

Visual and Ocular Effects

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Level of Evidence Conclusions

- **Animal Studies**

- Initial time period (>24 hours to 7 days): Inadequate level of evidence
- Intermediate time period (8 days to 1 year): Inadequate level of evidence
- Extended time period (>1 year): Inadequate level of evidence

- **Human Studies**

- Initial time period (>24 hours to 7 days): Moderate level of evidence
- Intermediate time period (8 days to 1 year): Moderate level of evidence
- Extended time period (>1 year): Inadequate level of evidence



Animal Data

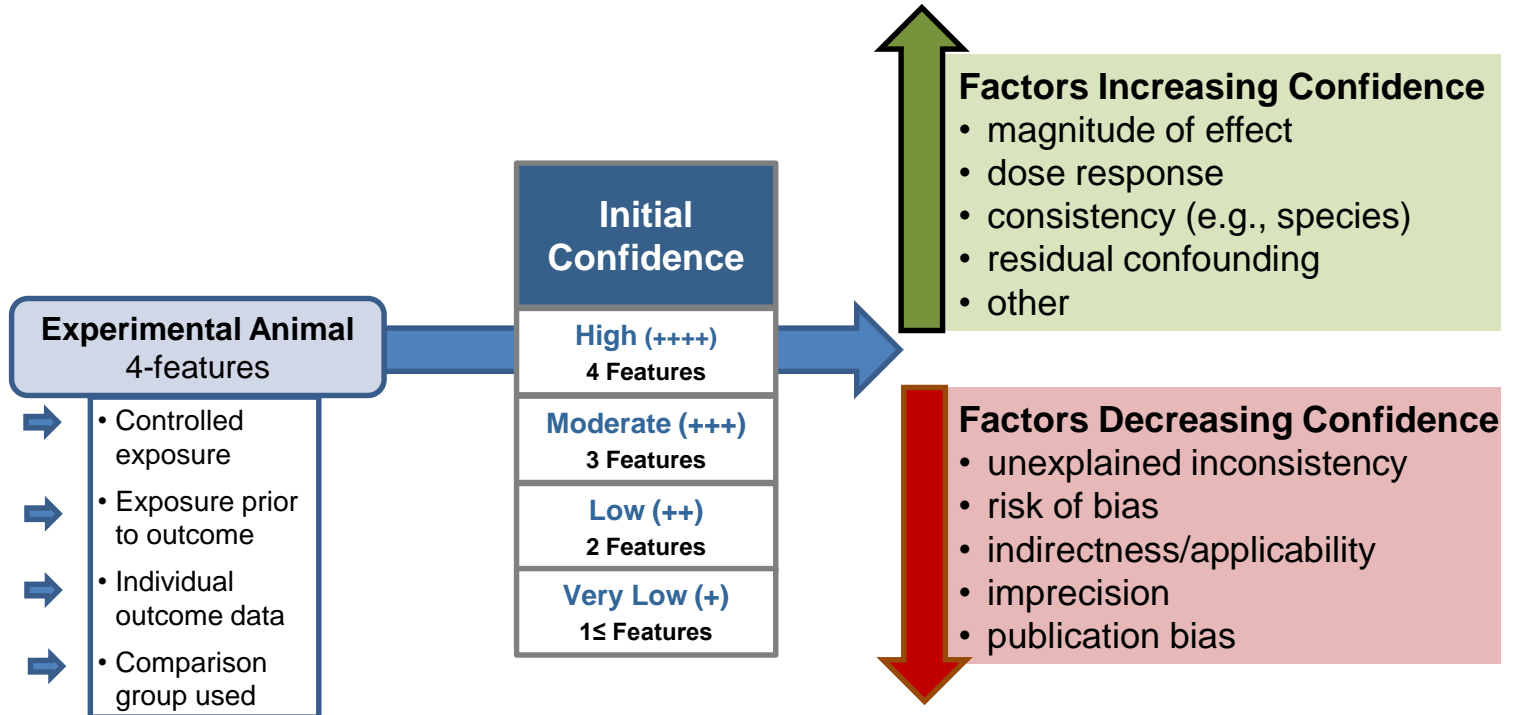
- Bodies of evidence
 - **Initial time period:** 3 studies
 - **Intermediate time period:** 1 study
 - **Extended time period:** 1 study
- Effects:
 - **Initial:** No or inconsistent effects reported
 - No effects on pupil diameter in rats at 1–7 days in 2 studies
 - Increased pupil diameter in rats at 1–7 days in 1 study (Mioduszeewski 2002)
(pattern of effect does not correspond to human data and not clear if it is adverse or reflects recovery)
 - **Intermediate and Extended:** No effects observed
 - No effects on visual functional observational battery scores in 1 study (Kassa 2001)
3–12 months after acute sarin exposure



Confidence Considerations to Support Level of Evidence

Animal – Visual and Ocular Effects

- **Initial time period:** 3 experimental animal studies
- **Intermediate and Extended time periods:** 1 experimental animal study





Confidence Considerations to Support Level of Evidence

Animal – Visual and Ocular Effects

- Factors that decreased confidence

Initial


- Unexplained Inconsistency ↓
 - Inconsistent results (no effect and increase)


**Intermediate
and
Extended**

- Unexplained Inconsistency ↓
 - No ability to evaluate consistency – single study
- Risk of Bias ↓↓
 - Probably high for all 3 key questions (randomization, exposure characterization, and outcome assessment)

- Factors that increased confidence

- No changes for any factors for all 3 time periods

- 
- unexplained inconsistency
 - risk of bias
 - indirectness/applicability
 - imprecision
 - publication bias

- 
- magnitude of effect
 - dose response
 - consistency (e.g., species)
 - residual confounding
 - other



Visual and Ocular Effects

Visual and Ocular Evidence Profile for Sarin

INITIAL CONFIDENCE for each body of evidence (# of studies)	Factors decreasing confidence “---” if no concern; “↓” if serious concern to downgrade confidence					Factors increasing confidence “---” if not present; “↑” if sufficient to upgrade confidence				FINAL CONFIDENCE RATING
	Risk of Bias	Unexplained Inconsistency	Indirectness	Imprecision	Publication Bias	Large Magnitude	Dose Response	Residual Confounding	Consistency Species/Model	
Animal										
Initial period - Initial High (3 mammal studies)	---	↓	---	---	---	---	---	---	---	Moderate
Intermediate period – Initial High (1 mammal study)	↓↓	↓	---	---	---	---	---	---	---	Very Low
Extended period – Initial High (1 mammal study)	↓↓	↓	---	---	---	---	---	---	---	Very Low

- No or inconsistent visual or ocular effects reported > 24 hours following acute sarin exposure
- Overall, **Inadequate to evaluate potential sarin-related effects** at all time periods based on the limited number of studies, risk-of-bias concerns, and no evidence of an effect that corresponds with the human data



Human Data

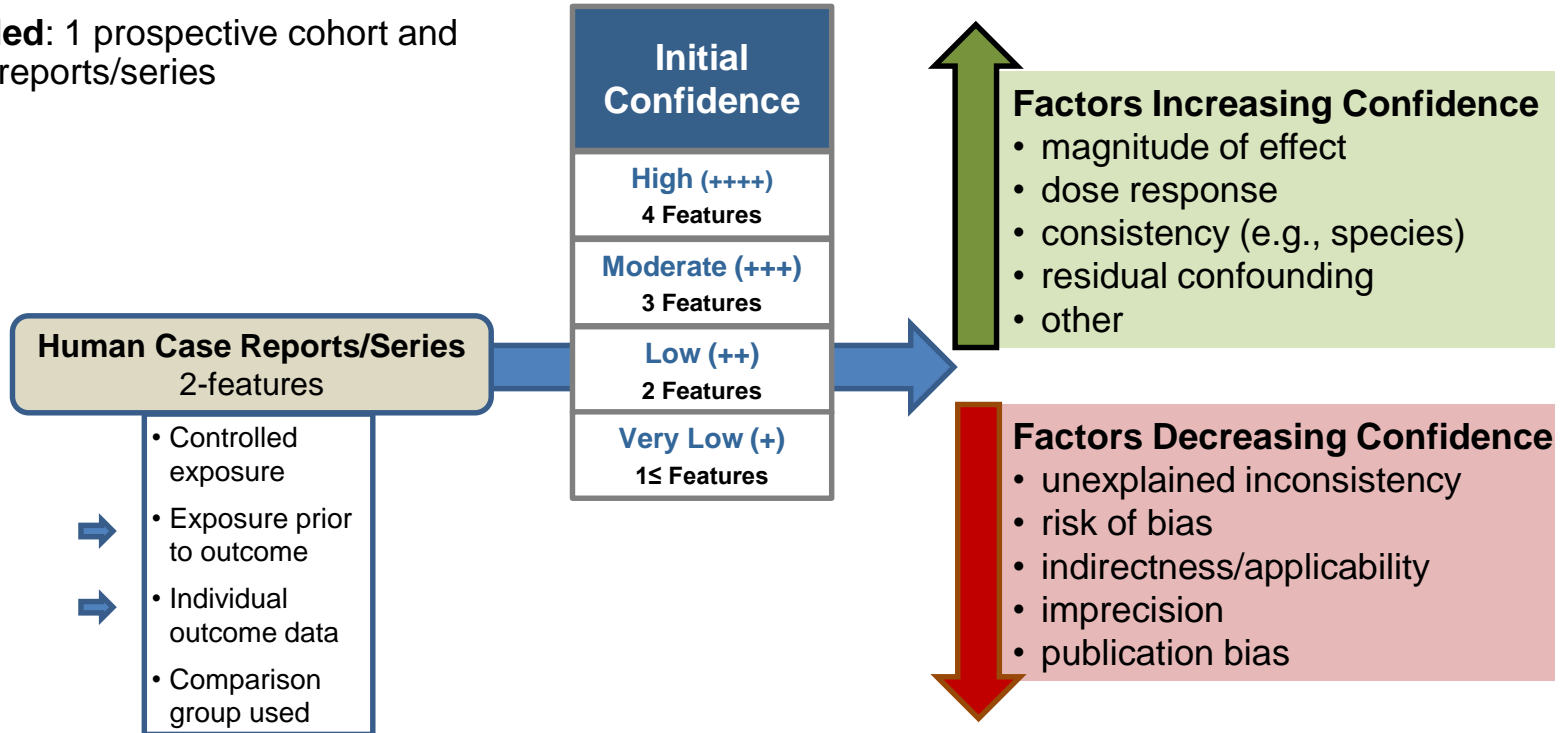
- Bodies of evidence
 - **Initial time period:** 5 case reports/series
 - **Intermediate time period:** 2 cross-sectional studies; 8 case reports/series
 - **Extended time period:** 1 prospective cohort study; 4 case reports/series
- Effects
 - **Initial:** Consistent evidence for pupil constriction (miosis) and evidence of other symptoms (e.g., blurred vision, ocular pain, difficulty focusing) 1–7 days following exposure
 - **Intermediate:** Consistent evidence for pupil constriction for weeks, suggests persistence following exposure; Then, pupil constriction not found at 1-2 months, suggests recovery
 - Slower visual evoked potentials (VEPs) reported at 6-8 months
 - Other symptoms reported in small percentages of subjects for months
 - **Extended:** Some evidence of symptoms in small percentage of study subjects 1–5 years following exposure



Confidence Considerations to Support Level of Evidence

Confidence Conclusions Primarily Based on:

- **Initial:** 5 case reports/series
- **Intermediate:** 2 cross-sectional studies
- **Extended:** 1 prospective cohort and 4 case reports/series

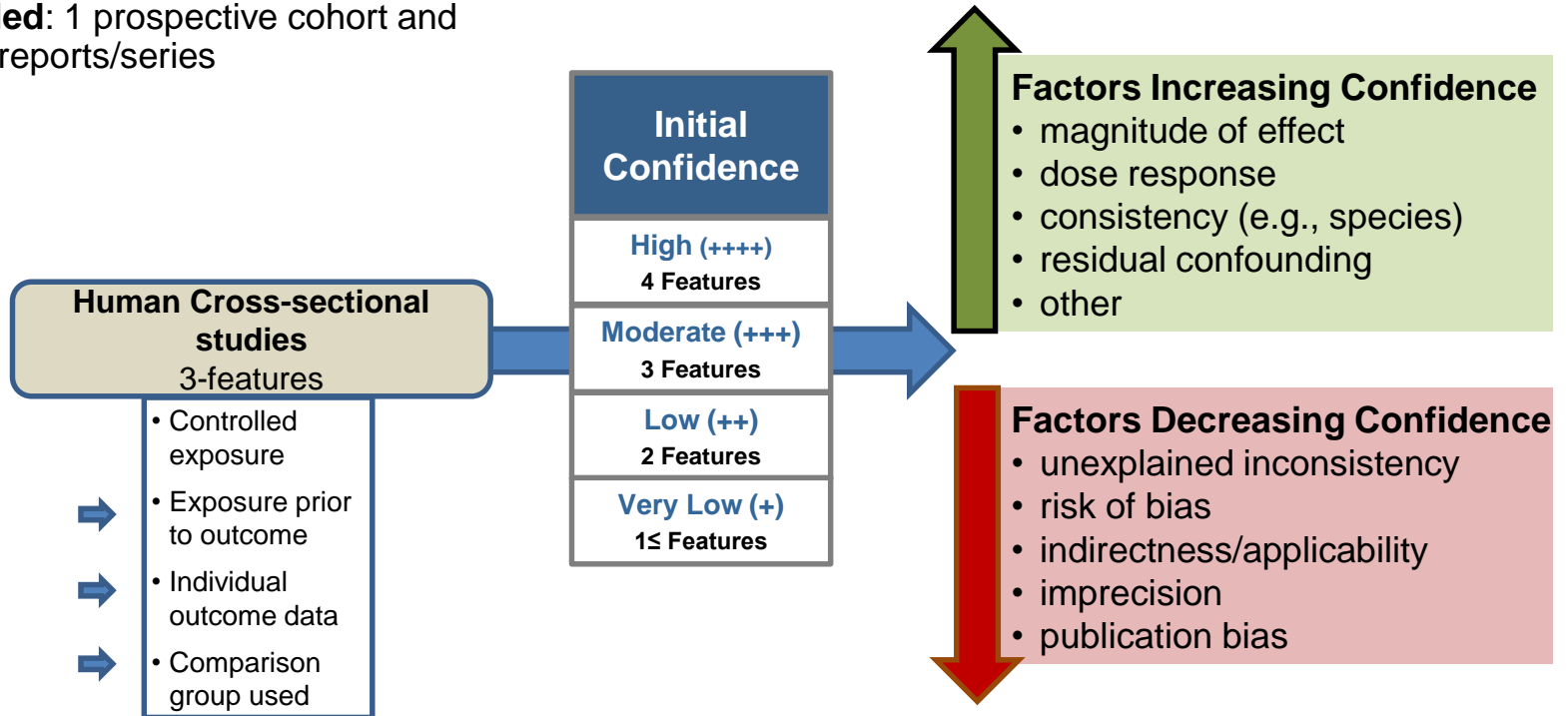




Confidence Considerations to Support Level of Evidence

Confidence Conclusions Primarily Based on:

- **Initial:** 5 case reports/series
- **Intermediate:** 2 cross-sectional studies
- **Extended:** 1 prospective cohort and 4 case reports/series





Confidence Considerations to Support Level of Evidence

Human – Visual and Ocular Effects


- Factors that decreased confidence

Intermediate
and Extended

- Risk of Bias (case reports/series) ↓
 - Probably high for 2 key questions in most studies (confounding and blinding of outcome assessors)

Extended

- Risk of Bias (single prospective cohort) ↓↓
 - Probably high or definitely high for 2 key questions and other serious risk-of-bias concerns


- 
- unexplained inconsistency
 - risk of bias
 - indirectness/applicability
 - imprecision
 - publication bias

- Factors that increased confidence

Initial

- Magnitude of Effect (upgrade considered*)
- Consistency ↑

** Decision to upgrade once based on magnitude of effect and consistency collectively, and supported by well-established response of immediate constriction of the pupils in the first 24 hours following acute sarin exposure*

- 
- magnitude of effect
 - dose response
 - consistency (e.g., species)
 - residual confounding
 - other



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	Risk of Bias	Unexplained Inconsistency	Indirectness	Imprecision	Publication Bias	Large Magnitude	Dose Response	Residual Confounding	Consistency Species/Model	
Human										
Initial period – Initial Low (5 case reports/series)	---	---	---	---	---	---	---	---	↑	Moderate
Intermediate period - Initial Moderate (2 cross-sectional studies)	---	---	---	---	---	---	---	---	---	Moderate
Intermediate period – Initial Low (8 case reports/series)	↓	---	---	---	---	---	---	---	---	Very Low
Extended period – Initial Moderate (1 prospective cohort study)	↓↓	---	---	---	---	---	---	---	---	Very Low
Extended period – Initial Low (4 case reports/series)	↓	---	---	---	---	---	---	---	---	Very Low

- **Moderate confidence** that acute sarin exposure is associated with visual or ocular effects from days to months following exposure
- **Limitations:** Risk-of-bias concerns, uncertainties related to study design for the case reports/series



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Questions?