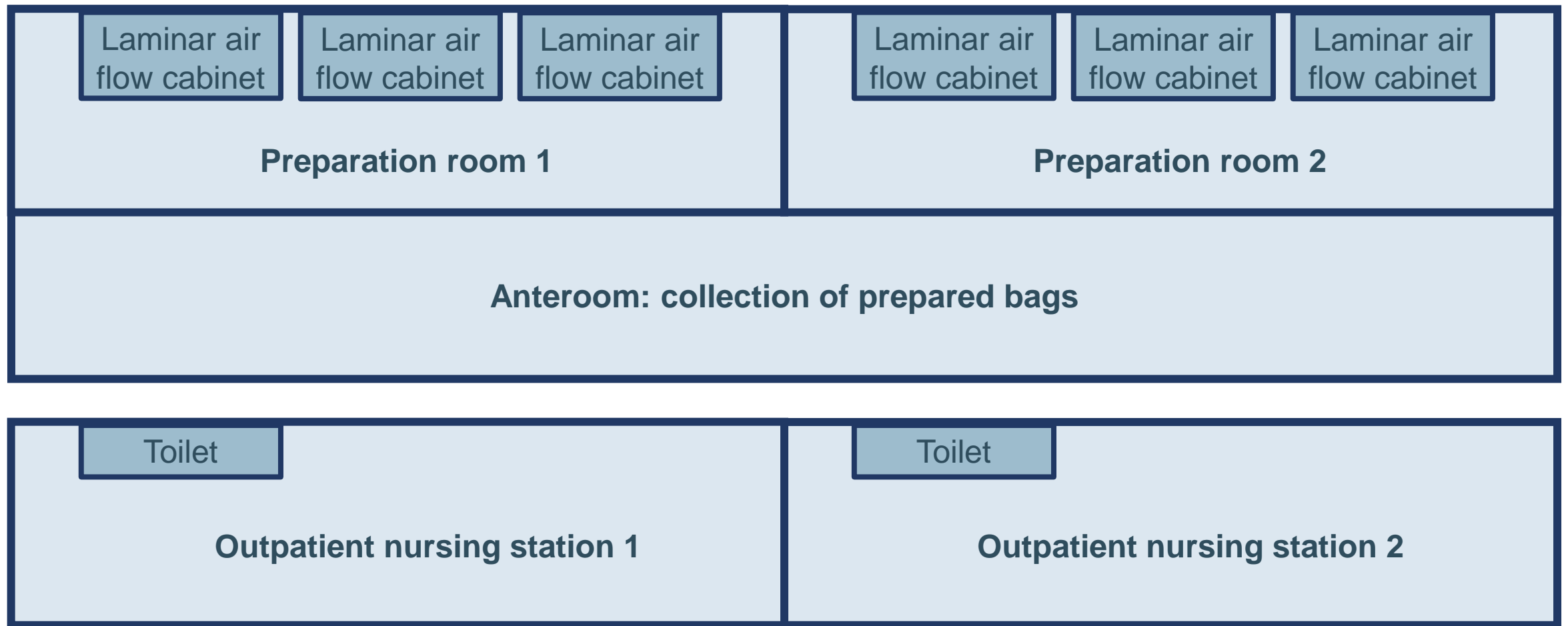
# Concentration ranges in surface samples

Concentration ranges in surface samples (ng/cm <sup>2</sup> )	
	<b>Algeria</b>
<b>Cyclophosphamide</b>	< LOQ - 208.85
<b>Ifosfamide</b>	< LOQ - 23.45
<b>Paclitaxel</b>	< LOQ - 76.76
<b>Methotrexate</b>	< LOQ - 10.49
<b>5-Fluorouracil</b>	< LOQ - 22.22

Concentrations	Action
< 0.1 ng/cm <sup>2</sup>	Repeat measurement 1x/year, revise after 4 years
0.1 - 10 ng/cm <sup>2</sup>	Risk estimation, possibly follow up in 3 - 6 months, take action if necessary
> 10 ng/cm <sup>2</sup>	<b>Take action and follow up</b>

→ **Need for action!**

# Belgium





# 3 types of samples



52



24



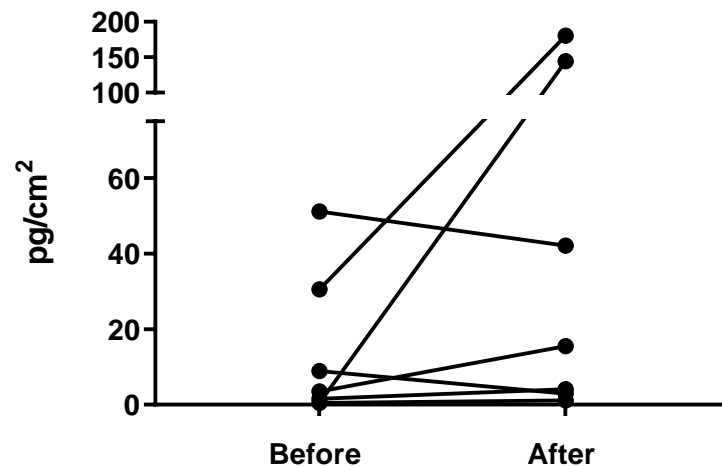
62



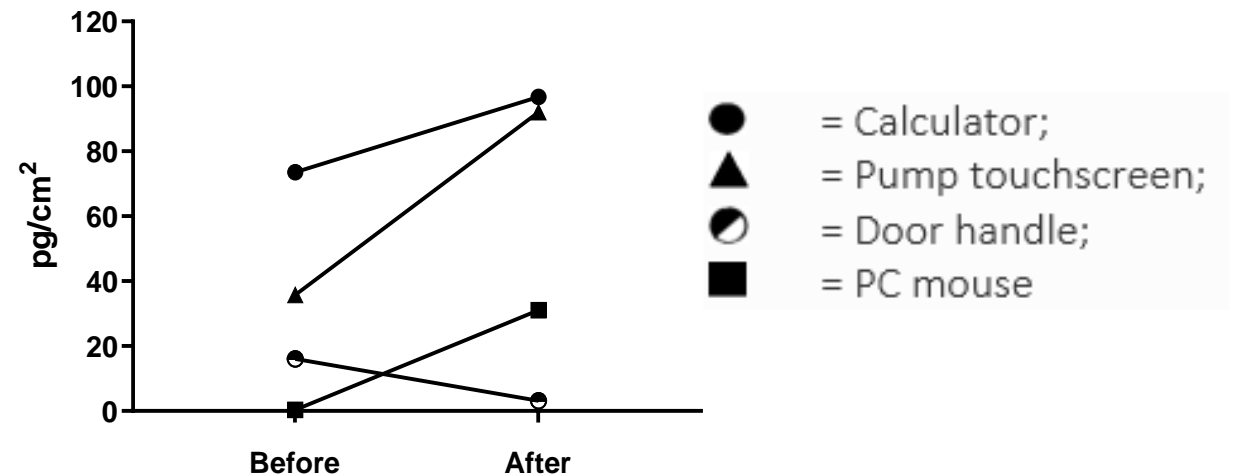
5-FU

# Very low levels of 5-FU confirm good practice of working and adequate cleaning

Laminar air flow cabinet in preparation rooms



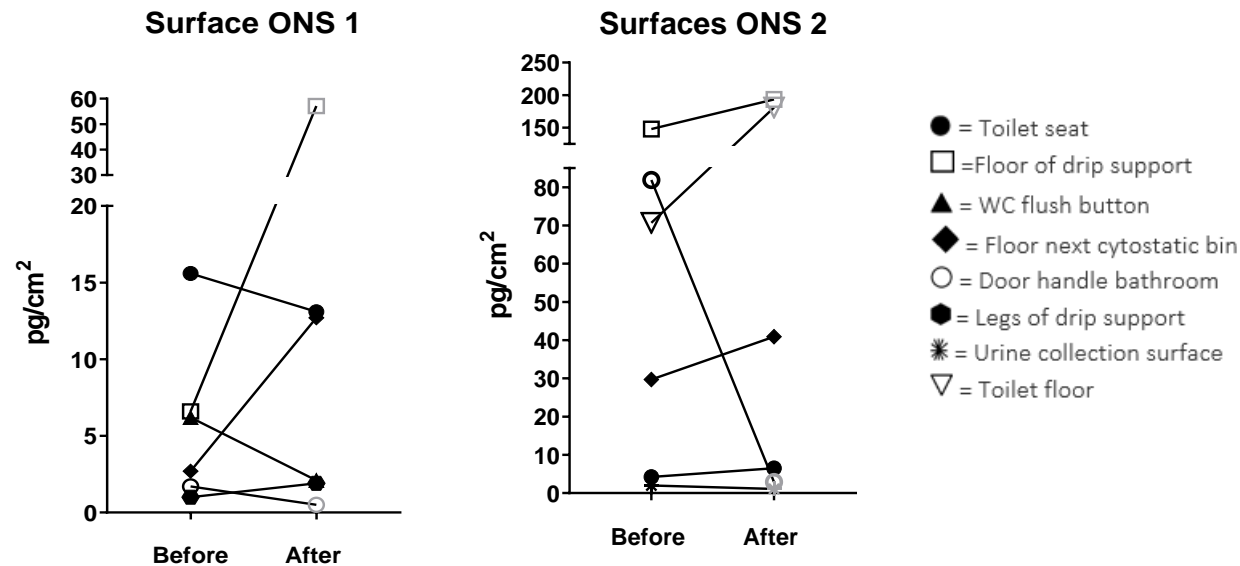
Frequently used devices in anteroom



- Low contamination → good practice of working and cleaning
  - Decreased concentration door handle after preparation → most touched → potential source for dermal exposure
- ! Contact point clave vial and box for infusion bags collection: 177800.86 pg/cm² → contamination may occur prior to receipt at the institution

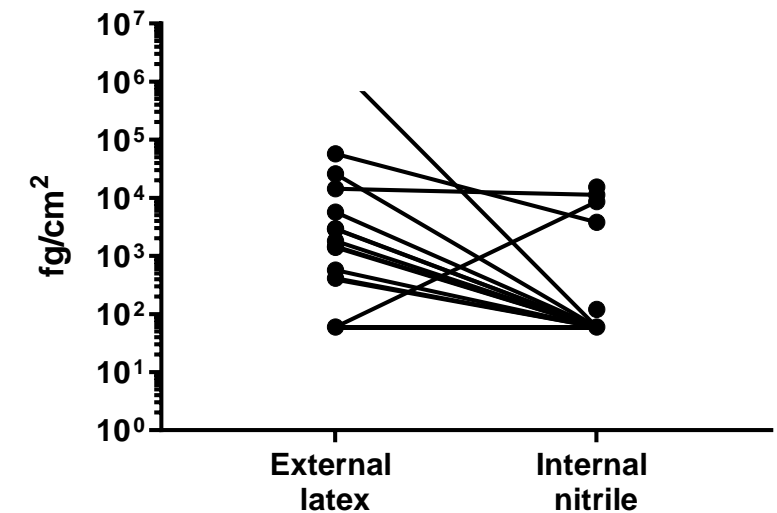
# Very low levels of 5-FU confirm good practice of working and adequate cleaning

## Outpatient nursing stations



## Gloves

### Gloves contamination



- Outpatient nursing stations → relatively low contamination in comparison with similar studies
- Dermal exposure: 3/24 > LOQ (0.38 – 1.18 pg/cm<sup>2</sup>)

# Concentration range 5-FU

Concentration ranges in surface samples (ng/cm <sup>2</sup> )	
<b>Belgium</b>	
<b>5-Fluorouracil</b>	< LOQ – 117.8

- 10/63 above 0.1 ng/cm<sup>2</sup>
- 9 samples between 0.1 and 10 ng/cm<sup>2</sup>
- 1 sample > 10 ng/cm<sup>2</sup>

Concentrations	Action
< 0.1 ng/cm <sup>2</sup>	Repeat measurement 1x/year, revise after 4 years
0.1 - 10 ng/cm <sup>2</sup>	Risk estimation, possibly follow up in 3 - 6 months, take action if necessary
> 10 ng/cm <sup>2</sup>	Take action and follow up

→ 53/63 surface samples < 0.1 ng/cm<sup>2</sup> → good practice of working and cleaning

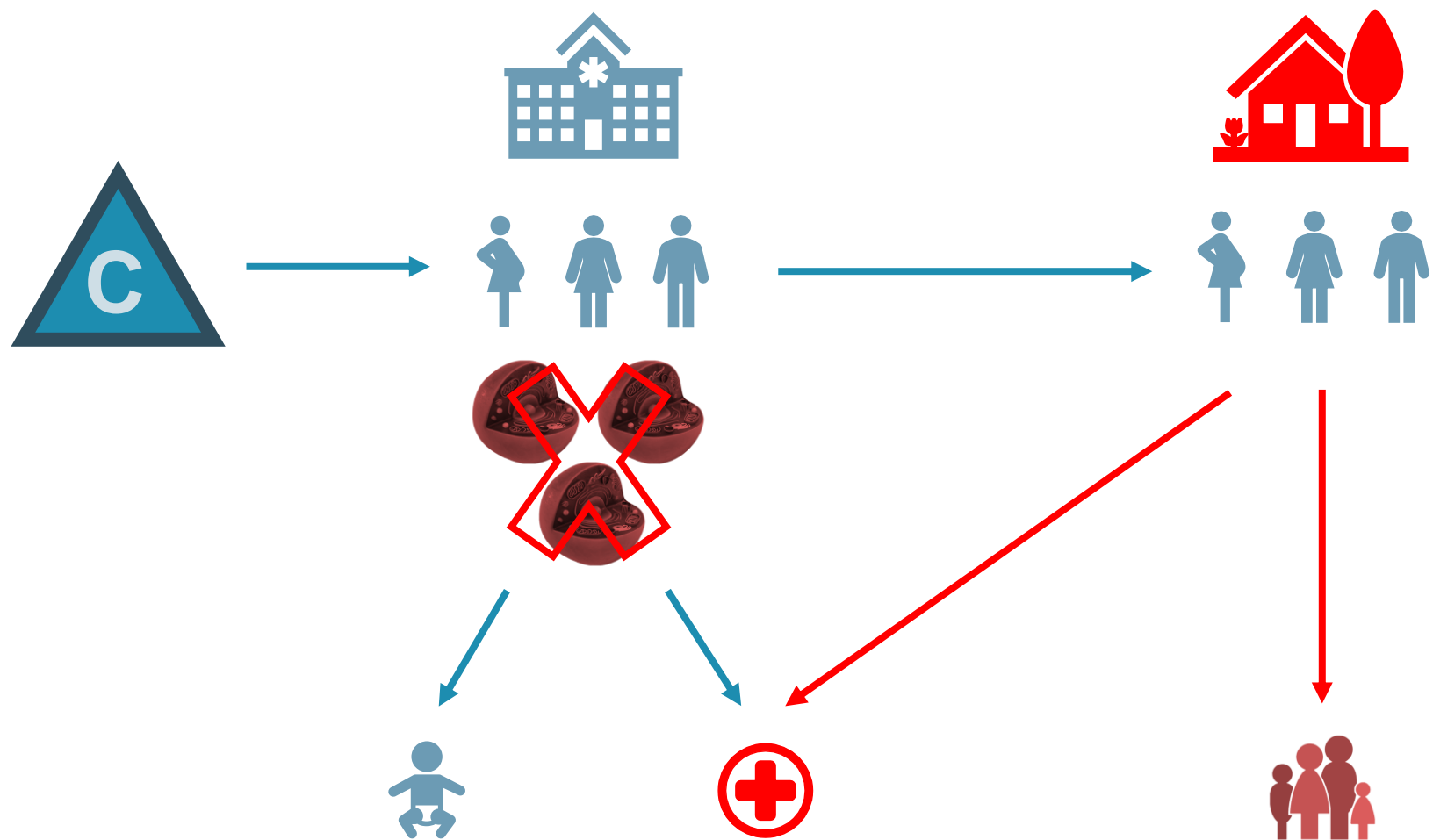
# Conclusion

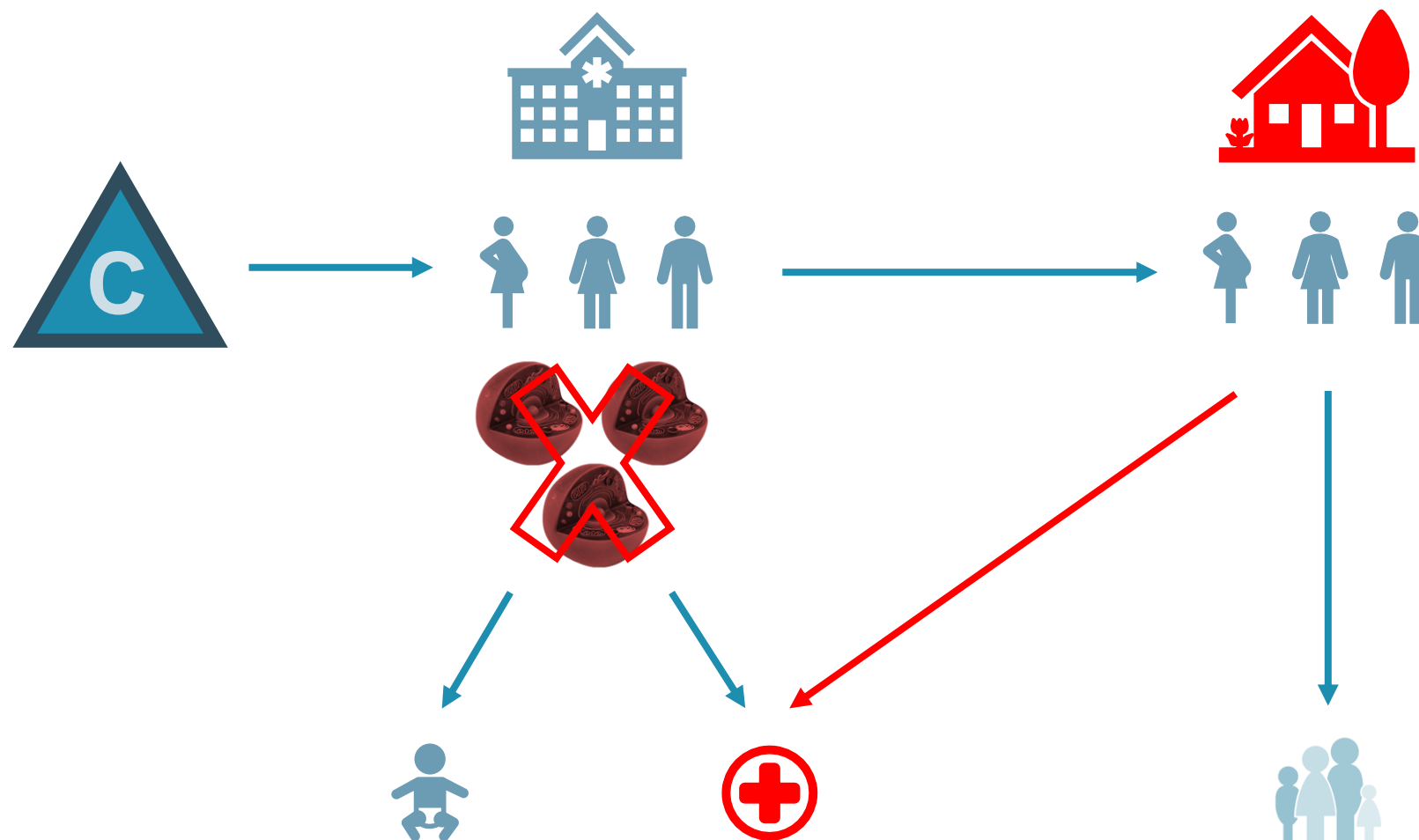
Concentration ranges in surface samples (ng/cm <sup>2</sup> )		
	Algeria	Belgium
<b>Cyclophosphamide</b>	< LOQ - 208.85	/
<b>Ifosfamide</b>	< LOQ - 23.45	/
<b>Paclitaxel</b>	< LOQ - 76.76	/
<b>Methotrexate</b>	< LOQ - 10.49	/
<b>5-Fluorouracil</b>	< LOQ - 22.22	< LOQ – 117.8
<b>&gt; 0.1 ng/cm<sup>2</sup> for 5-FU</b>	45%	16%

- Complement with biological monitoring → actual amount entering the body

# Occupational and non-occupational unintended exposure to antineoplastic drugs at home

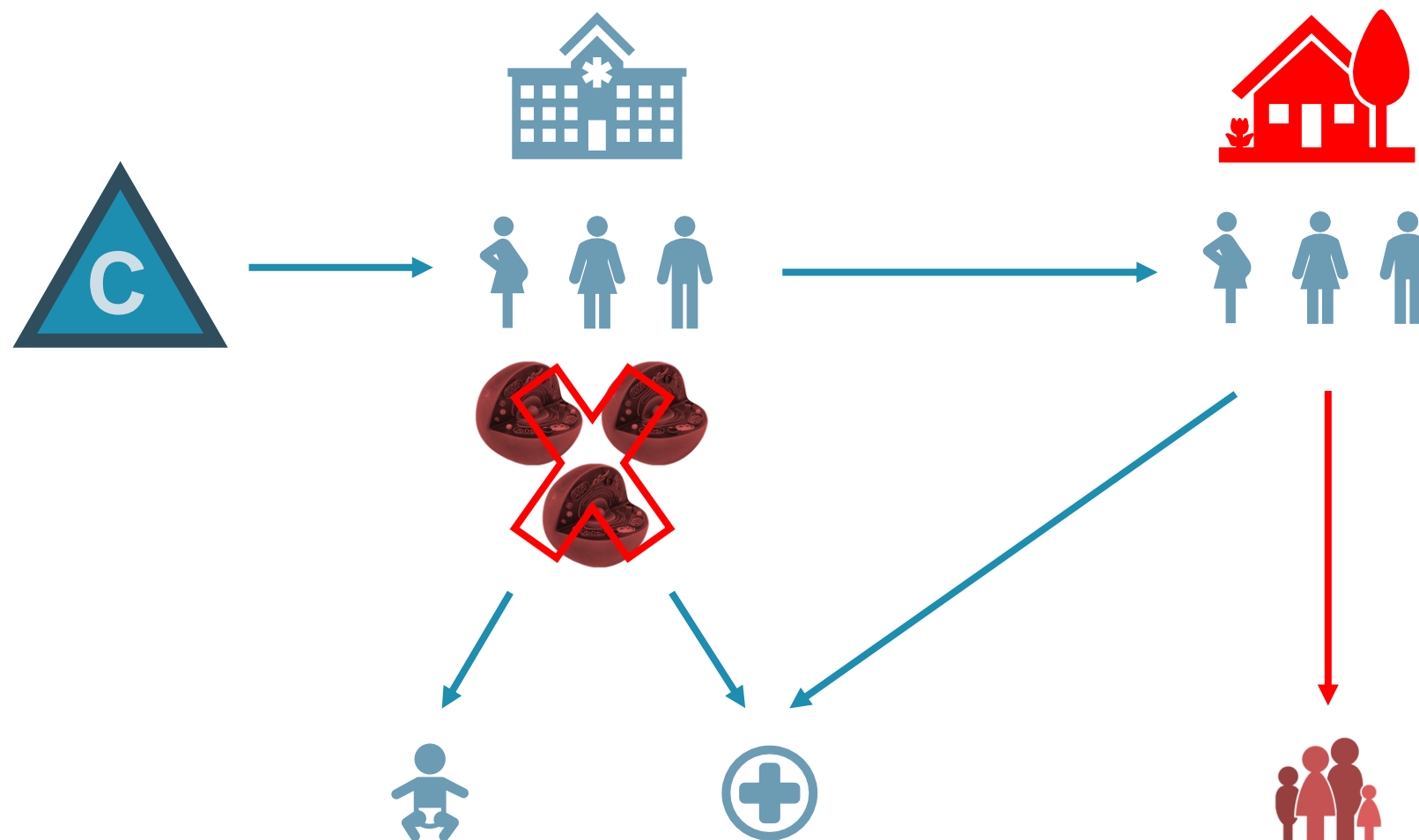






- Home = less controlled environment
- Exposure healthcare workers?
- Literature: clinical health effects and genotoxic effects  
→ increased risk for cancer development
- Health effects (genotoxic, epigenetic)?





- Home = less controlled environment
- Literature:
  - Limited number of studies
  - Variable results
  - Mainly small studies (3 – 13 family members)
  - Concentrations  $\geq$  healthcare workers

→ Exposure family members?  
→ Effects (genotoxic, epigenetic)?

# Conclusion

- Correct qualitative and quantitative information
- Mapping of exposure to and effects of cytostatic drugs
- In non-patient exposed groups (children exposed *in utero*, healthcare workers and family members of patients in home setting)
- Guidelines

# Hypothesis and aims



Unintended exposure to low cytostatic drug concentrations induces genotoxicity and epigenetic changes



**Exposure assessment:** determination of cytostatic drug concentration in the body and environment by biomonitoring and environmental monitoring



**Effect assessment:** link between cytostatic drug concentrations and DNA-adducts, chromosomal aberrations and alterations in DNA-methylation



## Unintended exposure to chemotherapeutics: an Algerian and Belgian example

Creta M.<sup>a</sup>, Verscheure E.<sup>a</sup>, Tans B.<sup>b</sup>, Devriese H.<sup>c</sup>, Devriendt A.<sup>d</sup>, Godderis L.<sup>a,c</sup>, Duca RC.<sup>a,e\*</sup>, Vanoirbeek JAJ.<sup>a\*</sup>

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<sup>5</sup>Idewe, External Service for Prevention and Protection at work, Heverlee, Belgium

Auteurs niet-gepubliceerde paper Matteo over 5-FU in UZ Leuven