Summary of Evidence to Recommendations Framework for Rabies Pre-Exposure Prophylaxis Vote

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Advisory Committee on Immunization Practices

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Recommendations passed

- ACIP recommends a 2-dose [0, 7 days] intramuscular rabies vaccine series in immunocompetent persons ≥18 years of age for whom rabies vaccine pre-exposure prophylaxis (PrEP) is indicated
- ACIP recommends an intramuscular booster dose of rabies vaccine, as an alternative to a titer check, for immunocompetent persons ≥ 18 years of age who have sustained and elevated risk for only recognized rabies exposures (i.e., those in risk category #3 of rabies PrEP recommendations table[*]). The booster dose should be administered no sooner than day 21 but no later than 3 years after the 2-dose PrEP series

[**]Risk category table in next slide

Risk category	Nature of Risk	Typical Population	Disease Biogeography[1]	Primary Immunogenicity PrEP	Long-term immunogenicity
#1: Elevated risk for unrecognized and recognized exposures including unusual / high risk exposures (e.g., aerosol exposures and high concentration rabies virus exposures)	Risk of virus exposure is continuous. Exposure is often in high concentrations and may go unrecognized, and can be unusual (e.g., aerosolized virus).	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	IM [0, 7 days]	Titers every 6 months (booster if titer <0.5 IU/mL)
#2: Elevated risk of both unrecognized and recognized exposures	Risk of virus exposure is episodic. Exposure typically recognized but could be unrecognized. Unusual exposures do not occur	Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entry into high density bat environments (e.g., bat biologist)	All geographic regions where bats are a reservoir for rabies[2]	IM [0, 7 days]	Titers every 2 years (booster if titer <0.5 IU/mL)
#3: Elevated risk of recognized exposures that is sustained	Risk of virus exposure greater than for population at large. Exposure is a recognized one.	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	All geographic regions where terrestrial[3] and non-terrestrial mammals are reservoirs for rabies	IM [0, 7 days]	Titer once at 1-3 years (booster if titer <0.5 IU/mL) **OR** Booster no sooner than day 21 and no later than year 3.
		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 endemic rabies		
#4: Elevated risk of recognized exposures that is not sustained (i.e., ≤ 3 years)	Risk of virus exposure greater than for population at large. Exposure is a recognized one and only present for up to 3 years after primary vaccination	Same as for #3 but with risk ≤ 3 years (e.g., short-term volunteer providing hands-on animal care or a traveler with no risky travel planned beyond 3 years	Same as for #3	IM [0, 7 days]	None
#5: 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	None	None

[1]For questions about the disease biogeography of the region where an exposure occurred, please contact your local or state health department

[2]Bats are reservoirs for rabies in all US states except Hawaii

[3]Terrestrial mammals are non-bat species (e.g., racoons, skunks, livestock)

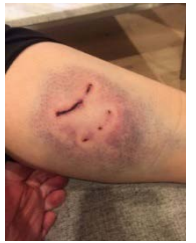
Proposed recommendations for June ACIP vote

- ACIP recommends a 2-dose [0, 7 days] intramuscular rabies vaccine series in immunocompetent persons <18 years of age for whom rabies vaccine pre-exposure prophylaxis (PrEP) is indicated
- ACIP recommends an intramuscular booster dose of rabies vaccine, as an alternative to a titer check, for immunocompetent persons < 18 years of age who have sustained and elevated risk for only recognized rabies exposures (i.e., those in risk category #3 of rabies PrEP recommendations table*). The booster dose should be administered no sooner than day 21 but no later than 3 years after the 2-dose PrEP series

*Risk category table in previous slide

PrEP in children

- Most common reason: Travel to canine rabies endemic countries
  - RIG is not available in some developing countries
  - Rabies vaccines may only be available in capital city resulting in a delay to PEP administration if travel is to rural regions
  - Children are at increased risk of multiple and severe bites including to face and neck



- Costs: PrEP for travel is typically paid out-of-pocket and can be costly because the 2008 ACIP PrEP schedule recommends 3 doses of vaccine over the course of 21-28 days

Estimated* PrEP use in the United States

- Doses: 170,000 including 500 booster doses
- Categories of people receiving PrEP: 60,535 / year
  - Travelers and “other risk groups”: 41,117
  - Veterinary technicians: 13,860
  - Veterinary students: 3,500
  - Animal control: 1,178
  - Rabies laboratory personnel: 480
  - Wildlife biologists: 400

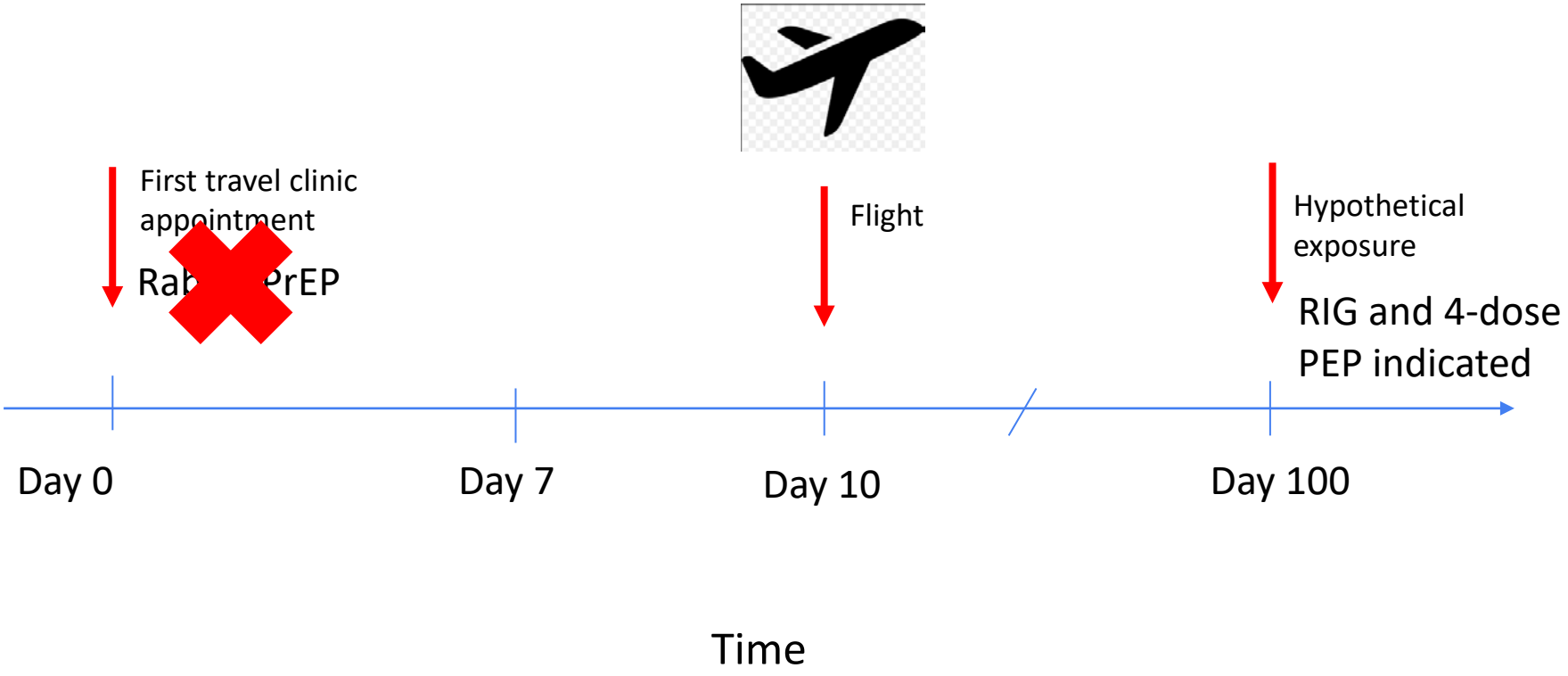
* Mathematical model based on workforce statistics produced by Bureau of Labor Statistics and market research provided by Bavarian Nordic

Conclusions from presentation about rabies PrEP and children during May ACIP meeting

- Primary immunogenicity
  - No difference between primary immunogenicity in children compared to adults for any given schedule
  - One observational study included in GRADE table for 2-dose series showed 190 (100%) children aged 5-13 years mounted titers ≥ 0.5 IU/mL cut-off after primary series

- Long-term immunogenicity
  - Titers in children may stay higher for longer
  - Since boostability is not a concern for adults, it should not be a concern for children

Impact of 3-dose series on PrEP administration



Impact of 2-dose series* on PrEP administration

First travel clinic appointment

Dose 1
Rabies PrEP

Dose 2
Rabies PrEP

Flight

Hypothetical exposure

2-dose PEP indicated

Day 0

Day 7

Day 10

Day 100

Time

*Persons at sustained risk for rabies beyond 3 years, would receive titer at 1-3 years (booster if <0.5 IU/mL) or booster no sooner than day 21 but no later than year 3 for long-term immunogenicity

Implications of not aligning adult and pediatric PrEP recommendations

- Discordant recommendations
  - Parents may get vaccinated but children would not
  - Children are believed to be at greater risk than adults but would not be vaccinated

- Setting precedent
  - No previous rabies PrEP or PEP recommendations have involved a different series for adults compared to children
  - Differing recommendations would lead to incorrect concern that more doses are needed for children than for adults

EtR for policy question #1: Primary immunogenicity

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 children# for whom rabies vaccine PreP is recommended?
Population	Children 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
#Persons <18 years of age

Problem: Rabies and PrEP

- Rabies is nearly always fatal
- PrEP is important component of preventing human rabies in U.S.
- Yellow Book specifically mentions children are at a particular risk for rabies
  - Inquisitive nature and attraction to animals
  - Inability to read behavioral cues from dogs and other animals
  - Increased likelihood for severe bites to high-risk anatomic regions (e.g., head and face) because of short stature
- Children often travel to canine rabies endemic regions
- Rabies modern cell culture vaccines are effective

EtR: Policy question #1

Domains	WG interpretation
Benefits: How substantial are the desired anticipated effects	Minimal; 100% of people seroconvert for proposed and for previous schedule
Harms: How substantial are undesirable anticipated effects?	Minimal; No expected safety concerns
Benefit / Harm: Do desirable effects outweigh undesirable effects?	Favors both
Overall certainty of the evidence for the critical outcome(s)?	Moderate certainty of evidence (Level 2) due to concerns for risk of bias

PrEP Policy Question #1

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.

PrEP Policy Question #1

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, Range 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, Range 18 – 65	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	Mean 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, Range 5 -13	190	190	HDCV, IM	1.00 [0.99, 1.01]	7/9 Minimal concerns
Vodopija, 1986	Mean NR, Range 19 -25	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.

Sabchareon et al

- HDCV in 190 school children
- After [0, 7 days] series, 100% of children had antibody titers ≥ 0.5 IU/mL

Group, variable	Day 28
CPRV	
n	195
Antibody titer ≥0.15 IU/mL*	100
Antibody titer ≥0.5 IU/mL†	100
HDCV	
n	190
Antibody titer ≥0.15 IU/mL*	100
Antibody titer ≥0.5 IU/mL†	100

Table from: Sabchareon A, Lang J, Attanath P et al. A new vero cell rabies vaccine: Results of a comparative trial with human diploid cell rabies vaccine in children. Clin Infec Dis. 1999; 29: 141-9.

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 Moderate	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	strong association	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 Low	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.

EtR: Policy question #1

Domains	WG interpretation
Values: Does the target population feel that desirable effects are large relative to undesirable effect?	Yes. Desirable effect is being vaccinated from rabies
Values: Is there important uncertainty about or variability in how much people value the main outcomes?	No. Target population values "protection" of children from rabies because this population is at a higher risk than adults during travel
Acceptability: Is the intervention acceptable to key stakeholders?	Yes. Shorter schedule preferred by patients & providers and will enable more children to be vaccinated before risky travel
Resource Use: Is the intervention a reasonable and efficient allocation of resources?	Yes. Travel vaccination costs are typically out-of-pocket; fewer doses results in lower costs for individuals. Also, rabies vaccine shortages have occurred in U.S. so using fewer doses will result in efficient allocation of resources
Equity: What would be the impact on health equity?	Probably increased because of decreased costs
Feasibility: Is the intervention feasible to implement?	Yes. Shorter series than current series so it can be more easily implemented before travel

Balance of Consequences

☐ Undesirable consequences clearly outweigh desirable consequences in most settings	☐ Undesirable consequences probably outweigh desirable consequences in most settings	☐ Balance between desirable and undesirable consequences is closely balanced or uncertain
☐ Desirable consequences probably outweigh undesirable consequences in most settings	X **Desirable consequences clearly outweigh undesirable consequences in most settings**	☐ There is insufficient evidence to determine the balance of consequences

Proposed recommendation for vote

Recommendation	Work Group Interpretation
ACIP recommends a 2-dose [0, 7 days] intramuscular rabies vaccine series in immunocompetent persons <18 years of age for whom rabies vaccine pre-exposure prophylaxis (PrEP) is indicated	WG preference is for intervention

EtR for policy question #2: Long-term immunogenicity

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 children$ in the #3 risk category of people who receive PreP?
Population	Children 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
$ Persons < 18 years of age

Problem: Long-term immunogenicity for rabies

- Some children may make trips to developing countries (e.g., to visit grandparents) beyond 3 years
- Immunology suggests that anamnestic response to an exposure occurs
- WHO approved 2-dose series for this population
- WG opted for very cautious recommendation to ensure long-term immunogenicity for [0, 7 days] series
  - Strong data for long-term immunogenicity only exists for up to 3 years
  - Data shows that titer at ≥ 1 year, is marker of long-term immunogenicity
  - WG proposed
    - Titer at 1-3 years (and boost accordingly) OR
    - Booster no sooner than day 21 and no later than year 3

Long-term immunogenicity reported in recently published article*

- 6 persons who received [0, 7 days] IM series, were evaluated after 10-11 years
  - 3 male; 3 female
  - Ages 34-46
  - 5 had titers ≥ 0.5 IU/mL
  - All had 4-fold increase in titers after booster

- More data expected about long-term immunogenicity of 2-dose series because WHO recommendations made in 2018

*De Pijper et al, Long-term memory response after a single intramuscular rabies booster vaccination, 10-24 years after primary vaccination. Journal of Infectious Diseases. Epub January 2021

EtR: Policy question #2

Domains	WG interpretation
Benefits: How substantial are the desired anticipated effects	Moderate • Flexibility in receiving titer check (and only booster if indicated) versus a booster over a broad time period i.e., as soon as day 21 and as late as 3 years;100% of subjects mounted anamnestic response to booster at 1-3 years
Harms: How substantial are undesirable anticipated effects?	Minimal; No expected safety concerns
Benefit / Harm: Do desirable effects outweigh undesirable effects?	Favors intervention
Overall certainty for evidence: effectiveness	Low certainty of evidence (Level 3)

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	42	No comparison[1]	PCEC, IM	Not able to calculate[2]	8/9 Mild concerns
Soentjens, 2019	Median 29.0, NR	368	No comparison[1]	HDCV, IM	Not able to calculate[2]	8/9 Mild 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) : 410/410 (100%) seroconverstion with booster	Level 3 Low	CRITICAL

CI: Confidence interval

EtR: Policy question #2

Domain	WG interpretation
Target population sentiments: Does the target population feel desirable effects are large relative to undesirable effects	Probably yes • Stakeholders want to avoid acquiring high-stakes infection; children have many more years ahead of them making future travel more likely than an older adult who is vaccinated • Booster provides reassurance that outweighs any inconvenience
Target population sentiments: Is there important uncertainty about or variability in how much people value the main outcome(s)?	No: Target population values "protection" from rabies and there is likely no important variability
Acceptability: Is the intervention acceptable to stakeholders?	Yes: Stakeholders accustomed to accommodating third dose of rabie vaccine and will find it acceptable to have booster as an option, particularly given the flexibility for when that booster can be given
Resources: Reasonable and efficient allocation of resources?	Yes: Persons who do not have sustained risk for rabies will not requi the booster; additionally, because of the flexibility in the time point for this booster, it can be arranged at a time when there is no shortage o vaccines

EtR: Policy question #2

Domains	WG interpretation
Equity: What would be the impact on health equity?	Increased: Some PrEP costs are out-of-pocket. Because titer is offered as option, inequity could be resolved by choosing that option. Additionally, children without sustained risk for rabies will not need booster or titer and those who do require it, could defer receiving (and paying) up to 3 years later diffusing the costs over a longer time period
Feasibility: Is the intervention feasible to implement?	Yes: Administrators could opt to schedule booster dose at the time of primary vaccination if there is a concern for travelers not remembering to receive booster dose

Balance of Consequences

☐ Undesirable consequences clearly outweigh desirable consequences in most settings	☐ Undesirable consequences probably outweigh desirable consequences in most settings	☐ Balance between desirable and undesirable consequences is closely balanced or uncertain
☐ Desirable consequences probably outweigh undesirable consequences in most settings	☒ **Desirable consequences clearly outweigh undesirable consequences in most settings**	☐ There is insufficient evidence to determine the balance of consequences

Proposed recommendation for vote

Recommendation	Work Group Interpretation
ACIP recommends an intramuscular booster dose of rabies vaccine, as an alternative to a titer check, for immunocompetent persons >=18 years who have sustained and elevated risk for only recognized rabies exposures (i.e., those in risk category #3 of rabies PrEP recommendations table). The booster dose should be administered no sooner than day 21 but no later than 3 years after the 2-dose PrEP series.	WG preference is for intervention

Proposed recommendations for June ACIP vote

- ACIP recommends a 2-dose [0, 7 days] intramuscular rabies vaccine series in immunocompetent persons <18 years of age for whom rabies vaccine pre-exposure prophylaxis (PrEP) is indicated
- ACIP recommends an intramuscular booster dose of rabies vaccine, as an alternative to a titer check, for immunocompetent persons < 18 years of age who have sustained and elevated risk for only recognized rabies exposures (i.e., those in risk category #3 of rabies PrEP recommendations table ʃ). The booster dose should be administered no sooner than day 21 but no later than 3 years after the 2-dose PrEP series

ʃRisk category table in next slide

Risk category	Nature of Risk	Typical Population	Disease Biogeography[1]	Primary Immunogenicity PrEP	Long-term immunogenicity
#1: Elevated risk for unrecognized and recognized exposures including unusual / high risk exposures (e.g., aerosol exposures and high concentration rabies virus exposures)	Risk of virus exposure is continuous. Exposure is often in high concentrations and may go unrecognized, and can be unusual (e.g., aerosolized virus).	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	IM [0, 7 days]	Titers every 6 months (booster if titer <0.5 IU/mL)
#2: Elevated risk of both unrecognized and recognized exposures	Risk of virus exposure is episodic. Exposure typically recognized but could be unrecognized. Unusual exposures do not occur	Persons who frequently handle bats or at frequent risk for coming into contact with bats because of entry into high density bat environments (e.g., bat biologist)	All geographic regions where bats are a reservoir for rabies[2]	IM [0, 7 days]	Titers every 2 years (booster if titer <0.5 IU/mL)
#3: Elevated risk of recognized exposures that is sustained	Risk of virus exposure greater than for population at large. Exposure is a recognized one.	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	All geographic regions where terrestrial[3] and non-terrestrial mammals are reservoirs for rabies	IM [0, 7 days]	Titer once at 1-3 years (booster if titer <0.5 IU/mL) **OR** Booster no sooner than day 21 and no later than year 3.
		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 endemic rabies		
#4: Elevated risk of recognized exposures that is not sustained (i.e., ≤ 3 years)	Risk of virus exposure greater than for population at large. Exposure is a recognized one and only present for up to 3 years after primary vaccination	Same as for #3 but with risk ≤ 3 years (e.g., short-term volunteer providing hands-on animal care or a traveler with no risky travel planned beyond 3 years	Same as for #3	IM [0, 7 days]	None
#5: 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	None	None

[1]For questions about the disease biogeography of the region where an exposure occurred, please contact your local or state health department

[2]Bats are reservoirs for rabies in all US states except Hawaii

[3]Terrestrial mammals are non-bat species (e.g., racoons, skunks, livestock)

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Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.