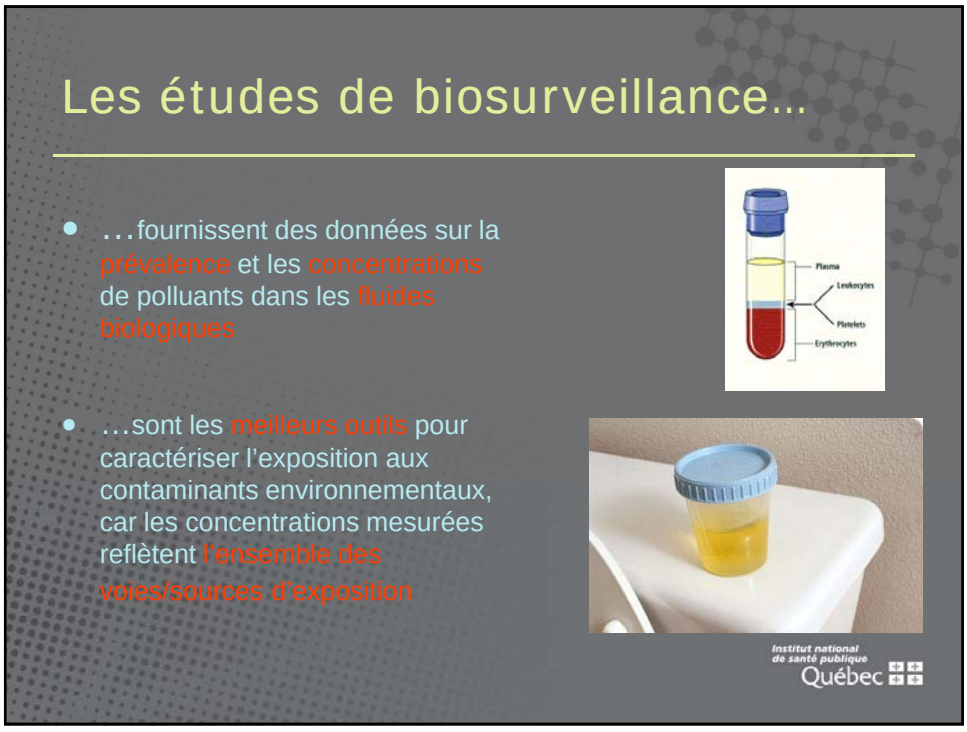
Cette présentation a été effectuée le 25 novembre 2013, au cours de la journée « La biosurveillance, un outil à exploiter en santé publique » dans le cadre des 17es Journées annuelles de santé publique (JASP 2013). L'ensemble des présentations est disponible sur le site Web des JASP à la section Archives au : http//jasp.inspq.qc.ca/.



Les études de biosurveillance…

- … permettent d'établir les niveaux d'exposition dans une population, par âge, sexe, ethnicité ou autres caractéristiques sociodémographiques

- …fournissent des résultats permettant:
  - d'établir des priorités de recherche
  - de mesurer les tendances temporelles
  - de vérifier l'efficacité de mesures de contrôle/politiques de santé publique

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Établir les priorités de recherche (Aylward et al. EHP, 2013; 121, 287-294)

Données du « National Report on Human Exposure to Environmental Chemicals » CDC 2012:

- Comparaison des concentrations de biomarqueurs avec des valeurs de références
- « Biomonitoring Equivalents » (BE):
  - Concentrations équivalentes à la RfD
  - Concentrations équivalentes à la « Risk-specific dose » - i.e. risque de cancer de 1 x 10^{-4} *

$$HQ = \frac{[\text{Biomarker}]}{BE}$$

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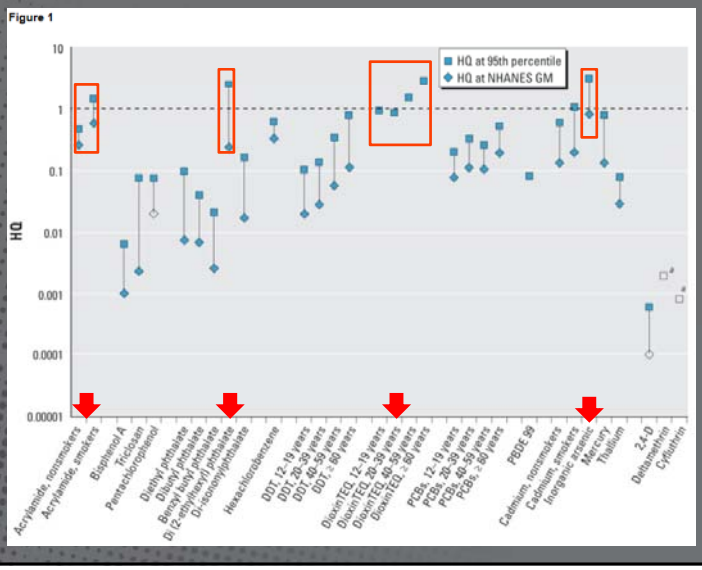
*Hays et al. Regul Toxicol Pharmacol, 2008; 51 (3 suppl): S4-S15.

HQ pour les données de NHANES
COV exclus



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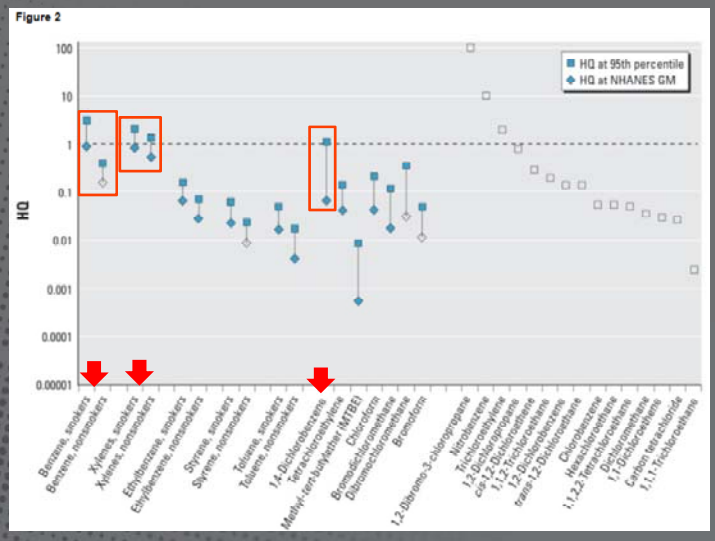
HQ pour les données de NHANES
COV



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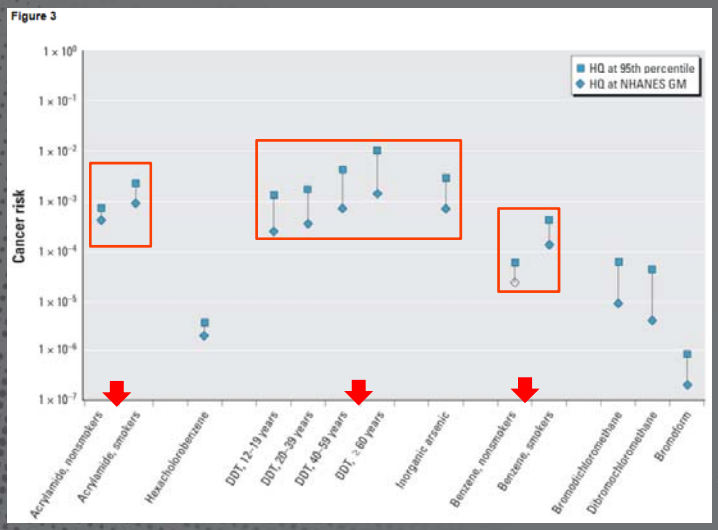
HQ pour les données de NHANES
Cancérigènes



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Tendances temporelles
Acides perfluoroalkylés aux É.U

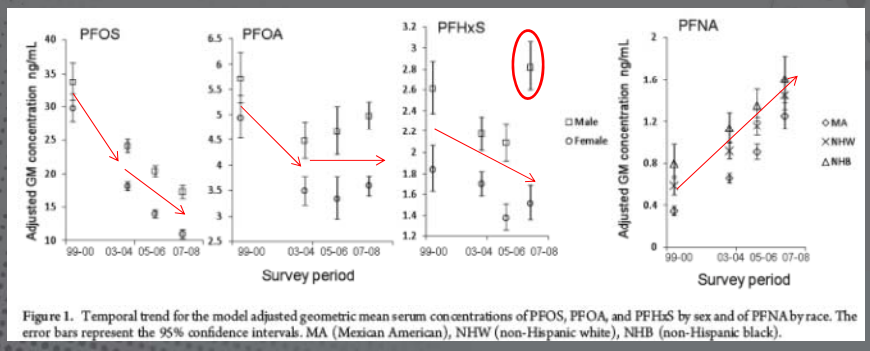

Figure 1. Temporal trend for the model adjusted geometric mean serum concentrations of PFOS, PFOA, and PFHxS by sex and of PFNA by race. The error bars represent the 95% confidence intervals. MA (Mexican American), NHW (non-Hispanic white), NHB (non-Hispanic black).

Kato K, et al.. Environ Sci Technol. 2011;45:8037-45.

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Convention de Stockholm
POPs

http://chm.pops.int/TheConvention

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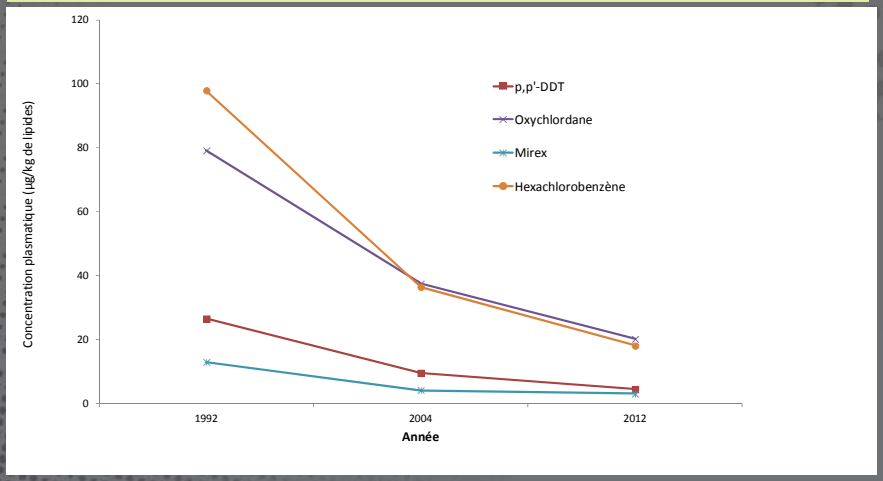
Tendances temporelles
Organochlorés au Nunavik



T. Adamou, Données non publiées

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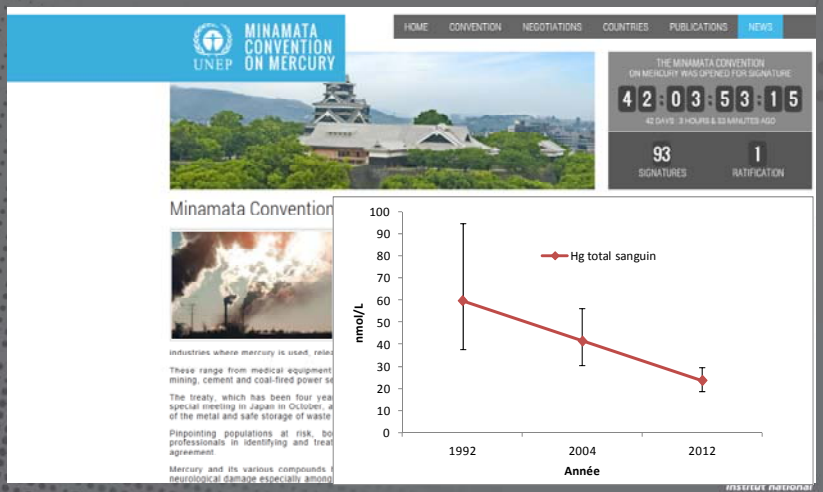
Convention de Minamata
Mercure



http://www.mercuryconvention.org/

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Les limites….

- La plupart des études de biosurveillance sont des études transversales
- Les concentrations de biomarqueurs et la présence de la maladie déterminés au même moment
- Inférence causale

1) Association statistique
2) Ordre temporel approprié
3) Explications alternatives

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BPA et maladies chroniques….

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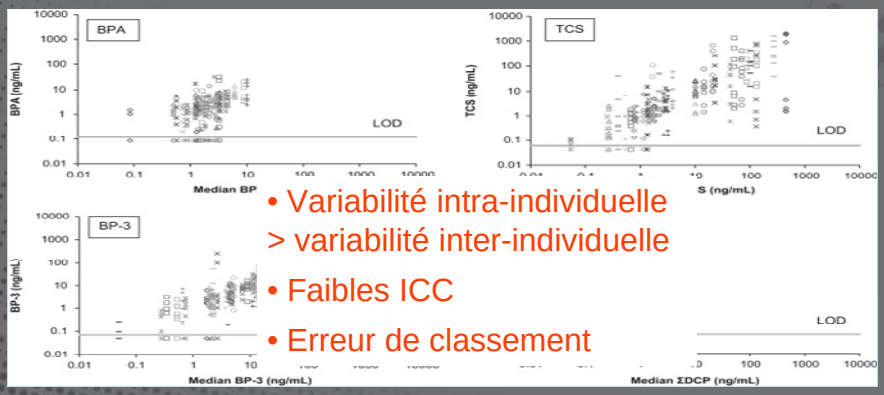
Variabilité des concentrations urinaires de BPA



- Variabilité intra-individuelle > variabilité inter-individuelle
- Faibles ICC
- Erreur de classement

Lassen et al. Environ Res. 2013;126:164-70.

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BPA et obésité chez les enfants/adolescents

ORIGINAL CONTRIBUTION

Association Between Urinary Bisphenol A Concentration and Obesity Prevalence in Children and Adolescents

Leonardo Trasande, MD, MPP
Teresa M. Attina, MD, PhD, MPH
Jun Blustein, MD, PhD

Context Bisphenol A (BPA), a manufactured chemical, ... carbonate-bottled liquids, and other consumer products ... BPA concentrations are associated with obesity and ... BPA exposure is plausibly linked to childhood obesity, ...

Objective To examine associations between urinary ... mass outcomes in children.

Design, Setting, and Participants Cross-sectional ... sentative subsample of 2838 participants aged 6 through ... for measurement of urinary BPA concentration in the 2... Nutrition Examination Survey.

Main Outcome Measures Body mass index (BMI) ... standardized z scores and used to classify participants a... centile for age/sex) or obese (BMI >95th percentile).

Results Median urinary BPA concentration was 2.8 n... 5.6). Of the participants, 1047 (34.1%; SE, 1.5%) were ... (SE, 1.3%]) were obese. Controlling for race/ethnicity, ... ority to income ratio, sex, serum cotinine level, caloric ... urinary creatinine level, children in the lowest urinary BPA ... prevalence of obesity (10.3% [95% CI, 7.5%-13.1%]; B... [95% CI, 14.5%-25.6%]; 3 (19.0% [95% CI, 13.7%-... CI, 16.4%-27.5%]). Similar patterns of association were ... examining the association between quartiled urinary BPA ... and in analyses that examined the logarithm of urinary BP... fence of obesity. Obesity was not associated with exposu... nals commonly used in other consumer products, such as ... fied analysis, significant associations between urinary BPA ... found among whites (P < .001) but not among blacks or ...

Conclusions Urinary BPA concentration was significantly associated with obesity in this cross-sectional study of children and adolescents. Explanations of the association cannot rule out the possibility that obese children ingest food with higher BPA content or have greater adipose stores of BPA.

Table 3. Association of Urinary Bisphenol A Concentration and Body Mass Outcomes From Full Multivariable Models[a]

	Body Mass Outcome				
		Overweight		Obesity	
	Increment in BMI z Score (95% CI)	OR (95% CI)	Prevalence (95% CI), %	OR (95% CI)	Prevalence (95% CI), %
Urinary bisphenol A concentration quartile					
1	1 [Reference]	1 [Reference]	31.1 (25.4 to 36.8)	1 [Reference]	10.3 (7.5 to 13.1)
2	0.12 (−0.02 to 0.27)	1.26 (0.96 to 1.64)	36.0 (30.8 to 41.2)	2.24 (1.54 to 3.24)[b]	20.1 (14.5 to 25.6)
3	0.16 (0.01 to 0.30)[c]	1.28 (0.98 to 1.66)	36.4 (29.9 to 42.8)	2.08 (1.46 to 2.96)[b]	19.0 (13.7 to 24.2)
4	0.22 (0.06 to 0.39)[d]	1.26 (0.86 to 1.82)	35.9 (29.7 to 42.2)	2.57 (1.72 to 3.83)[b]	22.3 (16.6 to 27.9)
Log-transformed bisphenol A concentration, ng/mL	0.06 (0.001 to 0.11)[c]	1.04 (0.92 to 1.18)		1.24 (1.08 to 1.44)[d]	

[a] For all models, n = 2614. All models control for sex, caloric intake, television watching, poverty to income ratio, parental education, serum cotinine level, urinary creatinine level, age, and race/ethnicity categories.
[b] $P < .001$.
[c] $P < .05$.
[d] $P < .01$.

• Données de NHANES 2003-2008: 2838 participants (6-19 ans)

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Un usage inapproprié des données de NHANES

OPEN ACCESS Freely available online PLOS ONE

Use of NHANES Data to Link Chemical Exposures to Chronic Diseases: A Cautionary Tale

Judy S. LaKind[1,2,3]*, Michael Goodman[4], Daniel Q. Naiman[5]

Abstract

Background The National Health and Nutrition Examination Survey (NHANES) is one example of cross-sectional datasets that have been used to draw causal inferences regarding environmental chemical exposures and adverse health outcomes. Our objectives were to analyze four NHANES datasets using consistent a priori selected methods to address the following questions: Is there a consistent association between urinary bisphenol A (BPA) measures and diabetes, coronary heart disease (CHD), and/or heart attack across surveys? Is NHANES an appropriate dataset for investigating associations between chemicals with short physiologic half-lives such as BPA and chronic diseases with multi-factorial etiologies? Data on urinary BPA and health outcomes from 2003–2004, 2005–2006, 2007–2008, and 2009–2010 were available.

Methodology and Findings Regression models were adjusted for creatinine, age, gender, race/ethnicity, education, income, smoking, heavy drinking, BMI, waist circumference, calorie intake, family history of heart attack, hypertension,

Conclusions: Using scientifically and clinically supportable exclusion criteria and outcome definitions, we consistently found no associations between urinary BPA and heart disease or diabetes. These results do not support associations and causal inferences reported in previous studies that used different criteria and definitions. We are not drawing conclusions regarding whether BPA is a risk factor for these diseases. We are stating the opposite–that using cross-sectional datasets like NHANES to draw such conclusions about short-lived environmental chemicals and chronic complex diseases is inappropriate. We need to expend resources on appropriately designed epidemiologic studies and toxicological explorations to understand whether these types of chemicals play a causal role in chronic diseases.

Funding: This research was supported by the Polycarbonate/BPA Global Group of the American Chemistry Council (http://plastics.americanchemistry.com/Product-Groups-and-Sustv/Polycarbonate-BPA-Global-Group). The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The funder was given the opportunity to proffer ONLY non-substantive editorial suggestions.

Introduction

The Centers for Disease Control and Prevention's (CDC) National Biomonitoring Program – part of the National Health and Nutrition Examination Survey (NHANES) – measures over 400 chemicals in people in the US. The scientific literature is replete with publications reporting associations between US population levels of chemicals in blood and/or urine and a health outcome or biochemical indicator using NHANES data [1,2,3,4,5,6,7,8]. Bisphenol A (BPA), a chemical primarily used to manufacture polycarbonate plastic and epoxy resins, has been the subject of extensive research and media attention and is one of the chemicals for which NHANES data have been used to examine such associations [9,10,11,12,13,14,15,16].

These studies [9,10,11] evaluated associations of urinary BPA concentrations with diabetes and cardiovascular disease using data from three different individual NHANES timeframes (2003–2004, 2005–2006, or 2007–2008). While the first of these studies [9] reported significant positive associations between urinary BPA and heart attack, coronary heart disease (CHD), angina, and diabetes for the 2003–2004 survey, the other studies which used data from the next two years revealed inconsistent results.

These studies varied in their methods with respect to subject inclusion criteria, case definitions and modeling strategies. Utilization of different methodologies is not inherently inappro-

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APPROCHE PROPOSÉE POUR LA RECHERCHE EN SANTÉ ENVIRONNEMENTALE

- Études prospectives avec des sous-groupes de participants pour étudier les relations entre des expositions environnementales et des biomarqueurs d'effets précoces
- Études cas-témoin nichées dans la cohorte pour étudier:
  - Les relations entre les maladies des biomarqueurs d'effets précoces modulés par les expositions environnementales
  - Les relations entre les maladies et ces expositions environnementales

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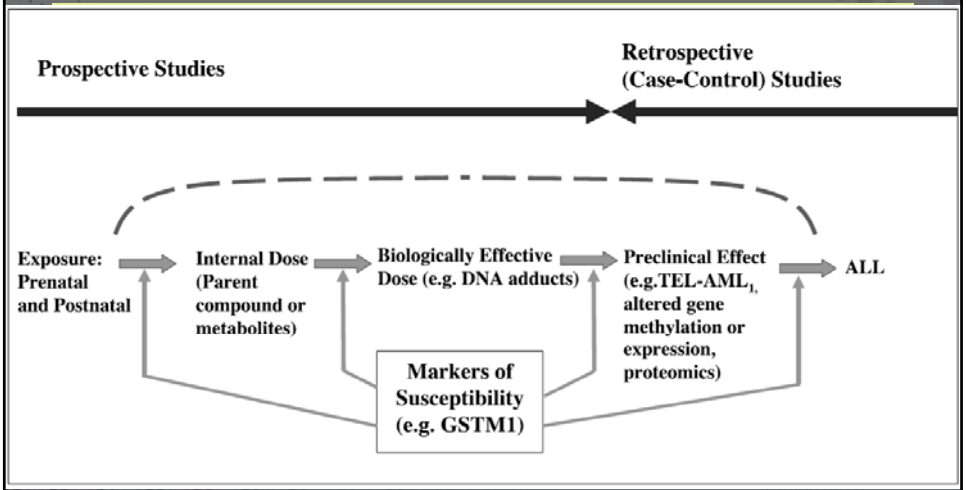
L'approche "Meet-in-the-Middle-Approach": L'exemple de la leucémie aigue lymphoblastique



Vineis, P. and Perera, F. CEBP, 2007; 16: 1954-65.

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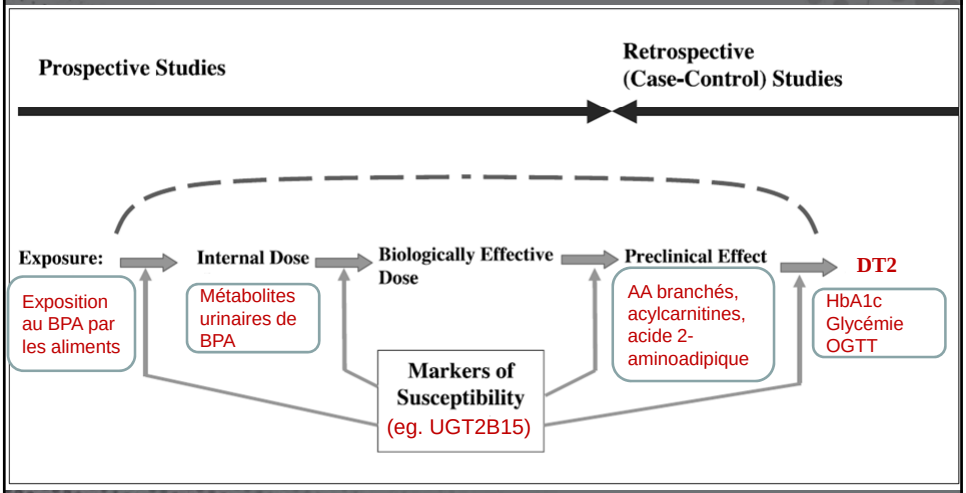
L'approche "Meet-in-the-Middle-Approach": Exposition au bisphénol A et diabète de type 2*



*Silver, MK et al.. PLoS One. 2011;6(10):e26868.

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Enquête canadienne longitudinale sur le vieillissement (ECLV)

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CONCLUSIONS

• Les études de biosurveillance constituent les outils de choix pour caractériser l'exposition des populations aux contaminants environnementaux

• Leur utilisation pour établir des relations entre les expositions environnementales et les maladies chroniques n'est pas appropriée

•Investissons dans les études prospectives en cours

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