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Economic Evaluation of Anti-Rabies Prophylaxis among children in India

Abhishek Royal^{1*}, Denny John², Omesh Bharti³, Retna Siwi Padmawati¹, Adi Utarini¹

¹ Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

² Amrita Institute of Medical Sciences & Research Centre, Kochi, India

³ Department of Health & Family Welfare, Government of Himachal Pradesh, Shimla, India

*Correspondence: abhishekroyal2010@gmail.com

Background:

- Rabies accounts for estimated 20,000 annual deaths in India.
- Children below 15 years of age contributes to 35% of these painful deaths.
- This study reports the costs and cost effectiveness of various Pre-Exposure Prophylaxis (PrEP) and Post-Exposure Prophylaxis (PEP) strategies to avert deaths due to rabies in children in India.

Methods:

- A decision tree model was developed for children in the age group of 0-5 years (U-5) and 5-15 years (U-15) to evaluate various PrEP + PEP and PEP only regimens recommended under WHO & National guidelines.
- The 2-site intradermal (ID) regimen administered on day 0 and 7 was considered as intervention [PrEP (I)].
- A burden of illness systematic review focused on India was conducted to identify relevant studies. Other literature, program reports and databases were additionally searched to identify data inputs.
- The data inputs, assumptions, and model structure was validated by the field experts.
- All costs were converted to 2020 International Dollars' value using implicit price deflators for PPP.
- ICER and cost of implementation at programmatic level was calculated for base case analysis along with one-way sensitivity, and scenario analyses for each regimen for the FY 2020-21
- The cost effectiveness was reported using WHO CET GDP based threshold approach[#].
- The data was analysed in MS Excel and Plant-a-tree add-in MS-Excel.

Table 1. Intervention and Comparator Arms

Arms	Strategy	Regimens
Intervention (PrEP I)	PrEP (ID); PEP (ID)	ARV at Day 0, 7 (2-site); ARV at Day 0 (4 site)
Comparator 1 (C1)	PrEP (ID); PEP (ID)	ARV at Day 0, 7, 21 (1-site); ARV at Day 0, 3 (1-site)
Comparator 2 (C2)	PrEP (IM); PEP (IM)	ARV at Day 0, 7 (1-site); ARV at Day 0, 3 (1-site)
Comparator 3 (C3)	PrEP (IM); PEP (IM)	ARV at Day 0, 7, 21 (1-site); ARV at Day 0, 3 (1-site)
Comparator 4 (C4)	PEP only (ID)	ARV at Day 0,3,7 (2-site) + RIG in Cat III exposure
Comparator 5 (C5)	PEP only (ID)	ARV at Day 0, 3, 7, 28 (2-site) + RIG in Cat III exposure
Comparator 6 (C6)	PEP only (IM)	ARV at Day 0, 3, 7, 14-28 (1-site) + RIG in Cat III exposure
Comparator 7 (C7)	PEP only (IM)	ARV at Day 0 (2-site) + Day 7, 21 (1-site) + RIG in Cat III exposure
Comparator 8 (C8)	PEP only (IM)	ARV at Day 0, 3, 7, 14, 28 (1-site) + RIG in Cat III exposure

ARV = Anti-Rabies Vaccination; ID = Intradermal; IM = Intramuscular

Results:

- PrEP (I) is reported to reduce U-5 and U-15 deaths up to 95.6% and 89.9% respectively
- The incremental DALYs averted per million population with implementation of PrEP (I) in U-5 and U-15 cohorts range between 187 and 35,399 and; 451 and 85,069 respectively.
- PrEP (I) is reported to be very cost effective in comparison with PEP regimens from societal perspective.
- PrEP (I) is not cost-effective over IM PrEP strategies in both the age groups
- Per capita cost of implementation of PrEP (I) is 18.83 USD and 19.19 USD for first year of implementation and is 33.9 times and 9.9 times higher than PEP regimens in U-5 and U-15 cohorts respectively.
- The cost of implementation of PrEP (I) strategy is lower than all other PrEP strategies in both the age groups.
- Implementation of local infiltration of equine rabies immunoglobulins in PEP was reported to be cost-effective over other forms of rabies immunoglobulins.

Table 2. Base Case Analysis (Societal Perspective) for U-5 & U-15 cohorts

	PrEP (Intervention)	PrEP (Comparator 1)	PrEP (Comparator 2)	PrEP (Comparator 3)	PEP (Comparator 4)	PEP (Comparator 5)	PEP (Comparator 6)	PEP (Comparator 7)	PEP (Comparator 8)
Cohort 1: Children in the age group of 0-5 years (U-5)									
Deaths (per million population)	99	143	104	104	987	1000	1011	1046	1046
DALYs (discounted)	3700.59	5345.3	3887.49	3887.49	36893.78	37379.72	37790.9	39099.19	39099.19
ICER (USD/DALYs averted)	-	7395.64	81416.27	202438.43	-904.51	-891.43	-880.6	-848.09	-848.01
Cost-Effectiveness [#]	-	Not cost effective	Not cost effective	Not cost effective	Very Cost Effective	Very Cost Effective	Very Cost Effective	Very Cost Effective	Very Cost Effective
Cohort 2: Children in the age group of 5-15 years (U-15)									
Deaths (per million population)	273	395	286	286	2524	2569	2607	2723	2723
DALYs (discounted)	9479.09	13715.17	9930.48	9930.48	87638.22	89200.71	90520.14	94547.89	94547.89
ICER (USD/DALYs averted)	-	2872.31	33736.29	83846.17	-383.97	-376.35	-370.02	-352.59	-352.36
Cost-Effectiveness [#]	-	Cost Effective	Not Cost Effective	Not Cost Effective	Very Cost Effective	Very Cost Effective	Very Cost Effective	Very Cost Effective	Very Cost Effective

Conclusion:

- Though the cost of implementation at programmatic level is higher in first year, PrEP (I) regimen is a cost-effective and life-saving strategy to avert painful deaths due to rabies in children in India.
- Implementation of PrEP (I) in school children can be an effective strategy in the age group of 5 – 15 years.
- Administration of PrEP in infants or children < 5 years in Universal Immunization Program can also be an effective strategy to avert rabies deaths in children in India

WHO CET - GDP based thresholds approach : interventions with an incremental cost per DALY averted less than the per capita GDP in low middle income countries (LMICs) are "very cost effective", and those costing less than triple the per capita GDP are "cost- effective"

Note: The study was conducted as master's in public health thesis in Universitas Gadjah Mada (Indonesia) and received research grant from WHO-TDR.