



NTP

National Toxicology Program

Implementation of Systematic Review by the National Toxicology Program Office of Health Assessment and Translation (OHAT)

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Division of the NTP
National Institute of Environmental Health Sciences

OpenTox USA
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Hamner Conference Center, North Carolina Biotechnology Center,
Raleigh-Durham, USA



Outline

- Overview of systematic review and OHAT framework for integrating evidence
- Assessing study quality and utility
- Data management and display software tools



Systematic Review

- A scientific investigation that focuses on a specific question, and uses explicit, pre-specified methods to identify, select, summarize, and assess the findings of similar studies
- Provides greater transparency
- Used to:
 - Reach evidence-based conclusions
 - Clarify need for additional research
 - May or may not result in quantitative meta-analysis
- Existing methodologies are primarily used for assessment of healthcare interventions
 - e.g., Cochrane, AHRQ, GRADE

What Does A Systematic Review Not Do?

- Does not eliminate the need for expert judgment
- Improves but does not guarantee reproducibility of conclusions across separate evaluations
 - Increased transparency does not necessarily eliminate differences in scientific judgment
- Existing methods do not provide guidance on how to
 - Reach hazard identification conclusions
 - Integrate evidence across human, animal, and mechanistic studies

OHAT Systematic Review and Evidence Integration Framework

Step 1: Prepare topic

Step 2: Search for and select studies

Step 3: Extract data from studies

Step 4: Assess individual study quality

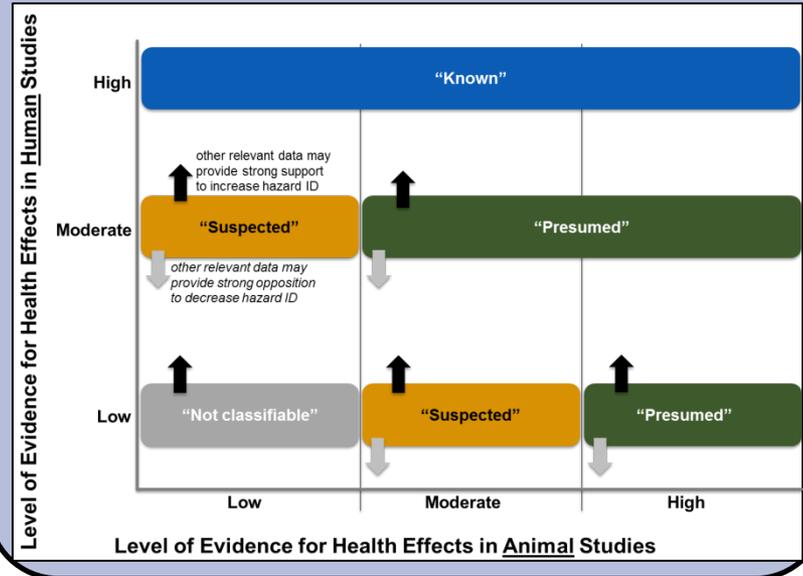
Step 5: Rate confidence in body of evidence (animal and human studies)

Initial Confidence by Key Features of Study Design	Factors Decreasing Confidence	Factors Increasing Confidence	Confidence in the Body of Evidence
High (++++) 4 Features	<ul style="list-style-type: none"> ❖ Risk of Bias ❖ Unexplained Inconsistency ❖ Indirectness ❖ Imprecision ❖ Publication Bias 	<ul style="list-style-type: none"> ❖ Large Magnitude of Effect ❖ Dose Response ❖ All Plausible Confounding <ul style="list-style-type: none"> • Studies report an effect and residual confounding is toward null • Studies report no effect and residual confounding is away from null ❖ Consistency <ul style="list-style-type: none"> • Across animal models or species • Across dissimilar populations • Across study design types ❖ Other <ul style="list-style-type: none"> e.g., particularly rare outcomes 	High (++++)
Moderate (+++) 3 Features			Moderate (+++)
Low (++) 2 Features			Low (++)
Very Low (+) ≤1 Features			Very Low (+)

- Features**
- Controlled exposure
 - Exposure prior to outcome
 - Individual outcome data
 - Comparison group used

Step 6: Translate confidence ratings into level of evidence for health effect

Step 7: Integrate evidence to develop hazard identification conclusions



Evaluating evidence for biological plausibility provided by *in vitro*, cellular, genomic, or mode of action data



Strong Support

- *Relevance of biological process or pathway to human health*
- *Consistency*
- *Relevance of concentration*
- *Potency*
- *Dose response*
- *Study quality*
- *Publication bias*

Weak Support

Factors considered parallel elements used to evaluate confidence in the other data streams

A conclusion of “strong” support may lead to a label of “suspected” in the absence of human or animal data

Evaluating Study Quality and Utility

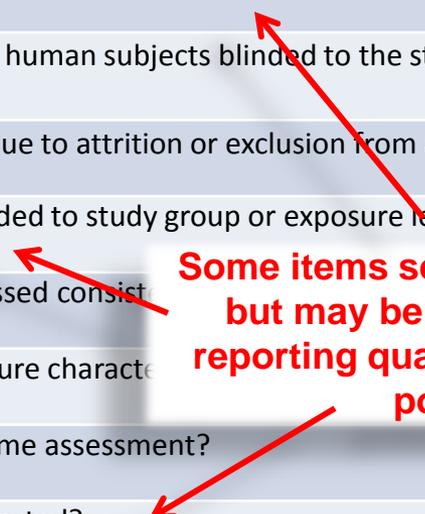
Definitions: Study Quality and Utility

- **Reporting quality:** How well was the study reported?
- **Internal validity or risk of bias:** How credible are the findings based on design and conduct of the study?
 - Reporting quality checklist \neq risk of bias tool
 - Non-reporting has negative impact on risk of bias (attempts will be made to follow up with study authors)
 - Single summary scores of studies strongly discouraged, domain-based approach recommended
- **Directness and applicability:** How well does the study address the topic under review?
 - Route, timing/duration of exposure and health outcome assessment
 - Upstream indicator of primary health outcome?
 - Relevance of animal model for human health

Same set of questions applied to different study designs

Risk of Bias Domain	Criterion	Animal	Controlled Exposure	Cohort	Case-Control	Cross-sectional	Case Series
Selection	Was administered dose or exposure level adequately randomized?	X	X				
	Was allocation to study groups adequately concealed?	X	X				
	Were the comparison groups appropriate?			X	X	X	
Confounding	Did the study design or analysis account for important confounding and modifying variables?	X	X	X	X	X	X
	Did researchers adjust or control for other exposures that are anticipated to bias results?	X	X	X	X	X	X
Performance	Were experimental conditions identical across study groups?	X	X				
	Did deviations from the study protocol impact the results?	X	X	X	X	X	X
	Were the research personnel and human subjects blinded to the study group during the study?	X	X				
Attrition	Were outcome data incomplete due to attrition or exclusion from analysis?	X	X	X	X	X	
Detection	Were the outcome assessors blinded to study group or exposure level?	X	X	X	X	X	X
	Were confounding variables assessed consistently across exposure measures						
	Can we be confident in the exposure characterization?						
	Can we be confident in the outcome assessment?	X	X	X	X	X	X
Reporting	Were all measured outcomes reported?	X	X	X	X	X	X
Other	Were there any other potential threats to internal validity (e.g., inappropriate statistical methods)?	X	X	X	X	X	X

Some items seem unlikely to be useful in short-term but may be useful in long-term, i.e., changes in reporting quality, develop empirical data to assess potential risk of bias of item



Current Tool: Response Format & Review Process

- Uses responses recommended by the Clarity Group
 - “definitely no” (●) risk of bias
 - “probably no” (●) risk of bias
 - “probably yes” (●) risk of bias (rule for non-reported elements)
 - “definitely yes” (●) risk of bias
- Rationale for selecting a response is noted
 - Based on instructions and expert judgment (e.g., members of review team, technical advisors)
- Risk of bias is independently assessed by 2 members of review team
 - Independent reviews discussed to develop draft response for report
- Risk of bias conclusions assessed by review team, technical advisors, and undergo external public peer-review

Risk of Bias Ratings Across Individual Studies

- ++ Definitely Low risk of bias
- + Probably Low risk of bias
- - Probably High risk of bias
- -- Definitely High risk of bias

Draft OHAT Risk of Bias Questions

○ Not applicable due to study design

NotGood , 2010

Bucher et al., 1999

Wolfe et al., 2000

Boyles et al., 2011

Thayer et al., 2008

Selection Bias

Was administered dose or exposure level adequately randomized?

○ ○ ○ ○ ○

Was allocation to study groups adequately concealed?

○ ○ ○ ○ ○

Were the comparison groups appropriate?

+ ● ++ + ● -- +

Confounding Bias

Did the study design or analysis account for important confounding and modifying variables?

- ● ++ - ● -- +

Did researchers adjust or control for other exposures that are anticipated to bias results?

- ● ++ - - ● --

Performance Bias

Were experimental conditions identical across study groups?

○ ○ ○ ○ ○

Did deviations from the study protocol impact the results?

- ● ++ + - -

Were the research personnel and human subjects blinded to the study group during the study?

○ ○ ○ ○ ○

Attrition / Exclusion Bias

Were outcome data incomplete due to attrition or exclusion from analysis?

● -- ● ++ - + +

Information / Detection Bias

Were outcome assessors blinded to study group or exposure group?

+ ● ++ + + +

Were confounding variables assessed consistently across groups using valid and reliable measures?

● -- ● ++ + ● ++ ● ++

Can we be confident in the exposure characterization?

- ● ++ ● -- - +

Can we be confident in the outcome assessment?

- ● ++ - + -

Selective Reporting Bias

Were all measured outcomes reported?

+ ● ++ + - +

Study Quality and Utility are Assessed in Several Different Steps

Step 1: Prepare topic

Step 2: Search for and select studies

Step 3: Extract data from studies

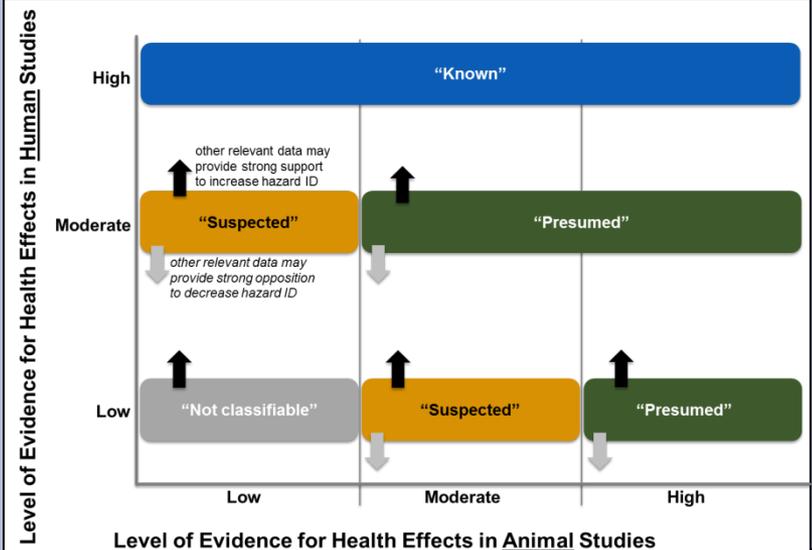
Step 4: Assess individual study quality (risk of bias)

Step 5: Rate confidence in body of evidence (animal and human studies)

Initial Confidence by Key Features of Study Design	Factors Decreasing Confidence	Factors Increasing Confidence	Confidence in the Body of Evidence
High (++++) 4 Features	❖ Risk of Bias ❖ Unexplained Inconsistency ❖ Indirectness ❖ Imprecision	❖ Large Magnitude of Effect ❖ Dose Response ❖ All Plausible Confounding • Studies report an effect and residual confounding is toward null • Studies report no effect and residual confounding is away from null	High (++++)
Moderate (+++) 3 Features Features: • Controlled exposure • Exposure prior to outcome • Individual outcome data • Comparison group used	❖ Publication Bias	❖ Consistency • Across animal models or species • Across dissimilar populations • Across study design types ❖ Other e.g., particularly rare outcomes	Moderate (+++)
Low (++) 2 Features			Low (++)
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Software Tools to Manage Systematic Review, Data Collection, & Visual Display

Data Management Goals

- Create data repositories of extracted data
 - Reduce duplication of effort – data extraction currently done by people = \$\$\$\$\$
- Disseminate data files of extracted data to public
 - Increase transparency
 - Facilitate independent and supplemental analysis of data
 - Data would reside in CEBS (and potentially other places)
- Create more concise reports
 - Use figures and tables to summarize studies
 - Web-based reports
 - Interactive modules (e.g. HAWC)

Data Management & Display Tools

- Distiller Systematic Review® Software = systematic review software to help manage screening process
- ICF International's DRAGON for data extraction and warehousing
- HAWC (Health Assessment Workspace Collaborative) for visual display and other analysis functions
 - Ivan Rusyn's talk in session C on Thursday

Distiller Systematic Review® Software

Distiller SR®

web-based

https://systematic-review.ca/Reports/ArticleProgress.php

Most Visited

DistillerSR

Project

air pollution

User kris.thayer (My Settings)

Messages Nothing new

tracks which studies were included/excluded and why

	Unreviewed	Some Reviews	Included	Excluded	Conflict	Fully Reviewed
Level 1 - Title & Abstract Screen	0	0	8842	9134	0	17976
Level 2 - Binning and PDF Screen	0	0	4675	3273	894	8842
Level 3 - Full Text Screen -Pregnancy Outcomes	412	13	2	0	0	2
	Unreviewed	Some Reviews	Included	Excluded	Conflict	Fully Reviewed

tracks conflicts

upload references from Endnote or other reference managers
— PDFs of articles can also be uploaded

Distiller SR® - Customizable Screening Level Forms

Y. Kim and B. K. Lee. 2011. Association between urinary arsenic and diabetes mellitus in the Korean general population according to KNHANES 2008. Sci Total Environ 409(19): 4054-62.

INTRODUCTION: We present data from the Korean National Health and Nutrition Examination Survey (KNHANES) 2008 on the associations between urinary arsenic and diabetes mellitus in a representative sample of the adult Korean population.

METHODS: This study was based on data obtained in KNHANES 2008, which was conducted for three years (2007-2009) using a rolling sampling design involving a complex, stratified, multistage, probability-cluster survey of a representative sample of the noninstitutionalized civilian population of South Korea.

RESULTS: Geometric means of total urinary arsenic concentration in females and total participants with diabetes mellitus were significantly higher than in participants without diabetes mellitus after adjustment for covariates, including age, seafood consumption, body mass index (BMI), hypertension, area of residence, regional area, education level, and smoking and drinking status. Multiple regression analysis after similar adjustment showed that total urinary arsenic concentration was associated with diabetes status in the females and total participants. In addition, after similar adjustment, the odds ratios (ORs) for diabetes mellitus in female participants and all participants were 1.502 (95% CI, 1.038-2.171) and 1.312 (95% CI, 1.040-1.655), respectively, for doubling of the level of urinary total arsenic concentration.

CONCLUSION: This study showed an association between total urinary arsenic concentration and the prevalence of diabetes mellitus in a representative sample of the adult population, especially women, with environmental arsenic exposure after adjustment for seafood intake and relevant diabetes risk factors.

and go to or [Skip to Next](#)

Do the title or abstract suggest the article contains original data related to a topic of interest?

- yes
- yes (non-English)
- yes, but is a review, commentary, or letter with no original data
- no, not relevant
- not directly relevant, but could be supportive material
- unsure

Add text here to described screening level criteria for relevance:

Inclusion criteria

- [bullet format](#)
- [bullet format](#)

Exclusion criteria

- [bullet format](#)
- [bullet format](#)

Comments

and go to or [Skip to Next](#)

Distiller SR® – Inclusion & Exclusion Settings

Answer	Type	Has Text	Order	Export Header	Calculation Value	Actions
yes	Include	<input type="checkbox"/> No Validation	1		0	Delete
yes (non-English)	Neutral	<input type="checkbox"/> No Validation	2		0	Delete
yes, but is a review, corr	Exclude	<input type="checkbox"/> No Validation	3		0	Delete
no, not relevant	Exclude	<input type="checkbox"/> No Validation	4		0	Delete
not directly relevant, but	Neutral	<input type="checkbox"/> No Validation	5		0	Delete
unsure	Neutral	<input type="checkbox"/> No Validation	6		0	Delete
	Neutral	<input type="checkbox"/> No Validation				
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	Neutral	<input type="checkbox"/> No Validation				

Cancel Save

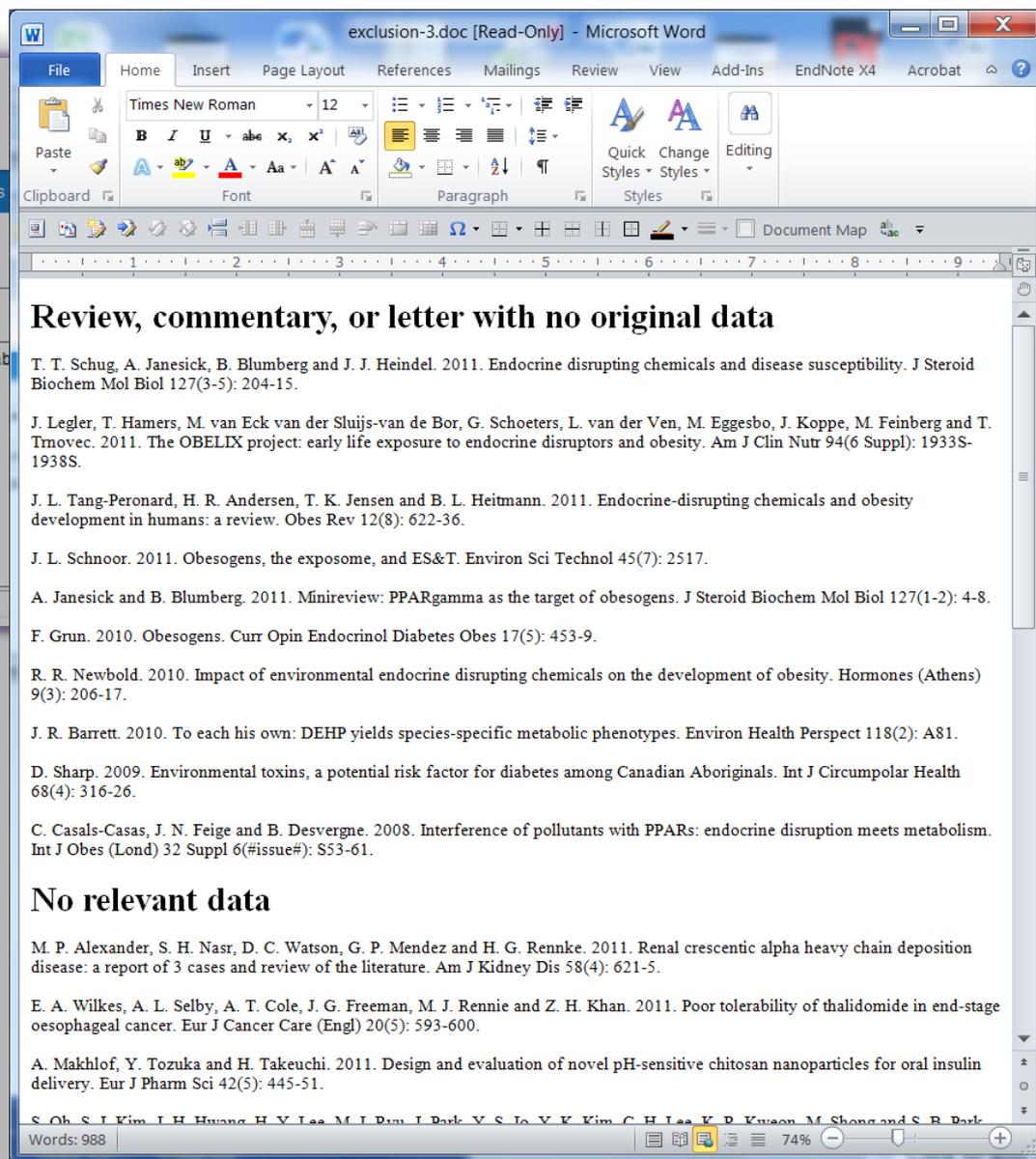
Distiller SR® - Exclusion Reports



The DistillerSR interface shows a navigation bar with 'Review', 'Datarama', 'Reports', 'References', and 'Forms'. The 'Reports' menu is open, listing options: Article Status, Exclusions, User Metrics, Kappa, Statistical, and User Workload. A table below shows exclusion data for Level 1, with 35 exclusions. A red arrow points from the 'Download Exclusion Document' button to the Microsoft Word document.

Level	Exclusions [?]	Form
Level 1	35	Abst Scre

Download Exclusion Document with format No Custom Format



The Microsoft Word document displays a list of excluded articles under the heading 'Review, commentary, or letter with no original data'. A second heading, 'No relevant data', is also visible. The status bar at the bottom indicates 988 words and 74% zoom.

Review, commentary, or letter with no original data

T. T. Schug, A. Janesick, B. Blumberg and J. J. Heindel. 2011. Endocrine disrupting chemicals and disease susceptibility. *J Steroid Biochem Mol Biol* 127(3-5): 204-15.

J. Legler, T. Hamers, M. van Eck van der Sluijs-van de Bor, G. Schoeters, L. van der Ven, M. Eggesbo, J. Koppe, M. Feinberg and T. Tmovec. 2011. The OBELIX project: early life exposure to endocrine disruptors and obesity. *Am J Clin Nutr* 94(6 Suppl): 1933S-1938S.

J. L. Tang-Peronard, H. R. Andersen, T. K. Jensen and B. L. Heitmann. 2011. Endocrine-disrupting chemicals and obesity development in humans: a review. *Obes Rev* 12(8): 622-36.

J. L. Schnoor. 2011. Obesogens, the exposome, and ES&T. *Environ Sci Technol* 45(7): 2517.

A. Janesick and B. Blumberg. 2011. Minireview: PPARgamma as the target of obesogens. *J Steroid Biochem Mol Biol* 127(1-2): 4-8.

F. Grun. 2010. Obesogens. *Curr Opin Endocrinol Diabetes Obes* 17(5): 453-9.

R. R. Newbold. 2010. Impact of environmental endocrine disrupting chemicals on the development of obesity. *Hormones (Athens)* 9(3): 206-17.

J. R. Barrett. 2010. To each his own: DEHP yields species-specific metabolic phenotypes. *Environ Health Perspect* 118(2): A81.

D. Sharp. 2009. Environmental toxins, a potential risk factor for diabetes among Canadian Aboriginals. *Int J Circumpolar Health* 68(4): 316-26.

C. Casals-Casas, J. N. Feige and B. Desvergne. 2008. Interference of pollutants with PPARs: endocrine disruption meets metabolism. *Int J Obes (Lond)* 32 Suppl 6(issue#): S53-61.

No relevant data

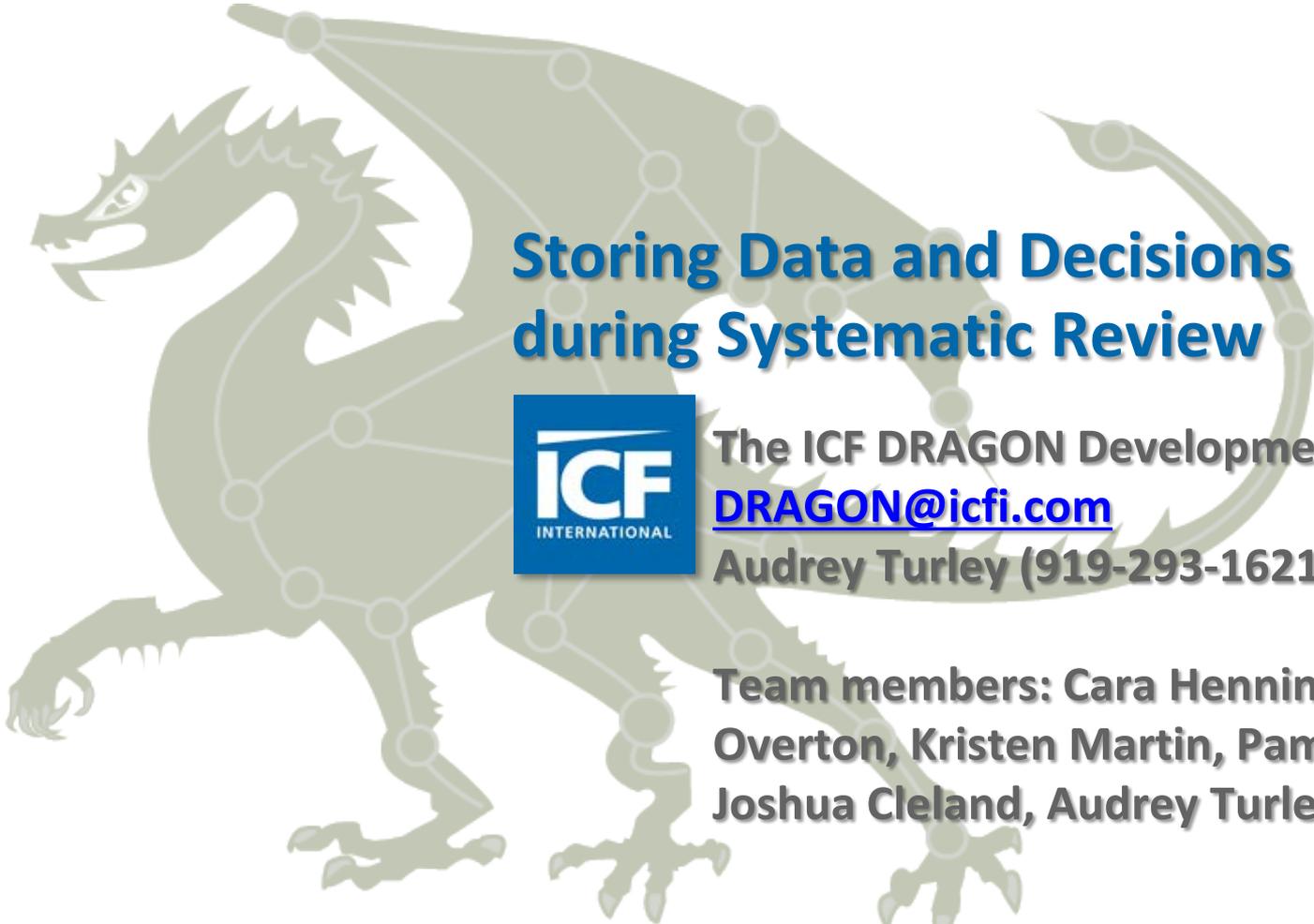
M. P. Alexander, S. H. Nasr, D. C. Watson, G. P. Mendez and H. G. Rennke. 2011. Renal crescentic alpha heavy chain deposition disease: a report of 3 cases and review of the literature. *Am J Kidney Dis* 58(4): 621-5.

E. A. Wilkes, A. L. Selby, A. T. Cole, J. G. Freeman, M. J. Rennie and Z. H. Khan. 2011. Poor tolerability of thalidomide in end-stage oesophageal cancer. *Eur J Cancer Care (Engl)* 20(5): 593-600.

A. Makhlof, Y. Tozuka and H. Takeuchi. 2011. Design and evaluation of novel pH-sensitive chitosan nanoparticles for oral insulin delivery. *Eur J Pharm Sci* 42(5): 445-51.

S. Oh, S. J. Kim, J. H. Hwang, H. Y. Lee, M. I. Park, J. Park, Y. S. Jo, Y. K. Kim, C. H. Lee, K. P. Kwon, M. Shong and S. B. Park

Words: 988 74%



Storing Data and Decisions during Systematic Review



The ICF DRAGON Development Team

DRAGON@icfi.com

Audrey Turley (919-293-1621)

Team members: Cara Henning, AJ Overton, Kristen Martin, Pam Ross, Joshua Cleland, Audrey Turley

DRAGON

Data Entry to Facilitate Creation of Evidence Tables

The AnimalDRAGON interface features a green header with a dragon logo and the text 'AnimalDRAGON'. On the left, there is a 'Login' section with fields for 'Assessment' and 'Username', and a 'Login' button. The main area is divided into two columns: 'Data Entry Tasks' and 'Administrative Tasks'. The 'Data Entry Tasks' column includes buttons for 'Add Data to Studies', 'Conduct BMDS', 'View Summary Table', and 'Export Data'. The 'Administrative Tasks' column includes buttons for 'Add Chemicals To Database', 'Add Studies To Database', 'Add/View Assessment(s)', 'QA Management', and 'View Tables'. At the bottom, there are buttons for 'Quick Start Guide' and 'Exit'.

The epiDRAGON interface features a green header with a dragon logo and the text 'epiDRAGON'. On the left, there is a vertical menu with buttons for 'View/Edit Study Data', 'Publication Data', 'QA Summary', 'View Lookup Data', 'Link to Backend', 'Export Data', 'About this Database', and 'Exit'. The main area is divided into two sections: 'Overview' and 'Quick Links'. The 'Overview' section shows statistics: 'Count of Studies: 13', 'QA Complete: 8', and 'QA Pending: 10'. The 'Quick Links' section is a table with columns for 'Study' and 'QA Complete', and buttons for 'View Data', 'Summary Table', and 'Evidence Table'.

Study	QA Complete
Ahwan et al., 2006	Pending
Bates, 2004	Pending
Chen et al., 2010 (urinary tract cancer)	Complete
Chen et al., In press	Pending
Chen, 2010	Complete
Chen, 2010 (diabetes)	Complete
Ferrecio et al., 2000	Pending
Kwok et al.	Pending
Lamm, 2004	Complete
Li et al., 2006	Pending
Medrano, 2010	Pending
Meliker et al. 2010	Pending

In vitro module under development

DRAGON Study Data

Go To:

Project: t-butanol, Study: Hard et al., 2011

Protocol Doses | Measured Endpoints | Protocol Results | Dose Conversions

Select Endpoint

Endpoint Details

Endpoint Name in Study

Gender Observation Time Units

Response Details Data not reported? **Analysis of Response** Data not evaluated?

Data Type NOEL

Trend Sig. LOEL

Table/Figure FEL

Stat. Method Dose Resp. Rel.

Power Text Reason not modeling?

Individual animal data reported? Attempt BMD?

Response Data Conduct/View Analysis

Dose	N	Incidence/Response	SD/SE	Type	Response Ur	Significance	AUC_Rpt	AU
0	50	3						
1.25	50	9				Not Sig.		
2.5	50	9				Not Sig.		
5	50	9				Not Sig.		

Mag. of Difference

Power Calculation Formula = $16 / (\text{mean} - (\text{mean} - (\text{magnitude_of_difference} * \text{mean})) / \text{sd})^2$

Manage Endpoints

Search for Endpoints

- By category
- By text

DRAGON Study Data Save Changes Undo C

Assessment: DEHP, Study: Moore et al., 2001 Viewing Dose Regimen

Study Dashboard | Study Protocol | **Measured Endpoints** | Results | Analysis

Select Endpoint Category: All Endpoints Search:

Double click a single endpoint, or select multiple and click "Add selected endpoints" [Add endpoints from existing dose regimen](#)

Select Endpoints [Add selected endpoints](#) [Clear All](#)

Endpoint	Example
adrenal gland: absolute weight	
adrenal gland: gross pathology	
adrenal gland: neoplastic lesions	
adrenal gland: nonneoplastic lesions	
adrenal gland: relative weight	
Age of sexual maturation	
alanine aminotransferase (ALT)	This can also be called glutamic pyruvic transaminase or GPT
albumin	
alkaline phosphatase (ALP)	This is sometimes also abbreviated ALK, but is not generally called another name

Measured Endpoints

View/Edit	System	Endpoint	Name in Study	ObsTime	Time Units	Not Reporte	Not Includer	Endpoint Notes
View/Edit	female reproductive system	implantations	Implantation sites per dam	PND 0	days	<input type="checkbox"/>	<input type="checkbox"/>	N = number of dams per group
View/Edit	development	parturition	Incidence of parturition	PND 0	days	<input type="checkbox"/>	<input type="checkbox"/>	Incidence provided as % incidence of parturition
View/Edit	development	undescended testes	Undescended testes per rat	PND 21	days	<input type="checkbox"/>	<input type="checkbox"/>	Data were digitized using GetData Graph Digitiz

Select Endpoint

Add Details

- Name in study
- Notes
- View/Edit more

Study Quality / Risk of Bias

Quality is assessed by two separate reviewers.

epiDRAGON Study Quality Save Ch

Assessment: BPA obes Go To:

Current Study: (Carwile and Michels 2011)

Review Level:

Selection -- Randomization (1 of 19) Go To:

Primary Question: Was administered dose or exposure level adequately randomized?

Rating:

Rationale:

Clarifying Questions
None

Factor	Rating
Randomization	++
Allocation Concealment	+
Comparison Group	n/a
Confounding (Design)	+
Unintended Exposure	+
Experimental Conditions	n/a
Protocol Deviations	++
Blinding (During Study)	n/a
Missing Outcome Data	+
Blinding (Outcome Assessment)	++
Confounding (Analysis)	++
Exposure Characterization	++
Outcome Assessment	++
Outcome Reporting	++
Internal Validity	++
Controlled Exposure	--
Exposure Timing	--
Individual-Level Data	++
Comparison Group Used	++

Enter rationale for rating here.

Study Quality / Risk of Bias: Management Console

DRAGON Study Quality Review

(Carwile and Michels 2011) -- Selection: Randomization

Studies for Quality Review

Study	Status
(Bhandari et al. 2013)	Pending
(Carwile and Michels 2011)	Pending
(Harley et al. 2013)	Pending
(Li et al. 2013)	Pending
(Maserejian et al. 2012)	Pending
(Shankar et al. 2012)	Pending

Pending only
 All studies

Study Quality Sufficiency Scores and Factor Selection

Factor	Final	Primary	Secondary
Randomization		++	
Allocation Concealment		+	
Comparison Group		n/a	
Confounding (Design)		+	
Unintended Exposure		+	
Experimental Conditions		n/a	
Protocol Deviations		++	
Blinding (During Study)		n/a	
Missing Outcome Data		+	
Blinding (Outcome Assessment)		++	
Confounding (Analysis)		++	
Exposure Characterization		++	
Outcome Assessment		++	
Outcome Reporting		++	
Internal Validity		++	
Controlled Exposure		--	
Exposure Timing		--	
Individual-Level Data		++	
Comparison Group Used		++	

Confirm and Complete Study Quality Review

Comments on inclusion/exclusions Include/Exclude

Review Completed by:

Date Completed:

Save and Complete Review

++ Rationale

Primary Review yes, "randomly assigned to treatment within their body weight stratum"

Secondary Review Rationale

Final Review Final Rationale

Consensus

Rationale Comments

Quality Control

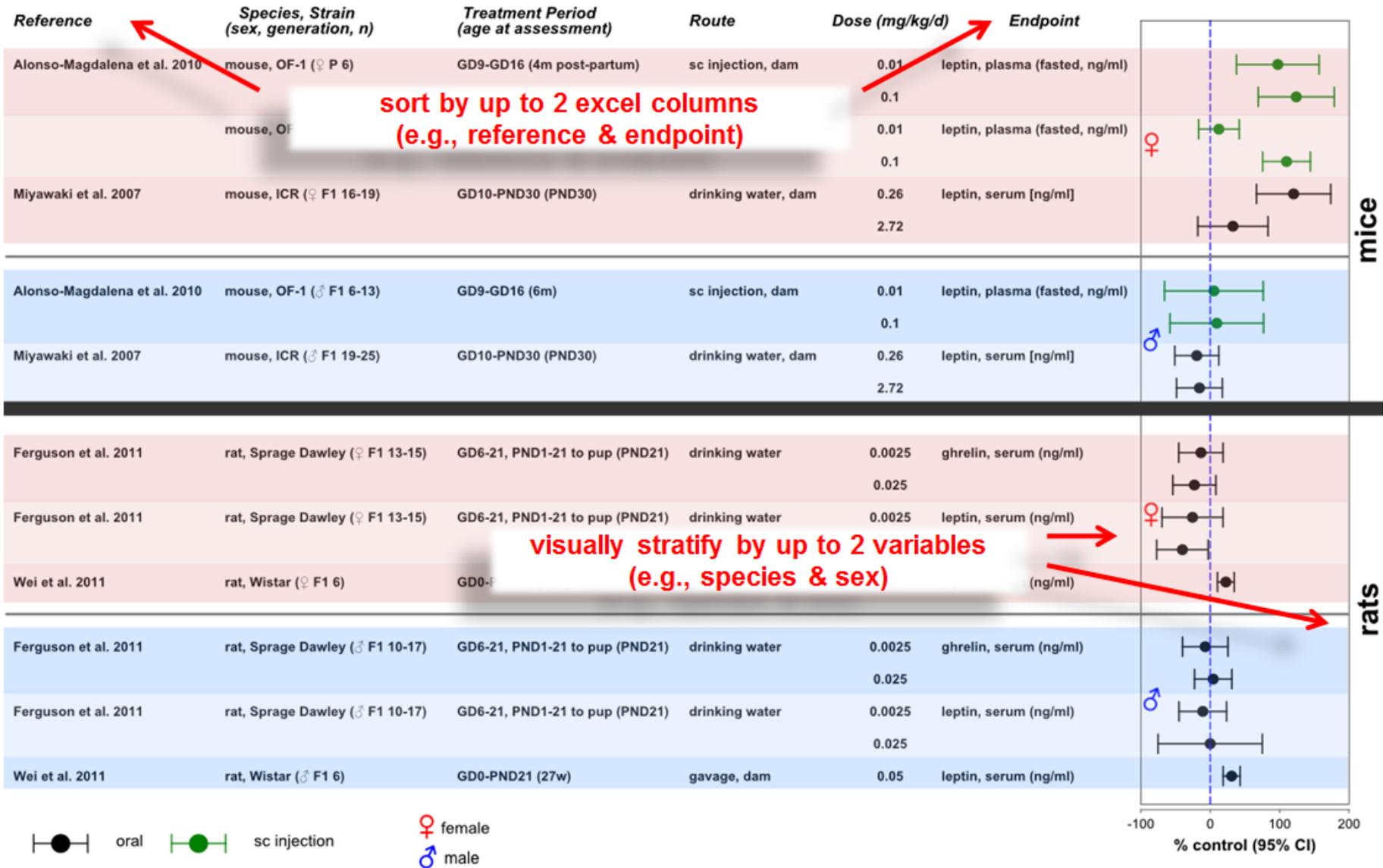
epiDRAGON QA Management

- QA Status: Pending

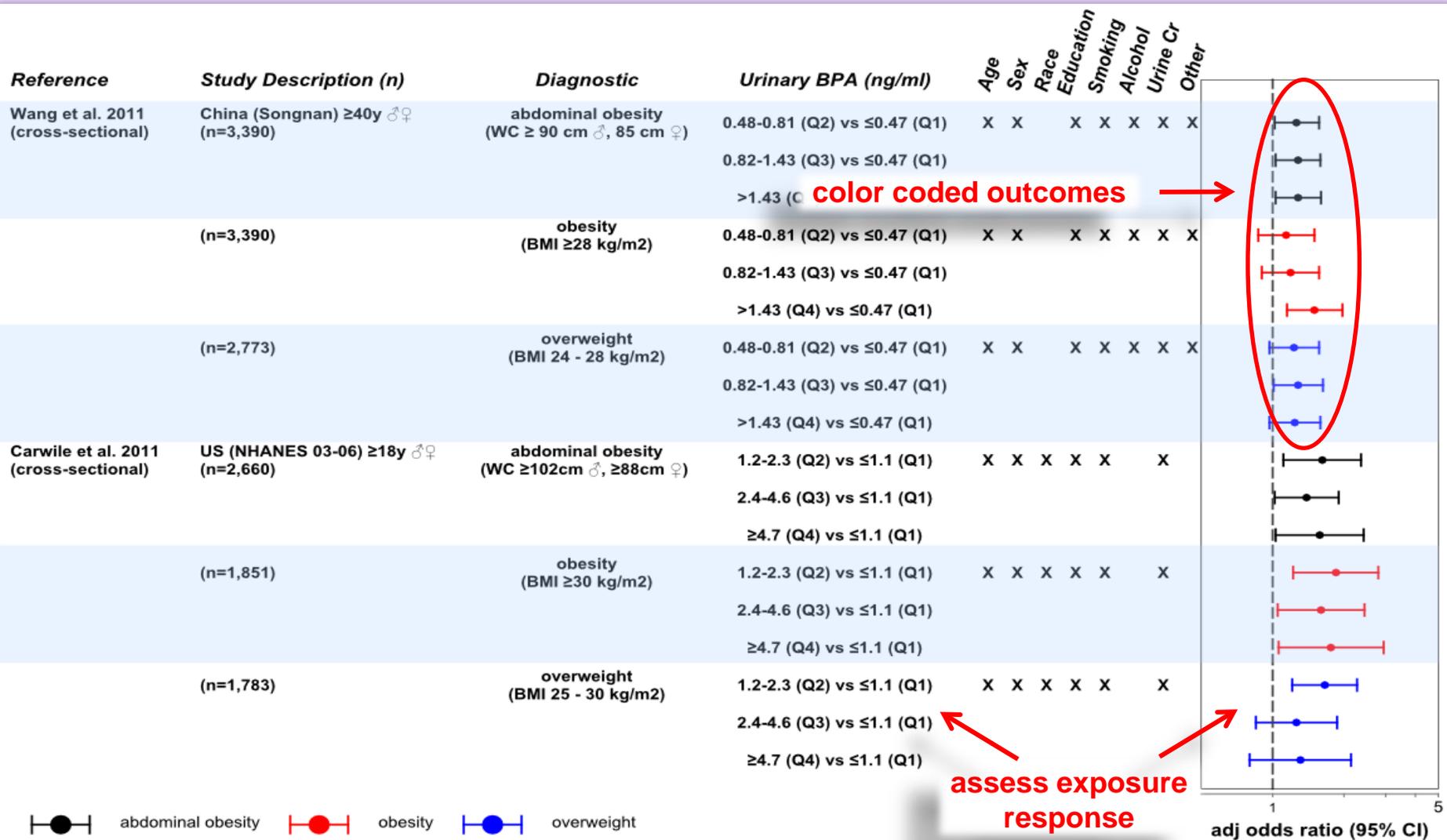
Short Citation	Data Group for QA				
	Study and Population	Study Effects	Exposure Information	Statistical Findings	Senior Review
	<input type="checkbox"/>				
Ahsan et al., 2006	<input type="checkbox"/>				
Bates, 2004	<input checked="" type="checkbox"/>				
Chen et al., 2010 (urinary tract cancer)	<input type="checkbox"/>				
Chen et al., in press	<input type="checkbox"/>				
Chen, 2010	<input checked="" type="checkbox"/>				
Chen, 2010 [diabetes]	<input checked="" type="checkbox"/>				
Ferreccio et al., 2000	<input type="checkbox"/>				
Kwok et al.	<input type="checkbox"/>				
Lamm, 2004	<input checked="" type="checkbox"/>				
Li et al., 2006	<input type="checkbox"/>				
Medrano, 2010	<input type="checkbox"/>				
Meliker et al. 2010	<input type="checkbox"/>				
Smith, 2006	<input checked="" type="checkbox"/>				
Tseng, 1996	<input checked="" type="checkbox"/>				
von Ehrenstein, 2006	<input checked="" type="checkbox"/>				
Wu et. al	<input type="checkbox"/>				
Xia, 2009	<input checked="" type="checkbox"/>				

**Interactive Visual Display Tools to Help
Evaluate Complex Data Sets
(MetaDataViewer/HAWC)**

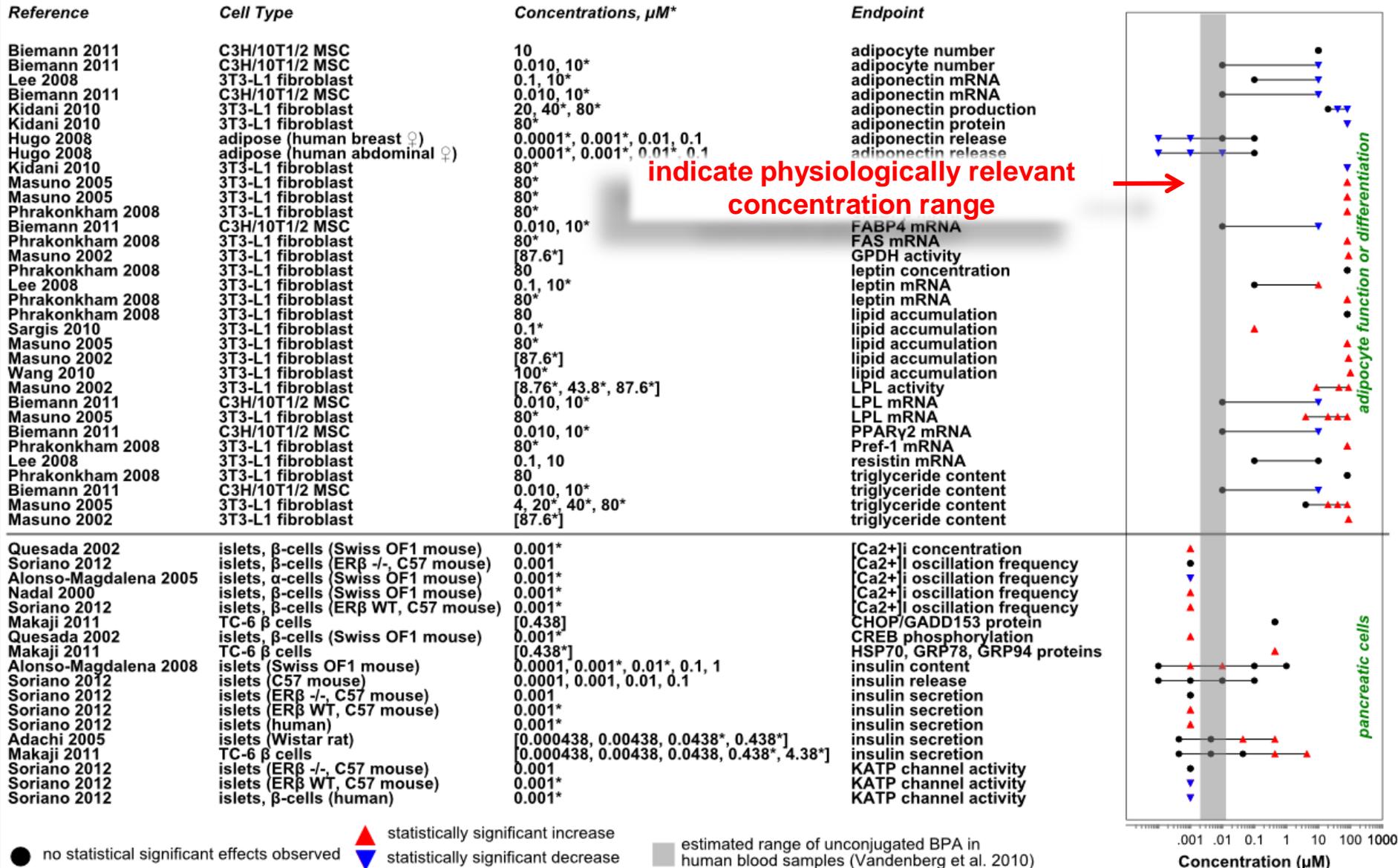
Animal Data



Human Data



In Vitro Data



Current Status & Next Steps

- See <http://ntp.niehs.nih.gov/go/38673> for documents and updates
- Draft OHAT Approach (posted February 2013)
 - Currently applying approach to 2 case-study protocols
 - BPA exposure and obesity
 - PFOA/PFOS exposure and immunotoxicity
 - Host “lessons learned” webinar (Spring/Summer 2014)
- “Beta testing” DRAGON and HAWC
- Working to improve transparency on how we consider other types of data, e.g., *in vitro*, HTS

Acknowledgements

- **Office of Health Assessment and Translation**

- Abee Boyles
- Kembra Howdeshell
- Andrew Rooney, Deputy Director
- Michael Shelby
- Kyla Taylor
- Kristina Thayer, Director
- Vickie Walker

- **Office of Liaison, Policy and Review**

- Mary Wolfe, Director
- Lori White

- **Technical Advisors and Experts**

- **Lisa Bero**, Director, San Francisco Branch, United States Cochrane Center at UC San Francisco
- **Gordon Guyatt**, Co-chair, GRADE Working Group, McMaster University
- **Malcolm Macleod**, CAMARADES Centre, University of Edinburgh
- **Karen Robinson**, Co-Director, Evidence-Based Practice Center, The Johns Hopkins Bloomberg School of Public Health
- **Holger Schünemann**, Co-chair, GRADE Working Group, McMaster University
- **Tracey Woodruff**, Director, Program on Reproductive Health and the Environment, UCSF

- **NTP BSC Working Group**

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