Grading of Recommendations Assessment, Development and Evaluation (GRADE): Rabies Pre-Exposure Prophylaxis

ACIP WG meeting

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Assumptions made by WG based on background presentations

- Rabies is 100% fatal
- Rabies vaccines are highly efficacious
- Multiple layers of preventing human rabies (e.g., PrEP, animal vaccinations for rabies, PPE while working with rabies virus, PEP)
- Goal of PrEP
  - Recognized exposures: Anamnestic response from PrEP + shortened PEP series
  - Unrecognized exposures: Sustained high titers such that “protection” provided by PrEP alone even if PEP is not administered
- ID data can be used to inform IM recommendations
- Increase in titer cut-off to 0.5 IU/mL has advantages and one potential disadvantage: booster could be indicated for a titer value that would have been considered acceptable in past

Proposed revisions

Risk category	Nature of Risk	Typical Population	Disease Biogeography[‡]	Primary Immunogenicity PrEP	Long-term immunogenicity
#1: Elevated risk for unrecognized and recognized exposures and	Risk of virus exposure is continuous. Exposure is often in high concentrations and may go unrecognized. Direct and indirect exposures.*	Laboratory personnel working with live rabies virus in research, diagnostic, or vaccine production capacities (e.g., necropsy of suspect rabid animal or working with rabies virus cultures)	Laboratory	Goal: Same primary series for 3 risk groups	Goal: Titers at different intervals and potentially for all 3 risk groups
#2: Elevated risk of both unrecognized and recognized exposures	Risk of virus exposure is episodic. Exposure typically recognized but could be unrecognized and is greater than for those in the Infrequent risk group. Direct exposures and rarely indirect exposures	Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entrance to high density bat environments (e.g., bat biologist)	All geographic regions where bats are a reservoir for rabies**		
#3: Elevated risk of recognized exposures	Risk of virus exposure greater than population at large. Exposure is a recognized one. Direct exposures.	Persons who work with animals • Animal care professionals (e.g., veterinarians, technicians, animal control officers) • Others who repeatedly handle terrestrial reservoir species (e.g., wildlife biologists, rehabilitators, and trappers) • Spelunkers • Veterinary students • Short-term / volunteer hands-on animal care workers where increased risk is expected for short time periods*	All geographic regions where terrestrial and non-terrestrial mammals are reservoirs for rabies		
		Travelers who will be performing activities (e.g., occupational or recreational) that put them at increased risk for exposure to rabid dogs and may have difficulty getting access to safe PEP (e.g., in rural area). Children may receive PrEP depending on the country to which they will travel (see CDC Traveler's Health destination pages)*	• Geographic regions internationally with canine rabies		
#4: Low risk of exposure / (i.e., general population)	Risk of virus exposure is uncommon. Bite or non-bite exposure	U.S. population at large	• Nationwide	• No pre-exposure prophylaxis • No serologic monitoring	n/a

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Policy question #1

Should a 2 dose pre-exposure prophylaxis (PrEP) series involving HDCV* or PCECV† IM [0, 7 days] replace the 3 dose series IM [0, 7, 21/28 days] for all those for whom rabies vaccine PrEP is recommended?

*Human diploid cell vaccine
† Purified chick embryo cell vaccine

PrEP policy question #1

	Policy question: Should a two dose pre-exposure prophylaxis (PrEP) series involving HDCV* or PCECV† IM [0, 7 days] replace the 3 dose series IM[0, 7, 21/28 days] for all those for whom rabies vaccine PreP is recommended?
Population	Persons for whom rabies vaccine PrEP is recommended

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Population	Persons for whom rabies vaccine PrEP is recommended
Intervention	[0, 7 days] rabies vaccine PrEP schedule
Comparison	[0, 7, 21/28 days] rabies vaccine PrEP schedule

*Human diploid cell vaccine
† Purified chick embryo cell vaccine

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Population	Persons for whom rabies vaccine PrEP is recommended
Intervention	[0, 7 days] rabies vaccine PrEP schedule
Comparison	[0, 7, 21/28 days] rabies vaccine PrEP schedule
Outcome	

*Human diploid cell vaccine
† Purified chick embryo cell vaccine

Critical outcomes

- Efficacy
  - Primary immunogenicity: Peak immunogenicity after completion of the primary vaccine series (i.e., at 2-4 weeks after completion of the primary series)

- Safety
  - None*

*adverse events were not included as an outcome because these vaccines have a track record for safety over many decades; summary data about the safety was presented from RCTs since the 2008 ACIP publication and also, from VAERS data and showed no change from previous)

PrEP policy question #1

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Population	Persons for whom rabies vaccine PrEP is recommended
Intervention	[0, 7 days] rabies vaccine PrEP schedule
Comparison	[0, 7, 21/28 days] rabies vaccine PrEP schedule
Outcome	Primary immunogenicity

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#2: Elevated risk of both unrecognized and recognized exposures	Risk of virus exposure is episodic. Exposure typically recognized but could be unrecognized and is greater than for those in the Infrequent risk group. Direct exposures and rarely indirect exposures	Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entrance to high density bat environments (e.g., bat biologist)	All geographic regions where bats are a reservoir for rabies**		
#3: Elevated risk of recognized exposures	Risk of virus exposure greater than population at large. Exposure is a recognized one. Direct exposures.	Persons who work with animals • Animal care professionals (e.g., veterinarians, technicians, animal control officers) • Others who repeatedly handle terrestrial reservoir species (e.g., wildlife biologists, rehabilitators, and trappers) • Spelunkers • Veterinary students • Short-term / volunteer hands-on animal care workers where increased risk is expected for short time periods*	All geographic regions where terrestrial and non-terrestrial mammals are reservoirs for rabies		
		Travelers who will be performing activities (e.g., occupational or recreational) that put them at increased risk for exposure to rabid dogs and may have difficulty getting access to safe PEP (e.g., in rural area). Children may receive PrEP depending on the country to which they will travel (see CDC Traveler's Health destination pages)*	• Geographic regions internationally with canine rabies		
#4: Low risk of exposure / (i.e., general population)	Risk of virus exposure is uncommon. Bite or non-bite exposure	U.S. population at large	• Nationwide	• No pre-exposure prophylaxis • No serologic monitoring	n/a

*Direct exposures are bite and non-bite (e.g., contamination of fresh open wound or mucous membranes with saliva), Indirect exposures (i.e. droplet)

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#2: Elevated risk of both unrecognized and recognized exposures	Risk of virus exposure is episodic. Exposure typically recognized but could be unrecognized and is greater than for those in the Infrequent risk group. Direct exposures and rarely indirect exposures	Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entrance to high density bat environments (e.g., bat biologist)	All geographic regions where bats are a reservoir for rabies**	Unrecognized and recognized exposures	
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		Travelers who will be performing activities (e.g., occupational or recreational) that put them at increased risk for exposure to rabid dogs and may have difficulty getting access to safe PEP (e.g., in rural area). Children may receive PrEP depending on the country to which they will travel (see CDC Traveler's Health destination pages)*	• Geographic regions internationally with canine rabies		
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Goal for Unrecognized exposures: Ensure titers are persistently high in case of PEP not being sought

Goal for recognized exposures: Ensure ability to mount an anamnestic response; titers need not be persistently high for anamnestic response

Ideal proposal:

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Long-term immunogenicity ensured through serial monitoring of titers for those at risk of unrecognized exposures

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How do we ensure long-term anamnestic response?

Ensuring long-term immunogenicity for those in risk group #3: titer check

- Data indicates that titer at the 1 year time point is indicative of long-term titers and ability to mount an anamnestic response

- In the absence of data confirming that the [0, 7 days] series, provides immunogenicity many years later, titers at 1 year time point indicate a person's long-term immunogenicity

% SCR2 for each year following a 1 year booster for a 2-dose HDCV primary series

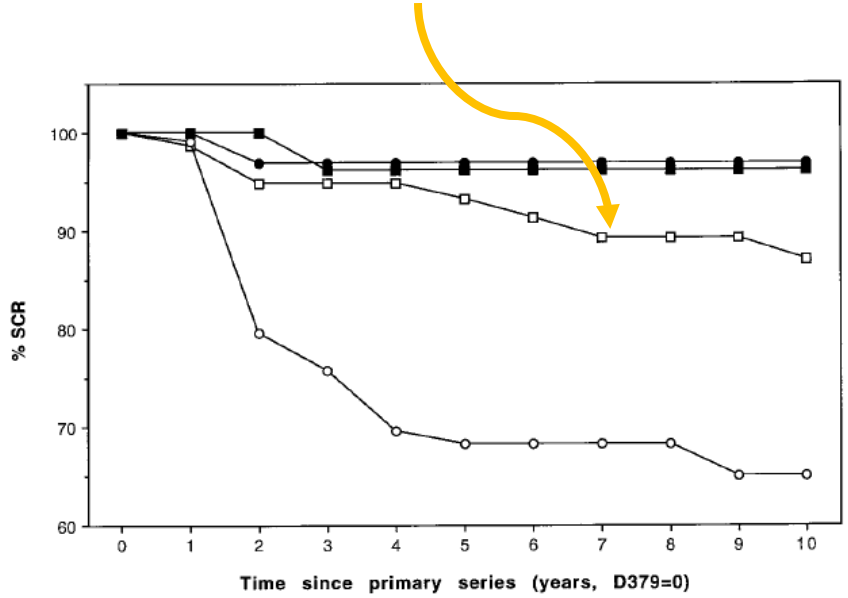

Figure: Evolution of seroconversion rate (% SCR) from day 379 (2 weeks after 1 year booster) to year 10

New data for titer check

- Data included in GRADE analysis shows primary immunogenicity is at least up to 3 years
- Taken together, WG felt titer value at any point during 1-3 years could be checked once to ensure long-term immunogenicity
- Booster is recommended if titers <0.5 IU/mL at the titer check
- No further titer checks indicated because persons in this risk group have only recognized exposures

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Long-term immunogenicity ensured through serial monitoring of titers for those at risk of unrecognized exposures

- WG concerned that population not previously accustomed to getting titer check for rabies PrEP may not do so
- Option for booster as an alternative to titer

Policy question #2

Should an IM booster dose of rabies vaccine (*PCECV or †HDCV) be recommended as an alternative to a titer check no sooner than day 21 and no later than 3 years after the two-dose pre-exposure (PrEP) series IM [0, 7 days] for those in the #3 risk category who receive PrEP?

*Human diploid cell vaccine
† Purified chick embryo cell vaccine

PrEP policy question #2

	Policy question: Should an IM booster dose of rabies vaccine (*PCECV or †HDCV) be recommended as an alternative to a titer check no sooner than day 21 and no later than 3 years after the two dose pre-exposure prophylaxis (PrEP) series IM [0, 7 days] for those in the #3 risk category of people who receive PrEP?
Population	Persons in #3 risk category
Intervention	6-12 months rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Comparison	No rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Outcome	Duration of effectiveness of immunogenicity

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Population	Persons in the #3 risk category for whom rabies vaccine PrEP is recommended
Intervention	Day 21- year 3 rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Comparison	No rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule

Outcome Duration of effectiveness of immunogenicity

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Population	Persons in the #3 risk category for whom rabies vaccine PrEP is recommended
Intervention	Day 21- year 3 rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Comparison	No rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Outcome	

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† Purified chick embryo cell vaccine

Critical outcomes

- Efficacy
  - Long-term immunogenicity (i.e., ability to mount an anamnestic response in response to a challenge like a rabies virus exposure or a booster dose of vaccine)

- Safety
  - None*

*adverse events were not included as an outcome because these vaccines have a track record for safety over many decades; summary data about the safety was presented from RCTs since the 2008 ACIP publication and also, from VAERS data and showed no change from previous)

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Population	Persons in the #3 risk category for whom rabies vaccine PrEP is recommended
Intervention	Day 21- year 3 rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Comparison	No rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Outcome	Long-term immunogenicity

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Evidence Retrieval

- Literature search of multiple biomedical and interdisciplinary bibliographic databases including: Medline, Embase, Cochrane Library, and WHO Index Medicus
- A broad and rigorous strategy incorporating terms related to the concept of pre-exposure vaccination against rabies virus using HDCV or PCECV vaccines
- Search was limited to 1965-2018 and without language restrictions to identify potentially relevant studies
- Results were compiled in an Endnote Library and duplicate records were removed
- Search updated through December 31, 2019 to screen recent records not captured in the original search

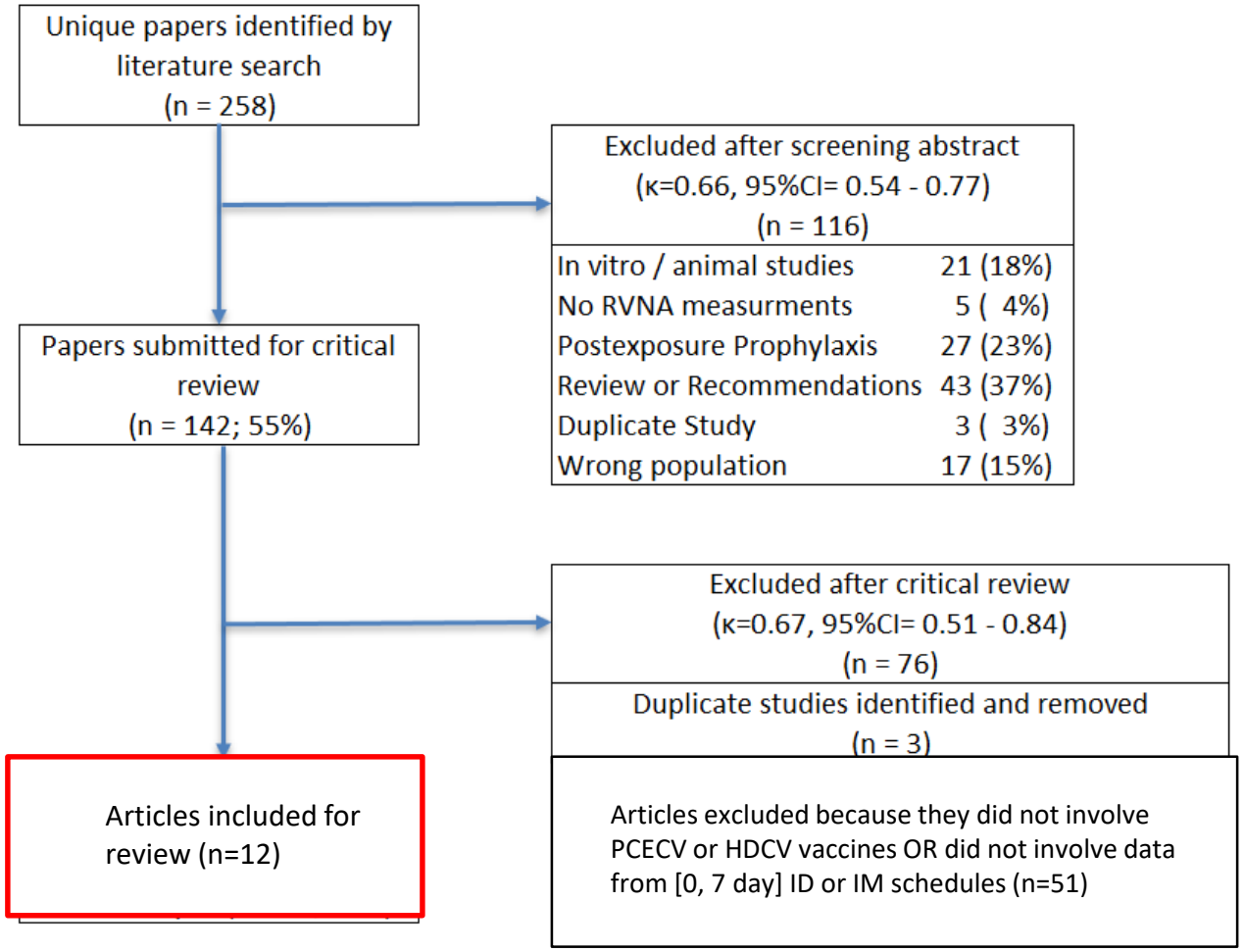
Evidence Retrieval

Records were included if they presented data on human rabies vaccines **and**:

- Involved immunocompetent adults 18 years of age or older[a]
- Included data for intervention of interest (HDCV or PCECV rabies vaccine, pre-exposure, intradermal [1-site or 2 site] or intramuscular [1-site], any PFU)
- Included data relevant to the outcome measures being assessed
- Planned categorization of primary data into comparative or single-arm studies; randomized control trials, prospective or retrospective cohort, case-control, cross-sectional studies [b]

a. Data from animal or *in vitro* studies or data from humans <18 years of age were excluded
b. Records that did not provide primary data (e.g. literature reviews or summaries, editorials, commentaries, opinions, clinical trial registries or protocols) and case reports or case studies were excluded

Study Selection



GRADE Evidence Assessment Criteria

- **Initial evidence type (certainty level) determined by study design**
  - Initial evidence type 1 (high certainty): A body of evidence from randomized controlled trials
  - Initial evidence type 3 (low certainty): A body of evidence from observational studies
- **Risk of bias:** Can include failure to conceal allocation, failure to blind, loss to follow-up. Risk of bias may vary across outcomes.
- **Inconsistency:** Criteria for evaluating include similarity of point estimates, extent of overlap of confidence intervals, and statistical criteria including tests of heterogeneity and I^2
- **Indirectness:** Considers the generalizability of the evidence to the original PICO components (i.e. pre-exposure immunization in the U.S. population)
- **Imprecision:** Considers the fragility of the relative and absolute effect measures based on the interpretation of the 95% CIs and the optimal information size.
- **Other considerations:** Includes publication bias or indications of dose-response gradient, large or very large magnitude of effect, and opposing residual confounding.

Overall evidence types (Certainty levels)

- **Type 1 (high certainty):** We are very confident that the true effect lies close to that of the estimate of the effect.
- **Type 2 (moderate certainty):** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- **Type 3 (low certainty):** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- **Type 4 (very low certainty):** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Not measuring how well the individual studies were conducted, but how much confidence we have in the estimates of effect across each outcome

Evidence Profile Notes

- GRADE was conducted as it pertains to the specific population, intervention, comparison, and outcome (PICO) of interest
- Randomized control trial (RCT) refers to a trial which randomizes participants to an active intervention or a placebo or unvaccinated comparator arm
- Observational studies (Obs) refer to one-arm studies, studies for whom participants were not randomized, or studies that did not provide disaggregated data to allow for the comparison between randomized arms
- Evidence was considered observational if only data from the study arm(s) involving one of the 2 US vaccines were included

Outcome for PrEP policy question #1

Table 1: PrEP policy question #1

	Policy question: Should a two dose pre-exposure prophylaxis (PrEP) series involving HDCV* or PCECV† IM [0, 7 days] replace the 3 dose series IM[0, 7, 21/28 days] for all those for whom rabies vaccine PrEP is recommended?
Population	Persons for whom rabies vaccine PrEP is recommended
Intervention	[0, 7 days] rabies vaccine PrEP schedule
Comparison	[0, 7, 21/28 days] rabies vaccine PrEP schedule
Outcome	Primary immunogenicity

*Human diploid cell vaccine
† Purified chick embryo cell vaccine

PrEP Policy Question #1

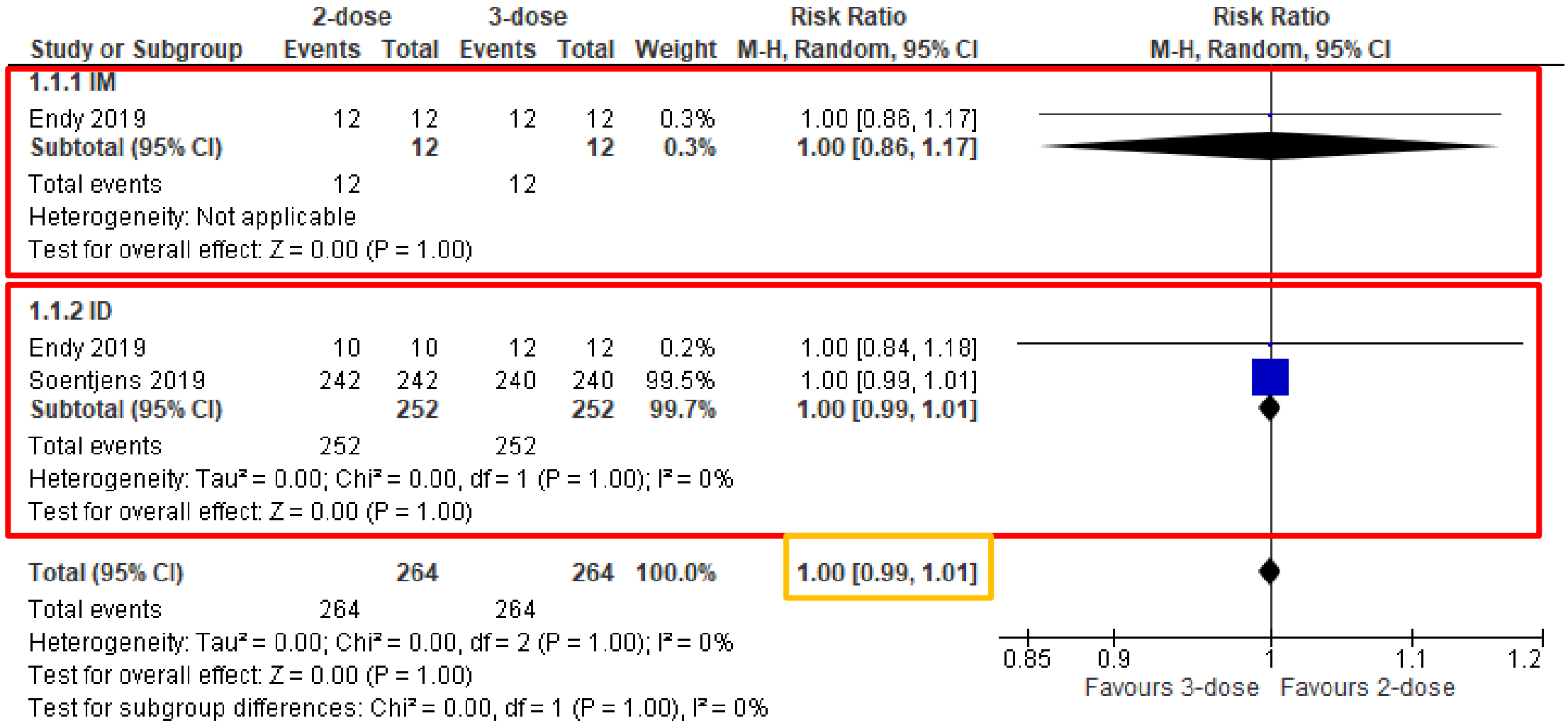
Table 3a: Summary of Randomized Control Trial Studies Reporting Outcome

Authors last name, pub year	Age (years)	N intervention	N comparison	Vaccine	Risk Ratio [95% CI]	Study limitations (Risk of Bias)
Endy, 2019	Mean 32.4, Range 18 - 59	22	24	PCEC, IM, ID	1.00 [0.89, 1.12]	Some concerns[1]
Soentjens, 2019	Median 29.0, Range NR	242	240	HDCV, ID	1.00 [0.99, 1.01]	Some concerns[2]

[1]Allocation concealment not reported. Study did not blind participants or healthcare personnel; however, unlikely that co-interventions would have influenced the outcome.

[2]Method of randomization and allocation not reported. Study did not blind participants or healthcare personnel; however, unlikely that co-interventions would have influenced the outcome.

Forest plot for two RCTs



PrEP Policy Question #1

Table 3b: Summary of Observational Studies Reporting Outcome

Authors last name, pub year	Age (years)	N intervention	N comparison	Vaccine	Risk Ratio [95% CI][1]	Study limitations (Study quality[2])
Ajjan, 1989	Mean 22, Range 19-41	72	69	HDCV, IM	1.00 [0.97, 1.03]	9/9 No concerns
Arora, 2004	Mean 26.2, NR	44	44	HDCV, IM	1.00 [0.96, 1.04]	9/9 No concerns
Briggs, 1996	NR	146	146	HDCV, IM	1.00 [0.99, 1.01]	9/9 No concerns
Cramer 2016	Mean 36.7, SD 12.9	371	364	PCEC, IM	0.99 [0.98, 1.01][4]	7/9 Minimal concerns
Hacibektasoglu, 1992	Mean 20, Range 18 - 24	30	30	HDCV, IM	0.90 [0.79, 1.03]	9/9 No concerns
Jaijaroensup, 1999	NR, Range 17 - 22	138	129	PCEC, IM, ID	0.94 [0.87, 1.02][4]	9/9 No concerns
Kitala, 1990	NR	37	37	HDCV, IM	1.00 [0.95, 1.05]	8/9 Minimal concerns
Recuenco, 2017	Median 41.0, Range 20 - 62	60	59	PCEC, IM, ID	1.00 [0.96, 1.05][4]	9/9 No concerns
Sabchareon, 1999	Mean 10, SD 1.3[3]	190	190	HDCV, IM	1.00 [0.99, 1.01]	7/9 Minimal concerns
Vodopija, 1986	NR	49	46	HDCV, PCEC, IM	1.00 [0.94, 1.06][4]	9/9 No concerns

[1]Data from observational studies, where intervention and comparison data were taken from the same people at different time points, were analyzed using M-H Risk Ratio random effects procedure. Due to unavailable raw data on pairing, a matched analysis was not possible.

[2]Study quality for observational studies was assessed using the Newcastle Ottawa Scale.

[3]Age for total study population was not reported in this paper. Numbers in this cell are from the study arm from which data were extracted.

[4]Studies contained multiple arms relative to the analysis. Risk ratio reflects pooled analysis from eligible arms.

Forest plot for 10 observational studies

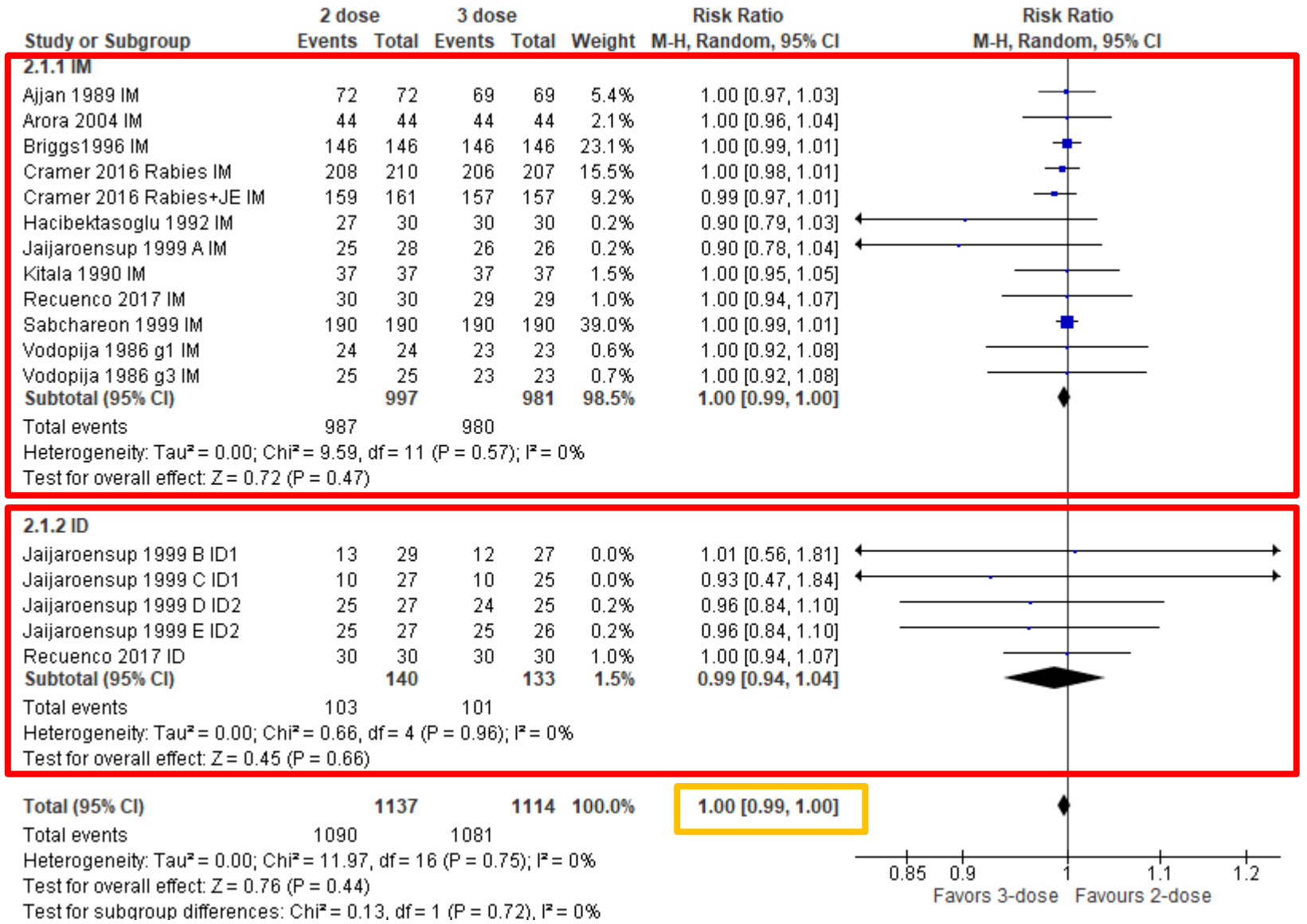


Table 4: Evidence table

Immunogenicity after [0, 7 days] PrEP series with HDCV or PCECV

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[0, 7 days] rabies vaccine PrEP schedule	[0, 7, 21/28 days] rabies vaccine PrEP schedule	Relative (95% CI)	Absolute (95% CI)		
Immunogenicity (RCTs) (follow up: range 2 weeks to 3 weeks; assessed with: titer level above 0.5)												
2 [1,2]	randomized trials	serious [a]	not serious	not serious	not serious	none	264/264 (100.0%)	264/264 (100.0%)	**RR 1.00** (0.99 to 1.01)	**0 fewer per 1,000** (from 10 fewer to 10 more)	Level 2	CRITICAL
Immunogenicity (observational studies) (follow up range: 2 to 3 weeks, assessed with titer level above 0.5)												
10 [3,4,5,6,7,8,9,10,11,12]	observational studies	not serious	not serious	not serious [b]	not serious	none	1090/1137 (95.9%)	1081/1114 (97.0%)	**RR 1.00** (0.99 to 1.00)	**0 fewer per 1,000** (from 10 fewer to 0 fewer)	Level 3	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Method of randomization and allocation not reported in Soentjens 2019 and allocation concealment not reported in Endy 2019. Neither study blinded participants or healthcare personnel; however, unlikely that co-interventions would have influenced the outcome.

b. Sabchareon 1999 study was conducted among children and the response may be more robust than in adults, which would potentially overestimate the immune response.

Table 4: Evidence table

Immunogenicity after [0, 7 days] PrEP series with HDCV or PCECV

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[0, 7 days] rabies vaccine PrEP schedule	[0, 7, 21/28 days] rabies vaccine PrEP schedule	Relative (95% CI)	Absolute (95% CI)		
Immunogenicity (RCTs) (follow up: range 2 weeks to 3 weeks; assessed with: titer level above 0.5)												
2 [1,2]	randomized trials	serious [a]	not serious	not serious	not serious	none	264/264 (100.0%)	264/264 (100.0%)	**RR 1.00** (0.99 to 1.01)	**0 fewer per 1,000** (from 10 fewer to 10 more)	Level 2	CRITICAL
Immunogenicity (observational studies) (follow up range: 2 to 3 weeks, assessed with titer level above 0.5)												
10 [3,4,5,6,7,8,9,10,11,12]	observational studies	not serious	not serious	not serious [b]	not serious	none	1090/1137 (95.9%)	1081/1114 (97.0%)	**RR 1.00** (0.99 to 1.00)	**0 fewer per 1,000** (from 10 fewer to 0 fewer)	Level 3	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Method of randomization and allocation not reported in Soentjens 2019 and allocation concealment not reported in Endy 2019. Neither study blinded participants or healthcare personnel; however, unlikely that co-interventions would have influenced the outcome.

b. Sabchareon 1999 study was conducted among children and the response may be more robust than in adults, which would potentially overestimate the immune response.

Table 4: Evidence table

Immunogenicity after [0, 7 days] PrEP series with HDCV or PCECV

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[0, 7 days] rabies vaccine PrEP schedule	[0, 7, 21/28 days] rabies vaccine PrEP schedule	Relative (95% CI)	Absolute (95% CI)		
Immunogenicity (RCTs) (follow up: range 2 weeks to 3 weeks; assessed with: titer level above 0.5)												
2 [1,2]	randomized trials	serious [a]	not serious	not serious	not serious	none	264/264 (100.0%)	264/264 (100.0%)	**RR 1.00** (0.99 to 1.01)	**0 fewer per 1,000** (from 10 fewer to 10 more)	Level 2	CRITICAL
Immunogenicity (observational studies) (follow up range: 2 to 3 weeks, assessed with titer level above 0.5)												
10 [3,4,5,6,7,8,9,10,11,12]	observational studies	not serious	not serious	not serious [b]	not serious	none	1090/1137 (95.9%)	1081/1114 (97.0%)	**RR 1.00** (0.99 to 1.00)	**0 fewer per 1,000** (from 10 fewer to 0 fewer)	Level 3	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Method of randomization and allocation not reported in Soentjens 2019 and allocation concealment not reported in Endy 2019. Neither study blinded participants or healthcare personnel; however, unlikely that co-interventions would have influenced the outcome.

b. Sabchareon 1999 study was conducted among children and the response may be more robust than in adults, which would potentially overestimate the immune response.

Outcome for PrEP policy question #2

PrEP policy question #2

	Policy question: Should an IM booster dose of rabies vaccine (*PCECV or †HDCV) be recommended as an alternative to a titer check no sooner than day 21 and no later than 3 years after the two dose pre-exposure prophylaxis (PrEP) series IM [0, 7 days] for those in the #3 risk category of people who receive PreP?
Population	Persons in the #3 risk category for whom rabies vaccine PrEP is recommended
Intervention	Day 21- year 3 rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Comparison	No rabies vaccine booster after [0, 7 days] rabies vaccine PrEP schedule
Outcome	Long-term immunogenicity

*Human diploid cell vaccine

† Purified chick embryo cell vaccine

PrEP Policy Question #2

Table 3: Summary of Studies Reporting Outcome

Authors last name, pub year	Age (years)	N intervention	N comparison	Comparator vaccine	Risk Ratio [95% CI]	Study limitations (Study quality[3])
Endy, 2019	Mean 32.4, Range 18 - 59	20	No comparison[1]	PCEC, IM	Not able to calculate[2]	8/9 Minimal concerns
Soentjens, 2019	Median 29.0, NR	183	No comparison[1]	HDCV, IM	Not able to calculate[2]	8/9 Minimal concerns

[1]No comparison data available for this policy question available in these studies.

[2]No comparison data available to calculate effect estimate.

[3]Study quality for observational studies was assessed using the Newcastle Ottawa Scale.

Table 4: Evidence table

Duration of immunogenicity after [0, 7 days] PrEP series with HDCV or PCECV

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Anamnestic response after booster (follow up: range 1 weeks to 3)									
2 [1,2]	observational studies	not serious	not serious	not serious	not serious	none	A historical control of trial participants receiving 2 doses of rabies vaccine resulting in 100% immunogenicity (n=264) at 1-3 weeks following vaccination schedule (Endy 2019, Soentjens 2019) : 203/203 (100%) seroconverstion with booster	Level 3	CRITICAL

CI: Confidence interval

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Thank you

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