Research Regulation in Nepal: Role of Nepal Health Research Council (NHRC)

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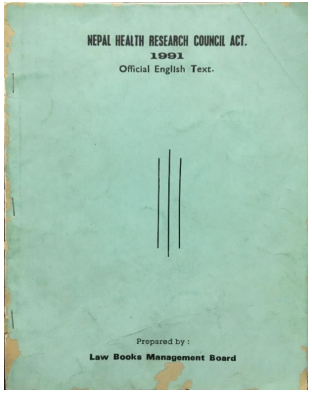
History of Health Research in Nepal

- 1951: Malaria survey in the Kathmandu Valley
  - ✓ Organized with the help of United States Operations Missions (now USAID)
- 1965-66: Nepal Health Survey
  - ✓ University of Hawaii and the Dooley Foundation
- 1976: Nepal Fertility Survey
  - ✓ University of California at Berkeley
- 1979-80: Nepal Blindness Survey
  - ✓ The first nationwide epidemiological survey of blindness
- 1988-90: Nepal Nutrition Intervention Project (NNIP)
  - ✓ USAID funded project on Vitamin A at Sarlahi district
  - ✓ Major research project in collaboration with Johns Hopkins University

Establishment of Nepal Health Research Council in the year 1991

- Autonomous government body by an act of parliament
- Apical body to promote and co-ordinate health research for the improvement of health status of Nepalese citizen



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NHRC ACT 1991

3. Establishment of Council: (1) The Nepal Health Research Council is hereby established to do, or cause to be done, high-level study and research works on health.

11. Permission to be Obtained to do Research Relating to Health:

(I) After the commencement of this Act, Individual or organization interested to do research in the field of health shall have to Obtain permission from the Council.

(II) The Council may also specify terms and conditions as prescribed while giving permission pursuant to sub- section (I).

12. Special Rights of the council: (1) The Council may issue necessary directives to the person or organization involved in the research work relating to health permitted for research pursuant to Section 11.

(2) In case any person or organization carries out research works without obtaining permission pursuant to Section 11 or does not abide by the terms and conditions as prescribed or directives of the Council, while carrying out the research work by obtaining permission, the council may warn such person or organization or prohibit to carry out the research work for a specified period.

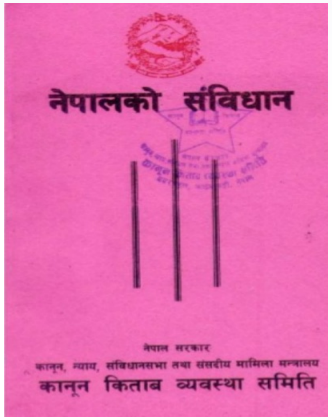
Constitution of Nepal

- **“Cooperation, Coordination, Coexistence”**

Article 51. Policies of the State

h) Policies relating to basic needs of citizens

(9) focus on health research and keep on increasing the number of health institutions and health workers in order to make health services widely available and qualitative



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The Fifteenth Plan

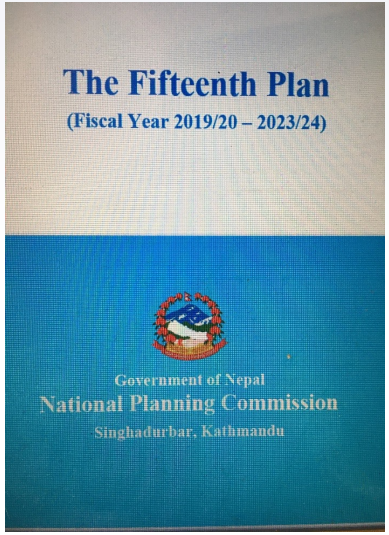
Chapter 7,
7.3 Health and Nutrition (Page 241)

10. *Strategy:* (Page 250)

To make timely revisions in the scope of the Nepal Health Research Council and develop and expand it to the provincial level.

Working Policies:

10.1 The structure of Nepal Health Research Council will be expanded to the provincial level coordinating with universities and the academic sector in health research for the formulation of evidence-based health policy and plans.



Nepal Health Policy-2019

6.14 Health researchers shall be made of international standards and the findings and the facts of such reports shall be efficiently used in policy formulation, planning and health system development;

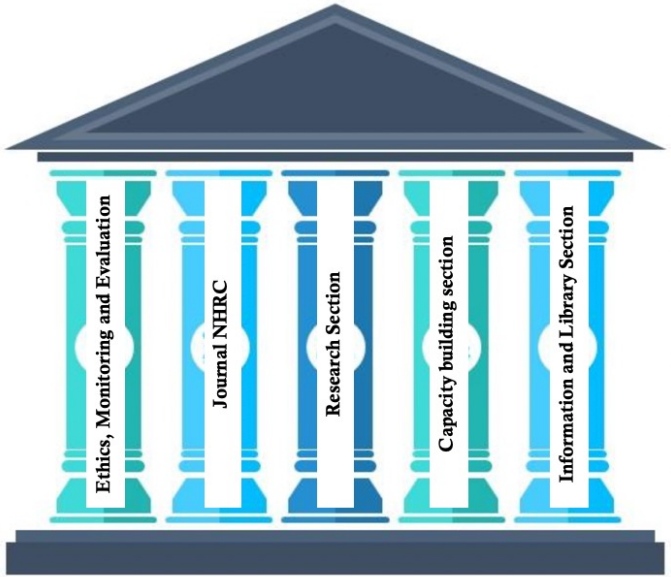
6.14.1 Institutional structure, capacity and scope of Nepal Health Research Council shall be updated, developed and expanded to federal structures and made as per the international standards

6.14.2 Capacity of all levels shall be developed in health researches; and health researchers and technical human resources shall be motivated to researches in coordination with academic and educational institutions

6.14.3 Results of health research conducted by all sectors and entities shall be integrated and those facts, reports and conclusions shall be used in formulation of policies and plans and health system development and expansion

6.14.4 Books, knowledge, skills on indigenous medicinal herbs, minerals, animal substances, Ayurveda and traditional health care shall be researched and recorded, protected and promoted as intellectual property.

NHRC Pillars



Ethics, Monitoring& Evaluation

Independent ERB board
56 IRCs in academic and research institutions
FERCAPP Accredited in 2019
Digital application system
Ethical approval and monitoring

Journal of NHRC

Biomedical Peer-reviewed journal
Open Access
Indexed and four issues per year
Co-operation with 4 international editors association

Health Research Section

Conducts and promotes research
Primary research on national priority areas
National and international collaboration
Establishment of center for Excellence
Communication of research findings

Capacity Building Section

Trainings
Health Research Grants

Information and Library Section

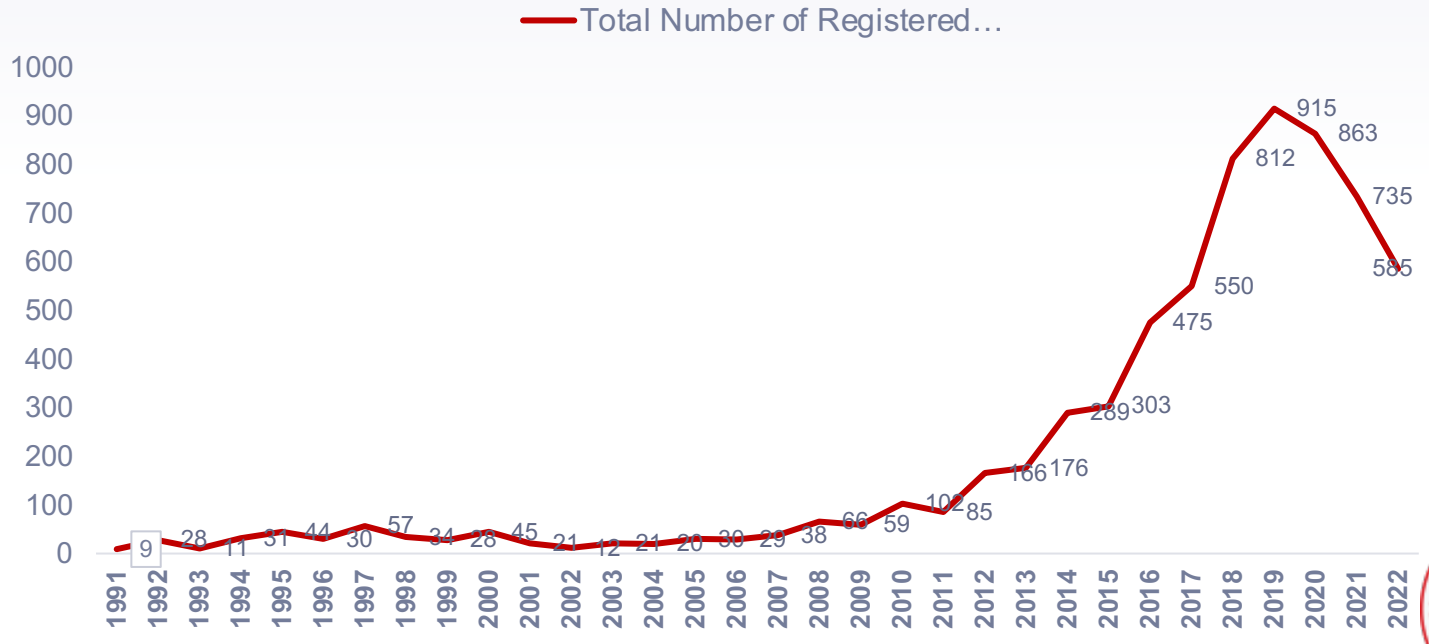
Integrated information
Technology accessible
Publicly available modern library

Evidence Generation and Promotion

- Periodic update of the national priority areas for health research (in coordination with MoHP, and stakeholders)
- Conduct and promote primary research on national priority areas
- Secretariat of Knowledge cafe' and Nepal Health Sector Strategic Plan Development
- National Summit of Health and Population Scientists in Nepal organized on annual basis
- Journal of Nepal Health Research Council- Peer-review & Publication -since 2002
- Policy Briefs

Trend of registered proposals in ERB

Over 2500 research proposals were also approved by IRCs in 2022



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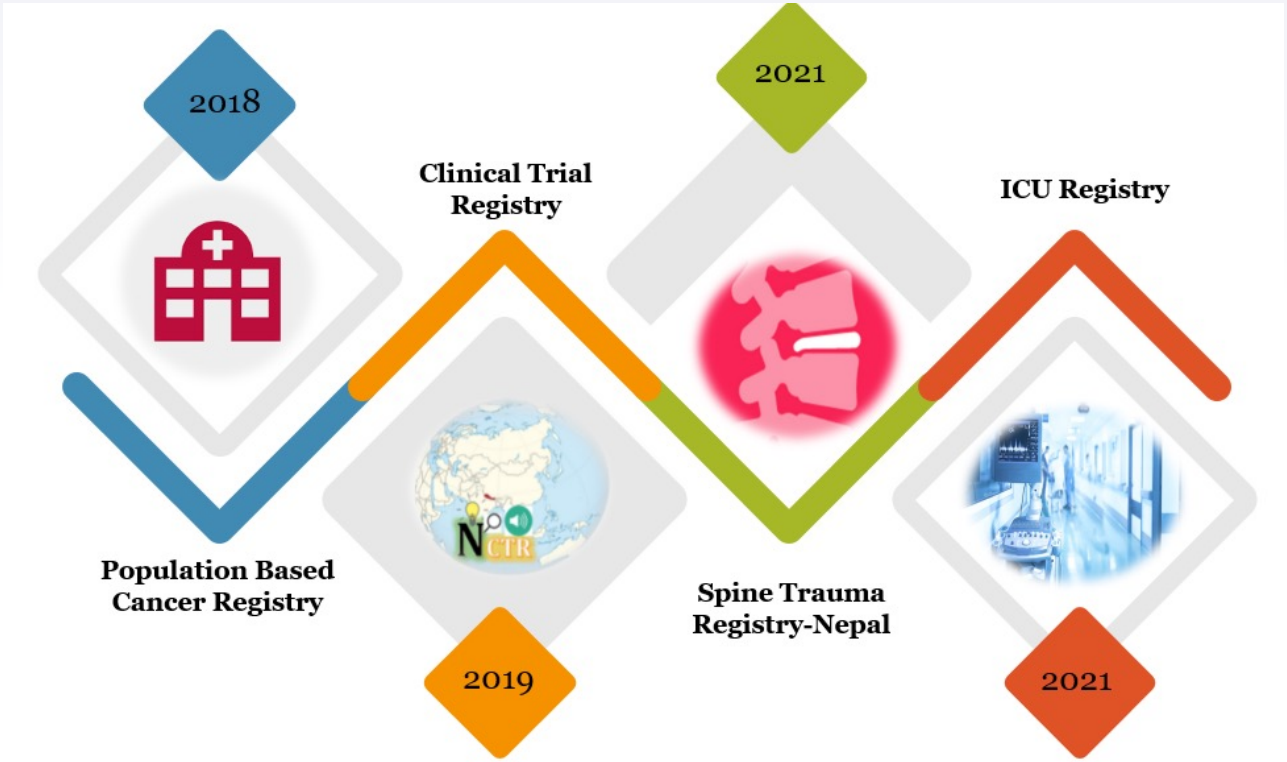
NHRC Registries



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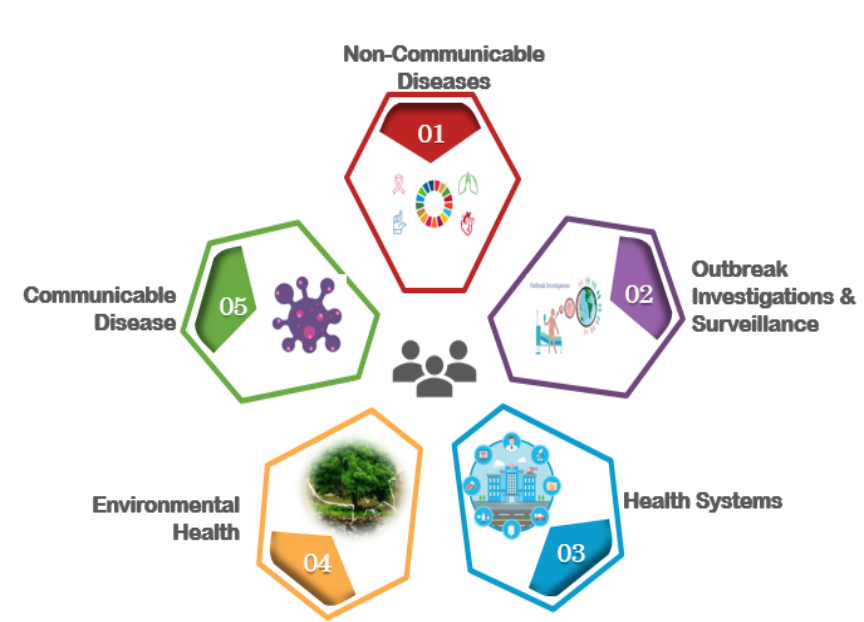
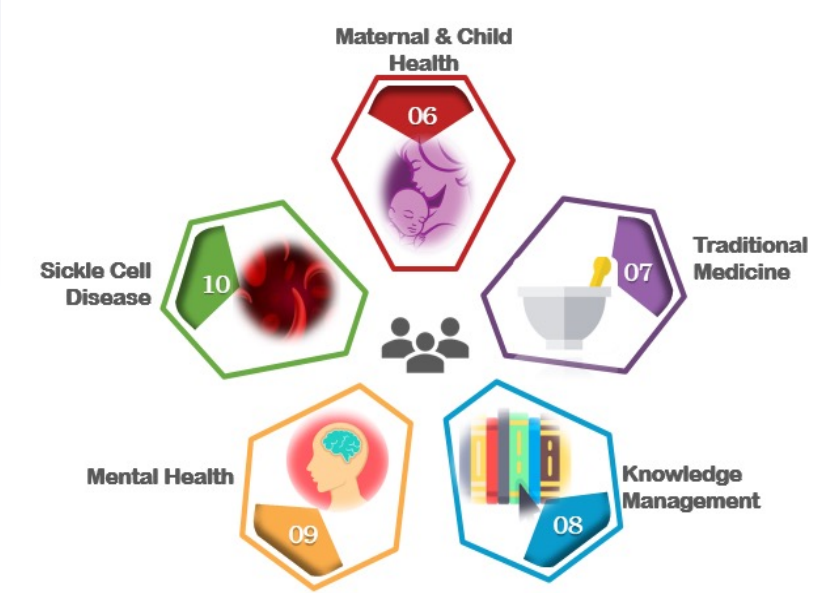
NHRC Research Projects





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Recent Global CR in Nepal

COVID-19 therapeutic trials led by NHRC

- Randomized evaluation of COVID-19 therapy
- An international randomized trial of additional treatments for COVID-19 in hospitalized patients who are all receiving the local standard of care: WHO solidarity Plus
- Efficacy of Favipiravir in Treatment of Mild & Moderate COVID-19 Infection in Nepal.
- Clinical evaluation of YASH-T decoction in management of mild to moderate COVID-19 cases: Open label controlled trial

NHRC approved COVID-19 therapeutic trial

- Australasian COVID-19 Trial (ASCOT) ADAptive Platform Trial

COVID-19 vaccine trials approved by NHRC

- Phase III efficacy trial of COVID-19 recombinant vaccine developed by Sanofi Pateur and GSK Bio
- Phase III efficacy trial of COVID-19 mRNA vaccine developed by Walvax Biotechnology

- Phase III efficacy trial of COVID-19 protein recombinant vaccine (sf9 cells)developed by WestVac Biopharma

Collaborative CR

- Epidemic Intelligence

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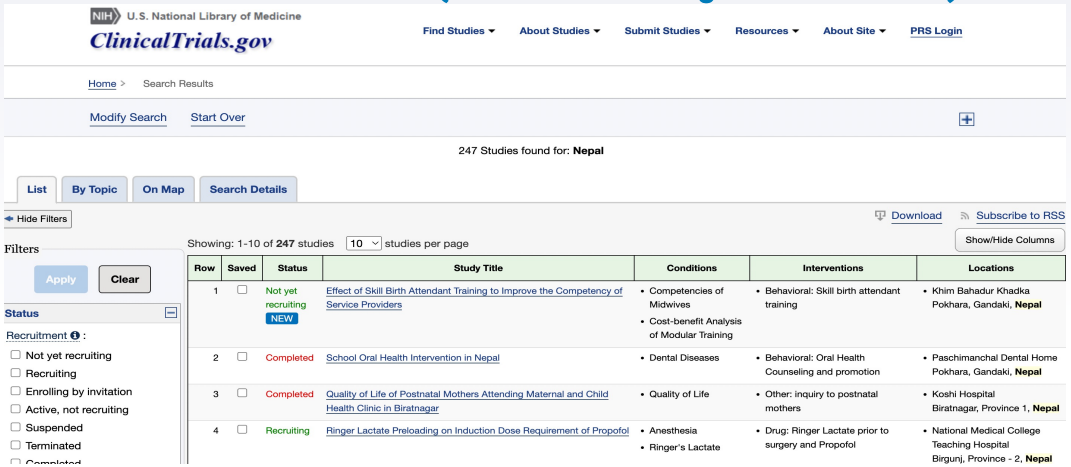
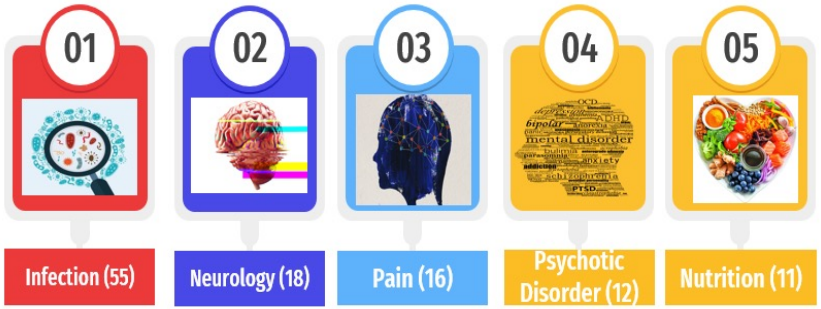
Registered Clinical Trials (28 May 2023)

- 247 studies registered
- 204 interventional studies
- 146 completed studies
- 38 trials recruiting participants
- 7 trials are active, not recruiting





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Recent Major Health Research Evidence

- **Chronic Disease Survey, 2016-2018**
  - Prevalence: COPD- 11.7%, DM- 8.5%, Chronic Kidney Diz- 6.0 %, CAD: 2.9%
- **STEPS Survey, 2019**
  - Current Tobacco user: 28.9%, Alcohol user (30 days): 20.8%, Overweight: 24.3%, HTN:24.5%, Average salt intake per day: 9.1gm/day
- **Mental Health Survey, 2019**
  - Prevalence of mental disorder : 4.3%
  - Life-time prevalence risk of mental disorder : 10%
- **rATA Project, 2022**
  - Prevalence of unmet need assistive product (AP)- 19.7%
  - Prevalence of use of AP: 27.7%

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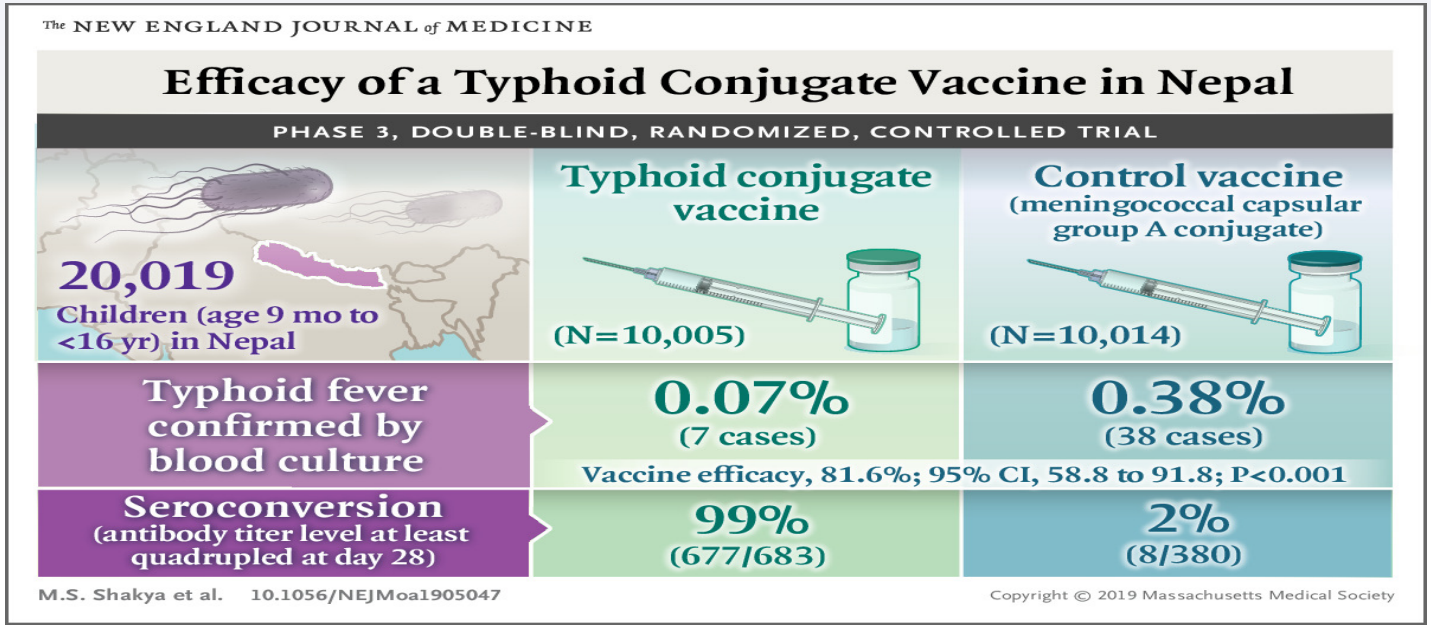
Phase III clinical trial with promising implications



Nepal Government approved the vaccine for routine immunization for children under age of 15 years.

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Phase IV clinical trial with promising implications

Summary

Background Influenza immunisation during pregnancy is recommended but not widely implemented in some low-income regions. We assessed the safety and efficacy in mothers and infants of year-round maternal influenza immunisation in Nepal, where influenza viruses circulate throughout the year.

Methods In this phase 4, randomised, placebo-controlled trial, we enrolled two consecutive sequential annual cohorts of pregnant women from the Sarlahi district in southern Nepal. We randomised mothers 1:1 to receive seasonally recommended trivalent inactivated influenza vaccine or saline placebo in blocks of eight, stratified by gestational age at enrolment (17–25 weeks *vs* 26–34 weeks). Women were eligible if they were married, 15–40 years of age, 17–34 weeks' gestation at enrolment, and had not previously received any influenza vaccine that season. We collected serum samples before and after immunisation, and cord blood from a subset of women and infants. Staff masked to allocation made home visits every week from enrolment to 6 months after delivery. Midnasal swabs for respiratory virus PCR testing were collected during maternal acute febrile respiratory infections, and from infants with any respiratory symptom. We assessed vaccine immunogenicity, safety, and three primary outcomes: the incidence of maternal influenza-like illness in pregnancy and 0–180 days postpartum, the incidence of low birthweight (<2500 g), and the incidence of laboratory-confirmed infant influenza disease from 0 to 180 days. This trial is registered with ClinicalTrials.gov, number NCT01034254.

Findings From April 25, 2011, to Sept 9, 2013, we enrolled 3693 women in two cohorts of 2090 (1041 assigned to placebo and 1049 to vaccine) and 1603 (805 assigned to placebo and 798 to vaccine), with 3646 liveborn infants (cohort 1, 999 in placebo group and 1010 in vaccine group; cohort 2, 805 in placebo group and 798 in vaccine group). Immunisation reduced maternal febrile influenza-like illness with an overall efficacy of 19% (95% CI 1 to 34) in the combined cohorts; 9% efficacy (–16 to 29) in the first cohort, and 36% efficacy (9 to 55) in the second cohort. For laboratory-confirmed influenza infections in infants aged 0–6 months, immunisation had an overall efficacy for the combined cohorts of 30% (95% CI 5 to 48); in the first cohort, the efficacy was 16% (–19 to 41), and in the second cohort it was 60% (26 to 88). Maternal immunisation reduced the rates of low birthweight by 15% (95% CI 3–25) in both cohorts combined. The rate of small for gestational age infants was not modified by immunisation. The number of adverse events was similar regardless of immunisation status. Miscarriage occurred in three (0·2%) participants in the placebo group versus five (0·3%) in the vaccine group, stillbirth occurred in 31 (1·7%) versus 33 (1·8%), and congenital defects occurred in 18 (1·0%) versus 20 (1·1%). Five women died in the placebo group and three died in the vaccine group. The number of infant deaths at age 0–6 months was similar in each group (50 in the placebo group and 61 in the vaccine group). No serious adverse events were associated with receipt of immunisation.

Interpretation Year-round maternal influenza immunisation significantly reduced maternal influenza-like illness, influenza in infants, and low birthweight over the entire course of the study, indicating the strategy could be useful in subtropical regions.

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Issues of health research in Nepal

- Inadequacies in accessing, utilization and generating evidence at the local and provincial levels, lack of priority-driven research areas
- Challenges to accessing and assessing scientific knowledge and synthesizing their findings
- Uptake of research findings in policy and planning
- Unethical practices/misconduct in medical research and publications
- Administrative challenges to conduct research
- Infrastructure challenges to conduct research
- Competencies of researchers to conduct research
- Communication with different stakeholders

Challenges of health research in Nepal

Substantial cost/limited funding for research	Disease heterogeneity & limited understandings	Limited cohort & geographic dispersion	Standardization of data and measures	Data ownership & sharing
• Impacts on research and innovation, • Inadequate data capture • Difficulties in capacity development and technology transfers	• Changing trend over time and differential impacts among dynamic population • Difficulty in disease characterization and diagnostic delays • Adversely affects diagnostic/drug development, study designs and duration	• Difficulty in resource allocation and mobilization • Hardships in completing robust study in limited population • Harder to detect and comprehend effects and outcomes	• Lack of adoption of Electronic Medical Record system in medical care • Challenges of accumulation, combination and comparison • Variances with data quality, utility and interpretation	• Benefits of research data compromised • Obscurity to data access and lack of control over subsequent data use

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Opportunities- Local Perspectives

- Collaborative partnership for basic to advance research
- Capacity building of health research investigators, ethics committee members , and regulators
- Revised medical curriculum with clinical research and medical statistics
- Legible laws and regulatory requirements
- Increased funding and priorities in advanced/implementation research
- Improve clinical trial/cohort studies enrolment
  - Inclusive inclusion criteria
  - Pragmatic trials
  - Improved incentives and addressing SDOH components
  - Systematic dissemination of information on ongoing studies, as well as findings of the completed studies

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Opportunities- Global Perspectives

- Emerging land in evidence development→ treatment-naïve cohort
- Large pool of heterogeneous population with richness in data (genetic variations, geographical diversity and ethnic inclusiveness)
- Cost effective structure for project implementation
- Opportunities to apply methodological advancements of advanced research studies
- Collaborative partnership for wider generalizability of research findings

Major Highlights: National Ethical Guidelines for Health Research in Nepal 2022

- Conducting Phase I and Phase II clinical trial
- Risk categorization:
  - Less than minimal risk
  - Minimal risk
  - Low risk
  - High risk
- Based on local needs and priorities
- Competencies of Researchers: Qualification, Experience and Training
- Roles and Responsibilities and Data Ownership
- Benefit: Strengthened institutional capacity
- Criteria set for IRCs for review

Ongoing Efforts for Research Regulation

- Update on Clinical trial Guideline published in 2005
- Academic and Provincial Grants
- Capacity building to promote research activities
  - Increase in training requirement and number of training conducted
  - Package development for Master Training of Trainers (MTOT)
    - Ethics and research methodology, GCP training

Issues in ethical review processing fees

Way Forward

- Adopt Electronic Health Record System in Nepal Health System and Research
- Adopt appropriate planning practices to ensure the contextual factors
- Advocacy for research education at all level of audiences
- Efforts to support local ownership and generation of health research of its own priorities (acute respiratory infections, dengue, malaria, tuberculosis, HIV, NCDs etc.)
- Appropriate strategies to enhance 'learning health system' through ethical and professional conduct of research
- Evidence Synthesis and Implementation Center

Collaboration Areas

Capacity Building

Trainings, Exchange of Researchers and Scholars, Develop Research labs, Registries (rare diseases, genomic medicine , etc.) Manufacturing Process Development (tech. transfer)

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Collaborative Research

Cohort studies, Lab research, Clinical Trials of biologics, Health Economics Study, Disease Surveillance

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Evidence Promotion

Sharing of scientific evidence and scholarly information, policy engagement, community engagement, media campaigns

- Government of Nepal, Nepal Health Research Council
- Ramshah Path, Kathmandu
- Call : 977-1-4254220 / 977-1-4254220
- Email : nhrc@nhrc.gov.np