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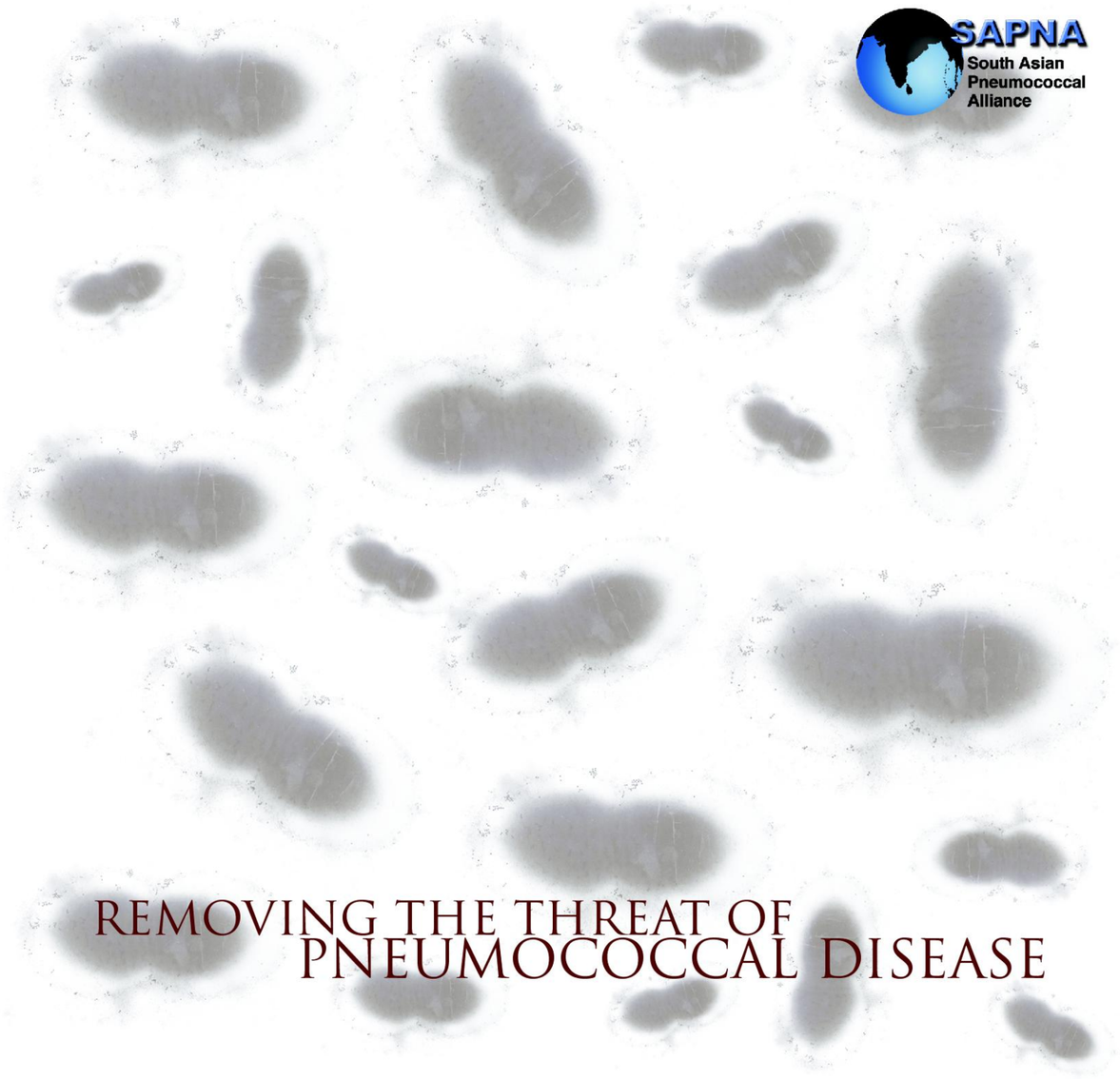
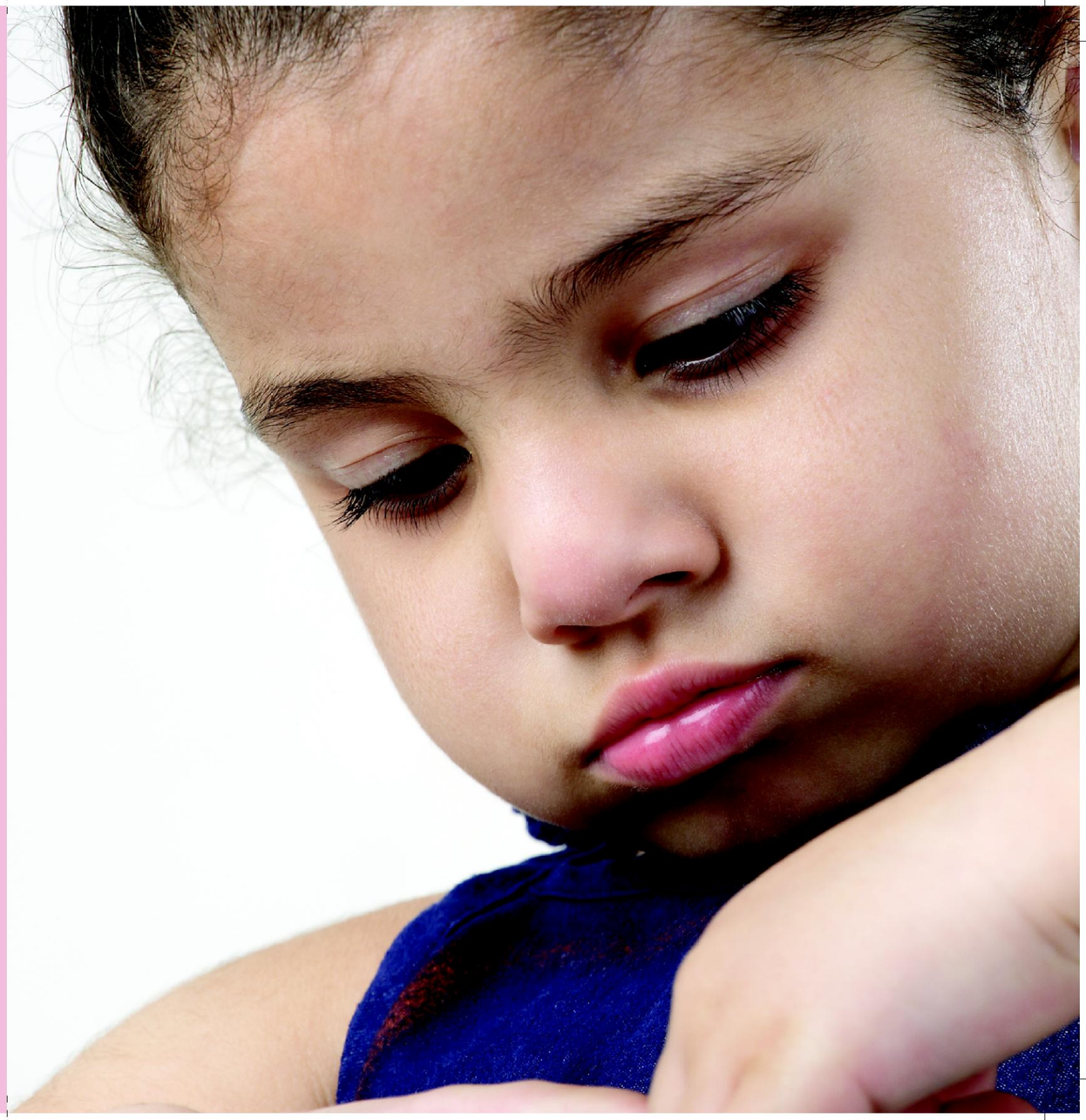
SAPNA
South Asian
Pneumococcal
Alliance



REMOVING THE THREAT OF PNEUMOCOCCAL DISEASE



SUGGESTED STEPS FOR MOVING FORWARD

1. In order to reduce the infant and child mortality and be on target with the Millennium Development Goals, the Government of India could formulate a **time table** for the introduction of pneumococcal vaccine in the national immunization program. This time table could include how India will utilize the pneumococcal conjugate vaccines using GAVI's offer and subsequently plan for the vaccine supply by Indian suppliers over the coming years.[3]
2. A strong emphasis on in-house **R&D** is needed in order to ensure that our production technologies for pneumococcal vaccine are in tune with the times, and to negotiate strategic partnerships with outside scientists or institutions and companies.
3. The Indian government should actively encourage independent **policy research**, cost benefit studies, and wider national consultations on various aspects of pneumococcal vaccination and public health so that it can take informed decisions on such matters.[3]

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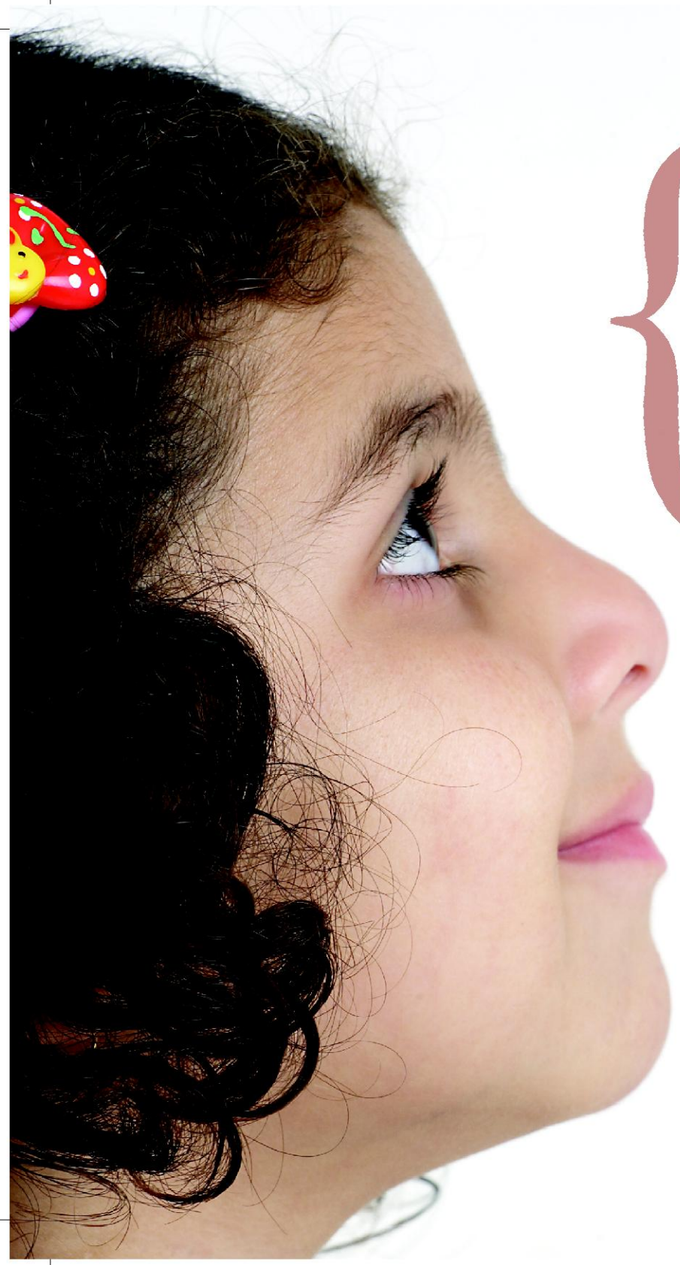
Dr. Kurien Thomas, *SAPNA Coordinator and Project Investigator*, "India should seriously consider introducing the pneumococcal vaccine for children, as pioneers of public health in the pursuit of the United Nations Millennium Development Goals. The Indian vaccine industry already provides many vaccines to India and the world, and will be able to provide the new pneumococcal vaccines at reasonable cost".

Dr. MK Lalitha, *Professor of Microbiology at Madras Medical Mission Hospital*, "The prevalence of Pneumococcal infection in our country is far higher than the available data, which is just the '*tip of the iceberg*'. This is due to a lack of standardized laboratory facilities across the country and variances in diagnostic practices."



44 MILLION INDIAN CHILDREN FALL ILL EVERY YEAR FROM PNEUMOCOCCAL PNEUMONIA. OF THESE, 123,000 TO 164,000 CHILDREN DIE IN INDIA ANNUALLY DUE TO PNEUMOCOCCAL PNEUMONIA; THAT IS, 450 CHILDREN DYING EVERY DAY, 19 CHILDREN EACH HOUR AND ALMOST 1 DEATH PER 3 MINUTES!

COST-EFFECTIVENESS OF PNEUMOCOCCAL VACCINE

The latest cost effectiveness study led by the Health Economists of WHO, Geneva has estimated that at a vaccine cost between $1 and $5 per dose, introduction of pneumococcal vaccine in the world's poorest countries will be cost effective and will substantially reduce childhood mortality.[7] **At a vaccine price of $5 per dose, pneumococcal vaccination was projected to be cost-effective for 71 of the 72 (99%) countries that are eligible for GAVI's support for immunization, and highly cost-effective for 68 (94%) of these countries. At $2.50 per dose, pneumococcal vaccine would be highly cost-effective in all countries apart from Cuba.** Vaccination was not cost saving but cost-effective over the vaccine cost range ($1 to $10 per dose) analyzed.[7]

GAVI'S OFFER

The GAVI Alliance makes new life-saving vaccines, such as Hib and pneumococcal conjugate vaccine, available to developing countries by purchasing the vaccines from suppliers and then providing them to low-income countries at heavily subsidized prices. Developing countries like India can procure pneumococcal conjugate vaccine with **financial support from the GAVI Alliance.** This offer will enable the Government of India to obtain pneumococcal vaccine at a price of **US$ 0.15 to 0.30 per dose**.[3] GAVI's funding is expected to continue at this level until 2015. It is expected that the developing countries would gradually increase their contributions to procure the vaccine.[3]

WAY FORWARD

India spends about 0.9% of its GDP and Rs. 200 per capita per annum on public health, against the WHO recommended 5% of GDP. While we are committed to increasing the public health expenditure up to 3% of GDP, we are likely to miss the Millennium Development Goals in terms of reducing child mortality. Considering the significant proportion of child mortality and morbidity contributed by pneumococcal disease, availability of a subsidized vaccine to prevent this and the major positive impact this will have on achieving the 4th Millennium Development Goal, it would be prudent to consider a timeline for introducing the pneumococcal vaccine in India at the earliest. India has a world class pharmaceutical and vaccine industry, which can be galvanized to provide the relevant vaccine for India and other countries in future, while the GAVI funding can take care of the period till 2015. Given the above facts, undue concern about financing and local suppliers may lead to unnecessary vaccine preventable child mortality due to delayed introduction until a local supplier has a licensed vaccine. Pneumococcal conjugate vaccine, if introduced, would help to greatly reduce this burden. It is to be noted that countries like Pakistan, Bangladesh, Sri Lanka and Nepal are already considering taking up the opportunity opened by the GAVI subsidy to introduce the pneumococcal vaccine in their public health programs. With a strong will and timely action, the current pneumococcal child morbidity and mortality in India can be reversed with this vaccine. In the near future, the world class Indian vaccine industry can even play a major role in meeting the global supply for shortfall of the pneumococcal vaccines.

Resistance to cotrimoxazole was noted to be high (69.2%) while resistance to penicillin was 7.6%, erythromycin 2.8% and chloramphenicol 11%.

The IBIS study has shown that:

1. Currently available 7-valent conjugate vaccine will **prevent** about **47%** of childhood IPD cases in India.
2. Candidate 10 and 13-valent conjugate vaccines under development would cover 72% of invasive STG identified in the IBIS study.
3. Resistance to commonly used antibiotics, such as penicillin, has been increasing over the years.

WHO RECOMMENDS PNEUMOCOCCAL VACCINE

WHO published an updated position paper on pneumococcal conjugate vaccines in March 2007. WHO strongly recommends use of pneumococcal conjugate vaccines in developing countries like India.[5] Since the burden of pneumonia is highest in countries with high under 5 mortality rates, **WHO considers it a high priority to include pneumococcal conjugate vaccine in national immunization programs of countries where under 5 mortality rate is greater than 50 per 1000 live births, or countries where more than 50,000 child deaths occur annually.** With an under 5 mortality rate of 85 per 1000 live births and over 2,210,000 deaths annually in children under 5 years, India meets the WHO's criteria for countries where pneumococcal vaccination should be a priority for introduction.[3]

EFFICACY OF PNEUMOCOCCAL VACCINE IN A DEVELOPING COUNTRY

A recent study of the **efficacy** of a nine-valent pneumococcal conjugate vaccine in The Gambia, Africa, found that the vaccine could significantly reduce the incidence of invasive pneumococcal disease caused by vaccine serotypes by 77% and for all-serotypes by 50%.[6] The vaccine efficacy for all-cause health-facility admissions was 15%, and **for overall child mortality** was **16%**.[6] This lends itself to the inference that India and other Millennium Development Goal (MDG) signatories in the region can **achieve their MDG Targets** with a pneumococcal vaccine, especially the fourth of the Millennium Development Goals, which aims to reduce child mortality in those aged under 5 by two-thirds between 1990 and 2015.

ABOUT INVASIVE PNEUMOCOCCAL DISEASE

Preventable Invasive Pneumococcal Disease (IPD) including meningitis, pneumonia and septicemia, caused by *Streptococcus pneumoniae* (pneumococcus), contributes significantly to morbidity and mortality in all age groups, particularly in children. WHO has estimated that nearly 1 million global deaths occur in children due to IPD and many of these occur in India and neighboring South Asian countries.

South Asian region holds 30% of the world's children. Invasive disease caused by *Streptococcus pneumoniae* is one of the important causes of childhood deaths in the region. In many developed countries, effective vaccination against this bacterium has dramatically reduced the burden of Pneumococcal disease.

Pneumonia remains the leading killer of children in India. Almost **25%** of all child deaths in India are due to pneumonia.[1] UNICEF report has estimated that **410,000** children under the age of 5 years die of pneumonia each year in India and approximately **123,000 to 164,000** of these deaths are due to pneumococcal pneumonia.[2,3] This high burden of pneumonia and pneumococcal disease calls for immediate action with dedicated resources, in order to prevent several thousands of childhood deaths in India every year.[3]

Effective vaccines are available against invasive pneumococcal disease, which would help in reducing high burden of childhood pneumonia in countries like India. New financing mechanisms have been developed by GAVI (Global Alliance on Vaccines and Immunization) to make these vaccines available to developing countries at affordable prices. The high disease burden and availability of effective vaccine at affordable price make it worthwhile to consider introduction of pneumococcal vaccine in national immunization program of India.[3]

Salient facts about pneumococcal pneumonia:

1. Invasive Pneumococcal Disease includes syndromes such as pneumonia, meningitis and sepsis/bacteremia
2. WHO estimates that almost one million children under 5 years of age die every year worldwide due to pneumococcal infections
3. 44 million Indian children fall ill every year from Pneumonia
4. It has been estimated that 410,000 children under the age of 5 years die of pneumonia every year in India
5. Of the above, 123,000 to 164,000 children die in India annually due to pneumococcal pneumonia; that is *450 children dying every day, 19 children each hour and almost 1 death per 3 minutes!*

ABOUT SAPNA

South Asian Pneumococcal Alliance (SAPNA) project is aimed at generating the epidemiological data on Pneumococcal disease in the South Asian countries *(www.indiaden.org/sapna/home/sapna3.html).* The program is funded by **Global Alliance on Vaccine and Immunization (GAVI)** through the **Pneumococcal Vaccines Accelerated Development and Introduction Plan (PneumoADIP)** at John's Hopkins School of Public Health. *(www.gavi.org, www.pneumoadip.org, www.preventpneumo.org).*

The goal of SAPNA project is to **generate local data** about pneumococcal disease that will help the policy makers of each participating country to consider use of pneumococcal conjugate vaccines. The program operates in 8 referral hospitals in India, Nepal and Sri Lanka, and has studied nearly 10,000 children since 2005, to gather hospital-based surveillance data about the regional patterns of invasive pneumococcal disease.

The program has generated important data to assist policy makers to introduce pneumococcal vaccination in children in the countries of India, Nepal and Sri Lanka to prevent serious infections caused by *S. pneumoniae.*

The main objectives of the SAPNA study are:

1. To generate local epidemiological data on invasive pneumococcal disease, particularly
   - Serotype distribution
   - Antimicrobial resistance.
2. To strengthen local capacity for national surveillance of vaccine preventable diseases.
3. To assist the development of national policy regarding control of pneumococcal disease.

ABOUT IBIS

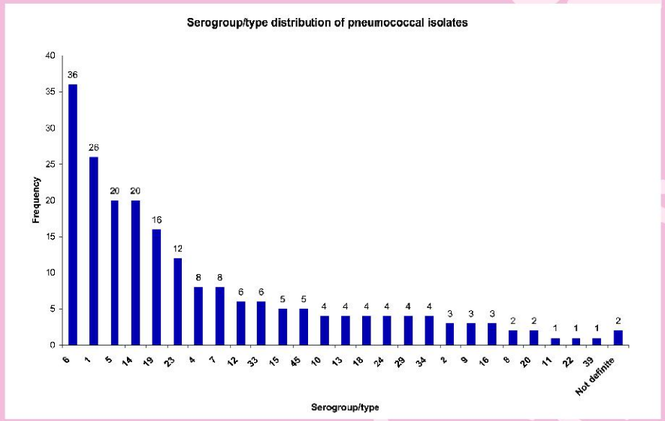
In India, a similar **Invasive Bacterial Infection Surveillance (IBIS)** network collected important data regarding serotype distribution and antimicrobial resistance of pneumococcal infections for more than 10 years. The program was funded by International Clinical Epidemiology Network (INCLEN) with financial assistance from United States Agency for International Development (USAID). This study is now being continued in India as SAPNA project with support from GAVI.

IF IT CHOOSES, THE GOVERNMENT OF INDIA COULD OBTAIN PNEUMOCOCCAL VACCINE FOR BETWEEN US$ 0.15 AND US$ 0.30 PER DOSE. INDIA CAN EVEN PLAY A MAJOR ROLE IN MEETING THE GLOBAL SHORTFALL IN THE SUPPLY OF PNEUMOCOCCAL VACCINES.

These data from across India show that pneumococci cause a high proportion of meningitis and severe pneumonia cases. These data are significant, since there are vaccines available which are widely used in developed countries to prevent childhood pneumococcal diseases.

Serogroup/type (STG) 6 (17.3%) was the most common serotype found in Indian children, followed by STG 1 (12.5%), 5 (9.6%), 14 (9.6%), 19 (7.7%), 23 (5.8%), 4 (3.8%) and 7 (3.8%).

FIGURE 7



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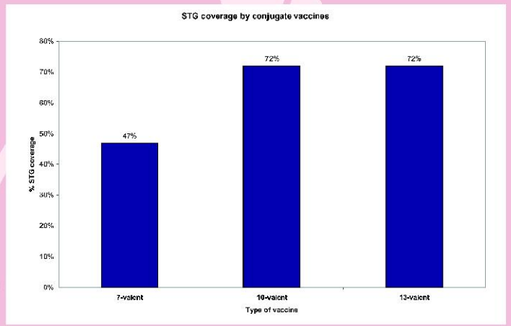
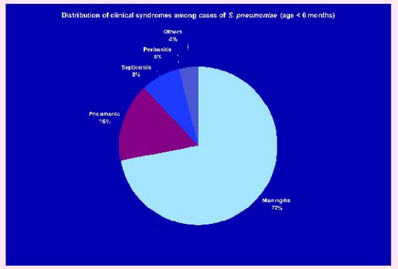


WHO CONSIDERS THE INCLUSION OF THE PNEUMOCOCCAL VACCINE IN NATIONAL IMMUNIZATION PROGRAMMES AS A PARTICULARLY HIGH PRIORITY IN COUNTRIES WITH UNDER - 5 MORTALITY >50 PER 1000 LIVE BIRTHS, OR > 50,000 CHILD DEATHS ANNUALLY

WITH AN INFANT MORTALITY RATE OF >60 PER 1000 LIVE BIRTHS AND OVER 400,000 CHILD DEATHS PER YEAR, INDIA MEETS THE WHO's CRITERIA FOR COUNTRIES WHERE PNEUMOCOCCAL VACCINATION SHOULD BE A PRIORITY FOR INTRODUCTION.

FIGURE 3



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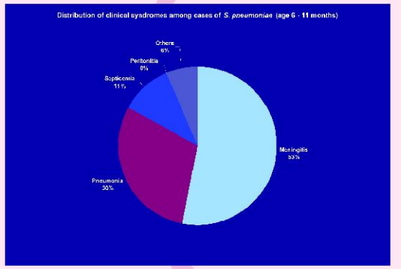

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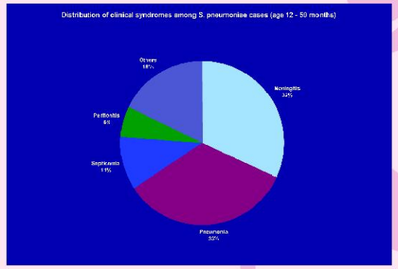
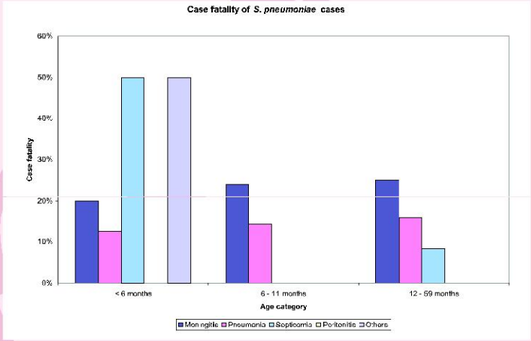


FIGURE 6



AT A VACCINE PRICE OF $5 PER DOSE, PNEUMOCOCCAL VACCINATION WAS PROJECTED TO BE COST-EFFECTIVE FOR 71 OF THE 72 (99%) COUNTRIES, AND HIGHLY COST-EFFECTIVE FOR 68 (94%) COUNTRIES. AT $2·50 PER DOSE, PNEUMOCOCCAL VACCINE WAS HIGHLY COST-EFFECTIVE IN ALL COUNTRIES APART FROM CUBA.

IBIS study was a prospective hospital-based surveillance of IPD.[4] Children with clinical or laboratory criteria for meningitis, pneumonia or other invasive infections were enrolled in IBIS study at hospitals in Delhi, Lucknow, Mumbai, Nagpur, Thiruvananthapurum and Vellore from 1993-2003.

Table 1 IBIS/SAPNA sites

Sr. No.	Name of the Institute	City
1	All India Institute of Medical Sciences	New Delhi
2	King George's Medical University	Lucknow
3	Lokmanya Tilak Municipal Medical College	Mumbai
4	Government Medical College	Nagpur
5	Trivandrum Medical College	Thiruvananthapuram
6	Christian Medical College	Vellore

Standard international microbiology procedures were followed to isolate pneumococci from CSF, blood and other normally sterile body fluids. Serotyping of pneumococcal isolates was done using antisera obtained from Staten Serum Institut, Denmark.

IBIS STUDY FINDINGS

There were 5,893 children (3626 male, 2267 female) below 5 years of age with suspected IPD enrolled in the IBIS study since 1993. Age distribution of children is given in Figure 1. *S. pneumoniae* were isolated from 210 specimens of either blood, CSF or other normally sterile body fluids. Age distribution of children in whom *S. pneumoniae* were isolated is given in Figure 2. Meningitis (47%), pneumonia (29%) and septicemia (10%) comprised 86% of the subjects in whom *S. pneumoniae* were isolated. Please refer to Table 2 for the details regarding outcomes of the illnesses.

FIGURE 1

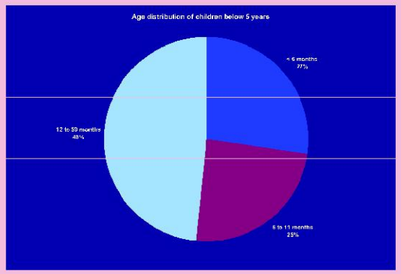


FIGURE 2

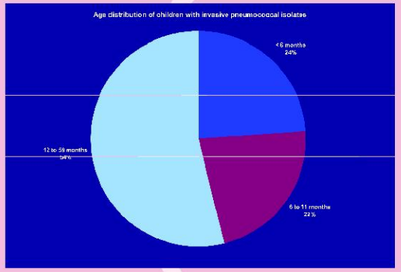


Table 2 Clinical syndromes by age group

	<6 months	Case Fatality	6 to 11 months	Case Fatality	12 to 59 months	Case Fatality	Total	Case Fatality
Meningitis	36 (37.1%)	20.0%	25 (25.8%)	24.0%	36 (37.1%)	25.0%	97	22.8%
Pneumonia	8 (13.3%)	12.5%	14 (23.3%)	14.2%	38 (63.3%)	15.8%	60	15.0%
Septicemia	4 (19.0%)	50.0%	5 (23.8%)	0.0%	12 (51.1%)	8.3%	21	14.3%
Peritonitis	0	–	0	–	7 (100%)	0.0%	7	0.0%
Others*	2 (8.0%)	50.0%	3 (12.0%)	0.0%	20 (80.0%)	0.0%	25	4.0%
Total	50	22.9%	47	17.0%	113	13.8%	210	16.2%

* Others (deep pus forming infections, bacteremia, pleural effusion, empyema, septic arthritis, abscess abdomen, hepatitis, subdural abscess, lymphoma, brain abscess, AGE, nephrotic syndrome, cellulitis, adenitis, LRI)

THE CURRENTLY AVAILABLE PNEUMOCOCCAL CONJUGATE VACCINE COULD SIGNIFICANTLY REDUCE THE INCIDENCE OF VACCINE-TYPE INVASIVE PNEUMOCOCCAL DISEASE BY 77%, BY 50% FOR ALL-SEROTYPE INVASIVE PNEUMOCOCCAL DISEASE, BY 15% FOR ALL-CAUSE HEALTH-FACILITY ADMISSIONS, AND BY 16% FOR OVERALL CHILD MORTALITY.