

Intersex wildlife as sentinels for human health and endocrine disruption near Superfund sites: A Systematic Review

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Study Question

Do wildlife in contaminated waters near Superfund sites have a higher prevalence/severity of intersex compared to the same wildlife farther away from Superfund sites?

Scope & Introduction



Superfund Chemicals

- Endocrine disrupting chemicals (EDCs) are long lasting and known to have reproductive and endocrine issues, even at low doses
- EDCs are widespread throughout US waterways at both high and low doses and are long lasting
- Often emitted Superfund Sites (EPA designated toxic waste sites)

Intersex Wildlife

- Wildlife are often used as sentinels for human health
- Intersex (testis contains oocytes/ovotestis) is one metric for endocrine disruption
- Literature has demonstrated a connection between intersex animals and endocrine disrupting chemicals in waterways

Human Health?

- Few links have been between elevated intersex and Superfund sites made but nothing consistent
- A systematic literature review is necessary to examine the link between intersex aquatic animals and highly contaminated Superfund sites.

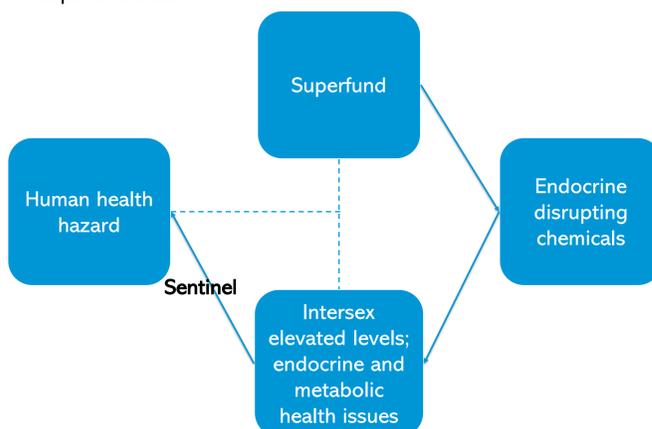


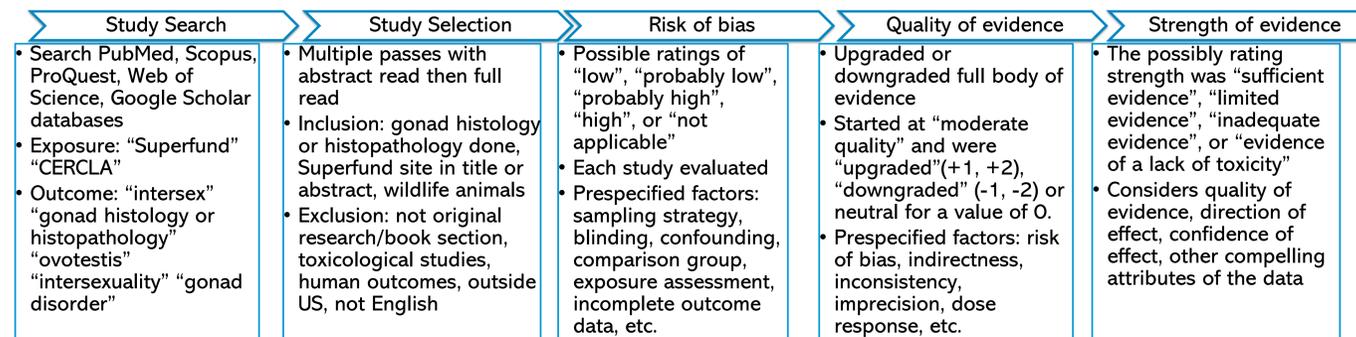
Figure 1. The relationship between Superfund, chemicals, intersex levels, and human health.

PECO Statement

Population	Exposure	Comparator	Outcome
Aquatic and semi-aquatic animals	Close to Superfund site on the waterway	Waterway far from Superfund sites	Prevalence or severity of intersex (ovotestis)

Methods

Based on Navigation Guide (Lam et al 2017) → modified for ecological studies and animal research



Results

First author (year)	Guillette (1994)	Reeder (1998)	Hinck (2004a)	Hinck (2004b)	Schmitt (2004)	Hinck (2006)	La Fiandra (2006)	Baldigo (2006)	Hinck (2007)	Lee Pow (2016)	LaPlaca (2017)	Pinkney (2017)
Species	Alligator	Frogs	Fish	Fish	Fish	Fish	Frogs	Fish	Fish	Fish	Fish	Fish
Location	Central Florida	Illinois	Alaska	NW USA	SW and Central US	SW US	New Hampshire	New York	Alaska	North Carolina	South Carolina	New York
Sample Size	50 eggs	96 juvenile frogs	217 fish	291 fish	386 fish	517 fish	207 total frogs	460 total	158 fish	403 total	60 total	411 total

Figure 2. Final studies, their species, location, and sample size in each study.

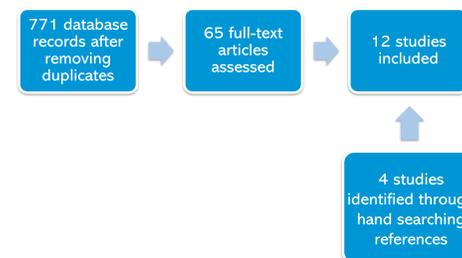


Figure 3. Flow chart of study selection and inclusion.

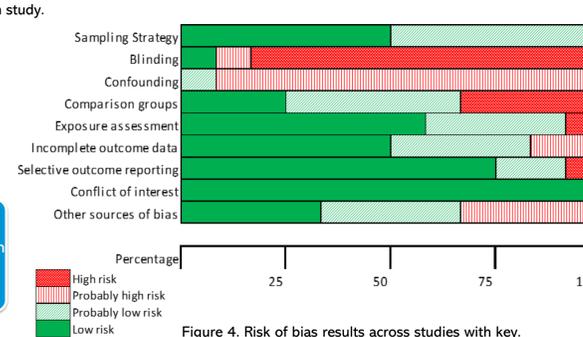


Figure 4. Risk of bias results across studies with key.

- **Quality of evidence: Low**
- Lack of control sites, high risk of confounding and blinding bias
- **Strength of evidence: Limited Evidence**
- Overall small positive relationship trend, no inverse

Discussion

Study Trends

- Studied were throughout the US and ranged from 50 eggs-517 fish
- Fish and amphibians were studied, with fish, specifically largemouth and smallmouth bass, the most frequently studied.
- 4/7 bass papers had significant results or general trend of higher intersex prevalence or severity compared to controls.
- 2/2 frog papers found no difference from the controls; 3/12 had no control comparison site; 2 pike fish species papers found no intersex at all
- 12/12 studies had intersex prevalence as an outcome, 3/12 studies also had intersex severity (from 2016-2017)

Knowledge Gaps

- No standard definition for proximity to a Superfund site
- Unknown background levels of intersex for each species
- Long term impacts of climate change on intersex
- Lack of control sites with surveillance papers

Recommendations

- Standardize methods: gonad histology, severity rankings, etc.
- Establish confounders
- Meta-analysis with current studies by species
- Examine links with certain EDC chemicals from Superfund sites
- Look for studies with human health concern: ex. breast cancer risk in the Great Lakes

Conclusions

Limitations of the systematic literature review

- Exposure of multiple chemicals
- Only English and in US
- Superfund only in title and abstract
- Other endocrine disruption indicators (ex. VTG levels)

Strengths of the systematic literature review

- First looking at this body of evidence
- Multiple animal species
- Strong sampling of evidence
- Clear eligibility criteria
- Ecological application of Navigation Guide

- Limited overall strength of evidence: small positive trend of higher intersex near Superfund sites
- Implications for an indicator of ecological health, watershed health, and human health
- More research is needed: meta-analysis with data from this review, separated by species
 - Should address limitations like adding other disruption indicators and multiple chemical exposures

References

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Acknowledgements & Contact Information

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