

# Literature Scoping and Evidence Mapping Approaches

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# What is a Systematic Evidence Map?

Exposure	Congenital Malformations		Endocrine System		Health Outcomes							Other Outcomes		Grand Total
	Animal	Human	Animal	Human	Growth	Nervous System	Prematurity- Neonatal Out	Reproductive System	Human	Animal	Human			
Evidence Stream														
170HPC	5	13	2		5	30	2	3	21	4		2	1	44
allylestrenol		2	2				3			2		1		10
chlormadinone acetate			1											1
cypoterone acetate	9		3		5		8			6		1		17
desogestrel						1								1
dienogest	1				1									1
ethynodiol diacetate			1				2					2		4
gestodene		4	1		4	1						2		9
levonorgestrel	1	3	3		2	3	2	1		1		1		9
lynestrenol	1	1			1									2
MDAP		1		1										1
megestrol acetate	1													1
MPA	7	4	5		6	5	4	7		4	2	3	1	26
norethindrone	3	2	3		3	1	2			6		1		10
norethindrone acetate	1				1		1			2		1		3
norethynodrel					1									1

- Systematic categorization of published literature
- Utilizes rigorous, objective and transparent methods
- Map key concepts related to a defined topic
  - Exposures
  - Health Outcomes
  - Evidence Stream
- Usually does not include study quality assessment



## Identify the Literature



### Considerations

- Broad search terms
- Focused search terms
- Search multiple databases
- Search single database



## Determine Relevant References



### Considerations

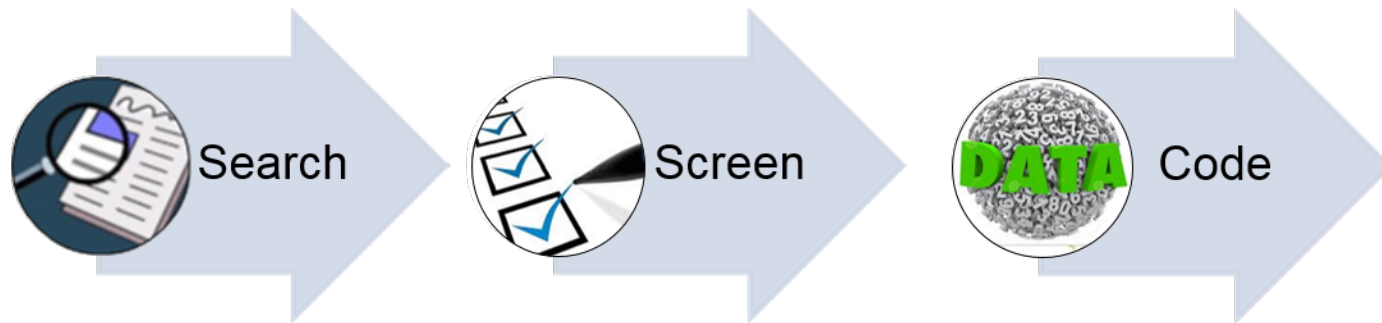
- Utilize active learning algorithms
- References are manually reviewed by 2 independent screeners
  - Title and Abstract
  - Full Text (PDF)

 SWIFT-ACTIVESCREENER

 **DistillerSR**



## Coding of Study Information (Categorization)



### Considerations

- Determine key concepts to inform decisions
  - Evidence stream
  - Exposures
  - Outcomes
- Tiered data coding – (broad vs specific)

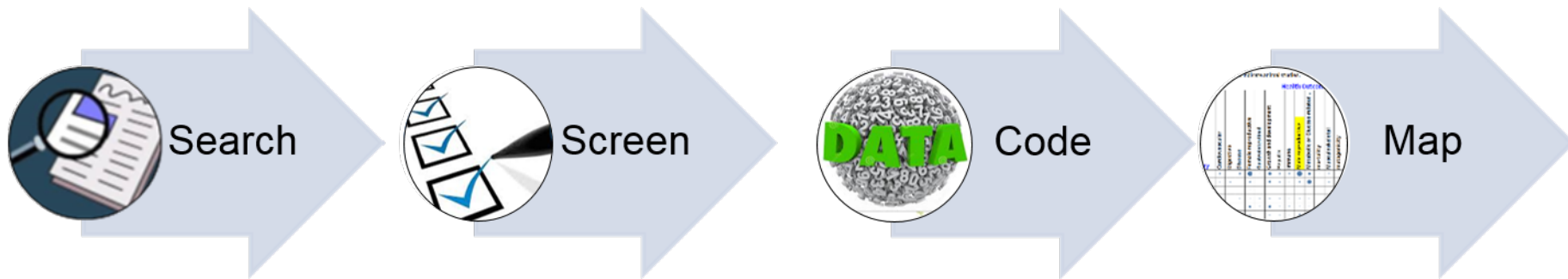
 **DistillerSR**





# Developing an Evidence Map

## Exploration of Study Information



## Considerations

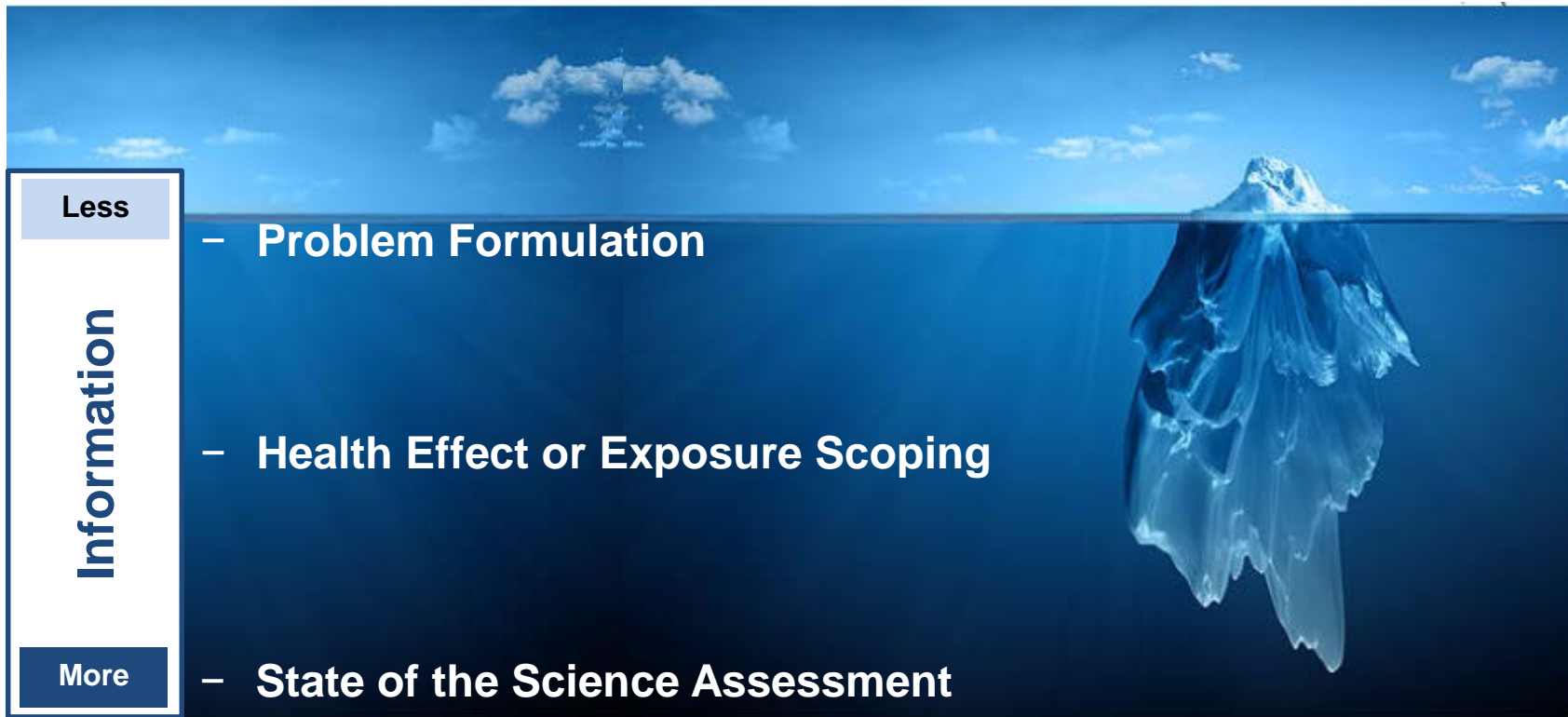
- Map Key concepts to create an interactive visual
- Share and explore data





# Systematic Evidence Maps are Fit for Purpose

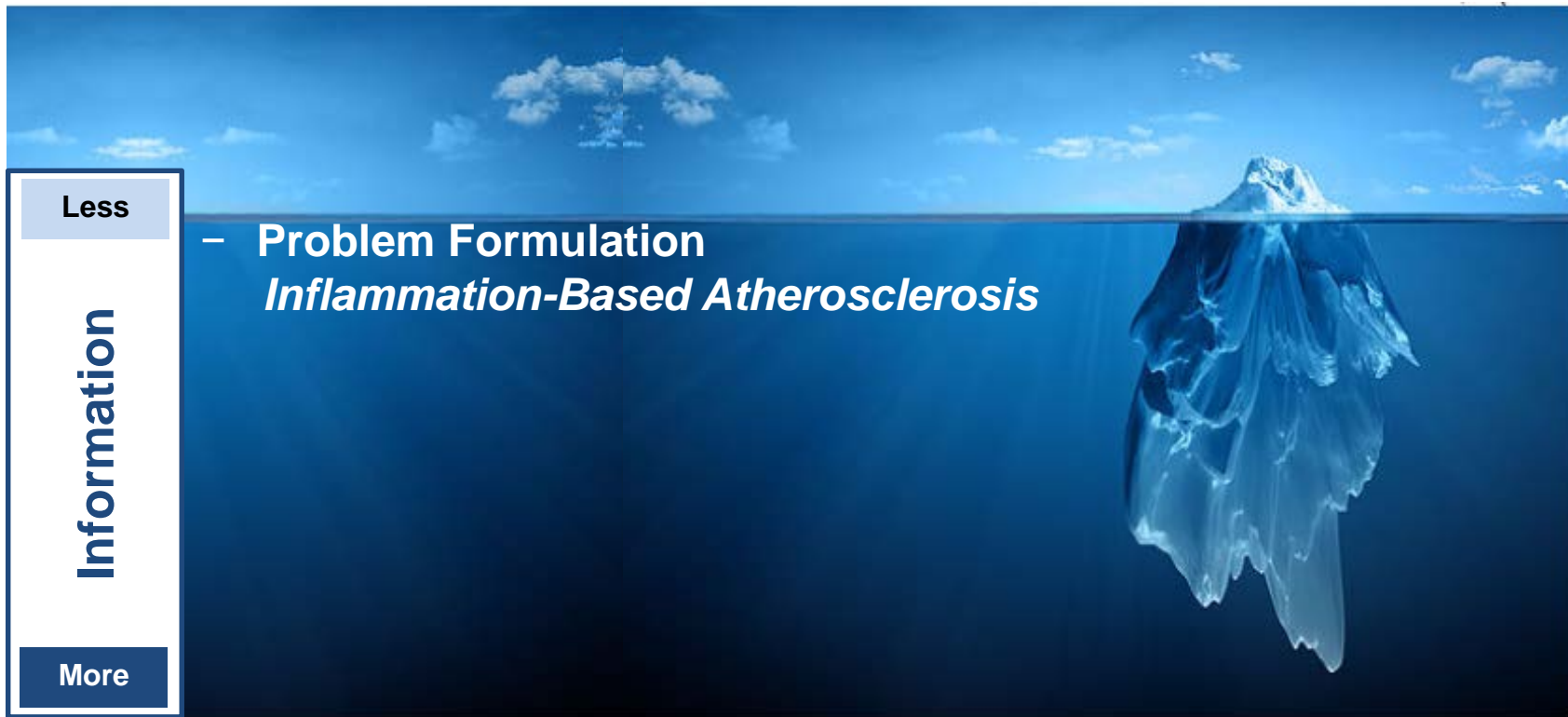
## Depth of Information to Support Decision Depends on Question





# Systematic Evidence Maps are Fit for Purpose

## Depth of Information to Support Decision Depends on Question





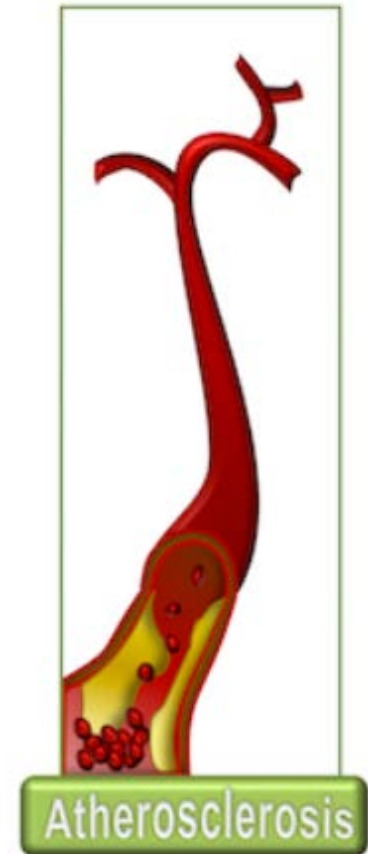


## Inflammation-Based Atherosclerosis

**Question:** Which environmental exposures have been investigated for associations with atherosclerosis?

- **Challenges:**  
Diverse exposures, outcomes, and markers of inflammation
- **Study Information:**
  - Exposures
  - Evaluation of inflammation markers

**Project Objective:** Determine environmental exposure with potential for full systematic review





# Inflammation-Based Atherosclerosis

## Problem Formulation

Support decision to determine systematic review focus

- Environmental exposures
- Key biomarker of inflammation-based atherosclerosis

Broad Exposure	Biomarker		
	C-reactive protein (CRP)	Fibrinogen	Interleukin 6 (IL-6)
Acrolein			
Air Pollution	•	•	•
Asbestos			•
biomass fuels	•		
biomass fuels (cookstove)	•		
cannabis smoking	•		
dioxins	•		•
Environmental Factors (not specified)	•		•
gas metal arc-stainless steel welding fume	•		
indoor smoke	•		
Ionizing Radiation (e.g. x-rays)	•		•
Metals	•	•	•
nicotine	•		•
PCBs	•		•
Polycyclic Aromatic Hydrocarbons (PAHs)	•	•	•
radiographic contrast media		•	
Smoking	•	•	•

Air Pollution

Metals

PAHs

Smoking



# Systematic Evidence Maps are Fit for Purpose

## Depth of Information to Support Decision Depends on Question





## Prenatal Exposure to Progestogens

**Question:** Which prenatal progestogens have been investigated for associations with adverse outcomes in the offspring?

- **Challenges:**  
Multiple progestogens, uses and windows of exposure
- **Study Information:**
  - Exposures
  - Administered use
  - Outcomes
  - Timing of exposure

**Project Objective:** Determine environmental exposure-outcome pair for full systematic review







# Exposures

### FILTER - Exposure Timing

during 1st trimester	27
2nd and/or 3rd trimester only	15
during pregnancy	7
Grand Total	46

# Scoping Review

- Tiered study categorization
- Extent of the evidence

Broad → Specific

		Exposures											
		17OHPG	allylestrenol	hydrogesterone	ethynodiol diacetate	levonorgestrel	lynestrenol	MDAP	MPA	norethindrone	progesterone	progestin	progestogen
Malformation Category	Specific Malformation												
digestive system malformations	rectal-anal atresia												1
	small bowel atresia												1
Down syndrome	Down syndrome												1
genital organ malformations	genital organ malformations	1						1			1	1	
		1	1	1	1		1			1	1	1	1
	inguinal hernia								1				1
	undescended testes								1			1	1
musculoskeletal system malformations	anterior abdominal wall malformations												1
	diaphragmatic hernia												1
	limb deficiencies				1	1							1

Broad → Specific



# Congenital Malformations in Humans

Malformation Category	Specific Malformation	17OHP	allylestrenol	dydrogesterone	ethynodiol diacetate	levonorgestrel	lynestrenol	MDAP	MPA	norethindrone	progesterone	progestin	progestogen
digestive system malformations	rectal-anal atresia												1
	small bowel atresia												1
Down syndrome	Down syndrome												1
genital organ malformations	genital organ malformations							1				1	
	hypospadias	1	1				1						1
	inguinal hernia								1				
	undescended testes								1				
musculoskeletal system malformations	anterior abdominal wall malformations												1
	diaphragmatic hernia												1
	limb deficiencies				1	1							1

## FILTER - Exposure Timing

during 1st trimester	27
2nd and/or 3rd trimester only	15
during pregnancy	7
Grand Total	46

## FILTER - Administration Reason

Contraception	5
Miscarriage or Preterm Birth	11
Miscarriage or Preterm Birth, Contraception, Pregnancy Test	1

## FILTER - Study List

Short Citation	Title
Carmichael (2005)	Maternal progestin intake and risk of hypospadias
Colvin (2010)	Linking a pharmaceutical claims database with a birth defects registry to investigate birth defect rates of suspected teratogens
Coomarasamy (2015)	A Randomized Trial of Progesterone in Women with Recurrent Miscarriages



# Systematic Evidence Maps are Fit for Purpose

Depth of Information to Support Decision Depends on Question







## Transgenerational Inheritance of Health Effects

**Question:** Which exposures and outcomes have been investigated using a transgenerational study design?

- **Challenges:**  
Specific study design; terminology, wide range of exposures and outcomes
- **Study Information:**
  - Exposures
  - Outcomes
  - Study Quality Assessment
  - Full Data extraction



**Project Objective:** Critical analysis on the extent of evidence and sufficiency of evidence for conclusions



# Evidence Map of Transgenerational Studies

Exposure Category	Health Outcome													
	Cardiovascular	Digestive	Disease	Female reproductive	Gastrointestinal	Growth and development	Hepatic	Immune	Male reproductive	Metabolic or Glucose-related ..	mortality	Musculoskeletal	mutagenicity	Neurological and sensory
chemical	•		•	•	•	•	•	•	•	•	•	•	•	•
diet and nutrition	•	•		•		•	•	•	•	•		•		
drugs of abuse				•									•	
mutagenic chemical			•	•	•	•	•	•	•	•		•	•	•
non-chemical stressor	•			•	•	•	•	•	•	•		•	•	•
radiation				•		•	•	•	•			•	•	•

## State of the Science

Map the evidence

- Extent of evidence
- Areas of consistency
- Critical assessment of Exposure + Outcome Pair



# Evidence Map of Transgenerational Studies

Exposure Category	Health Outcome																	
	Cardiovascular	Digestive	Disease	Female reproductive	Gastrointestinal	Growth and development	Hepatic	Immune	Male reproductive	Metabolic or Glucose-related ..	mortality	Musculoskeletal	mutagenicity	Neurological and sensory	Non-reproductive Endocrine	Renal	Reproductive	Respiratory
chemical	•		•	●	•	●	•	•	●	•	•	•	•	●	•	•	•	•
diet and nutrition	•	•		•		•	•	•	•	●		•			•	•		
drugs of abuse				•										•				
mutagenic chemical			•	•	•	•	•	•	•	•		•	•	•	•			
non-chemical stressor	•			●	•	●	•	•	•	•		•	•	●	•		•	
radiation				•		•	•	•	•			•	•	•			•	



### Exposure Category

# Map

# Data Extraction

EXPOSURE or STRESSOR

## OUTCOME

## STUDIES

# High Level Information





## Evidence Maps

- **Support A Wide Range Of Goals**
  - Level of detail and key concepts tailored to fit the question
- **Facilitate evidence synthesis for decision-making**
  - Categorize literature base
  - Support research initiatives
  - Focus resources more efficiently
- **Provide interactive exploration of the data**
  - Illustrates extent of the evidence (study quality and mechanisms)
  - Resource to scientific community and public



- **Solicit Input on Report Format**
  - Scoping review supported by an evidence map
- **Automation**
  - Active screening to reduce screening burden
  - Automate categorization and harmonize with NTP ontology efforts
  - Automate information extraction
- **Workflow Improvements**
  - “Living” scoping report – evidence surveillance
  - Literature analysis to inform hypothesis and research strategy



# NTP

National Toxicology Program

Exposure	Congenital Malformations		Endocrine System		Growth		Nervous System		Prepubertal/Neonatal Onset	Reproductive		Other Outcomes		Grand Total
	Animal	Human	Animal	Human	Animal	Human	Animal	Human	Human	Animal	Human	Animal	Human	
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cyproterone acetate	9		3				8			6		1		17
desogestrel						1								1
dienogest	1				1									1
drospirenone			1				2					2		4
dydrogesterone		4	1				1					2		9
ethynodiol diacetate		2												2
gestodene							1					1		1
levonorgestrel	1	3	3		2	3	2	1		1		1		9
lynestrenol	1	1			1									2
MDAP		1		1										1
megestrol acetate	1													
MPA	7	4	5		6	5	4	7		4	2	3	1	26

Thank you  
Questions?

