Hepatitis B vaccination of newborns in rural China: evaluation of an out-of-cold-chain delivery strategy

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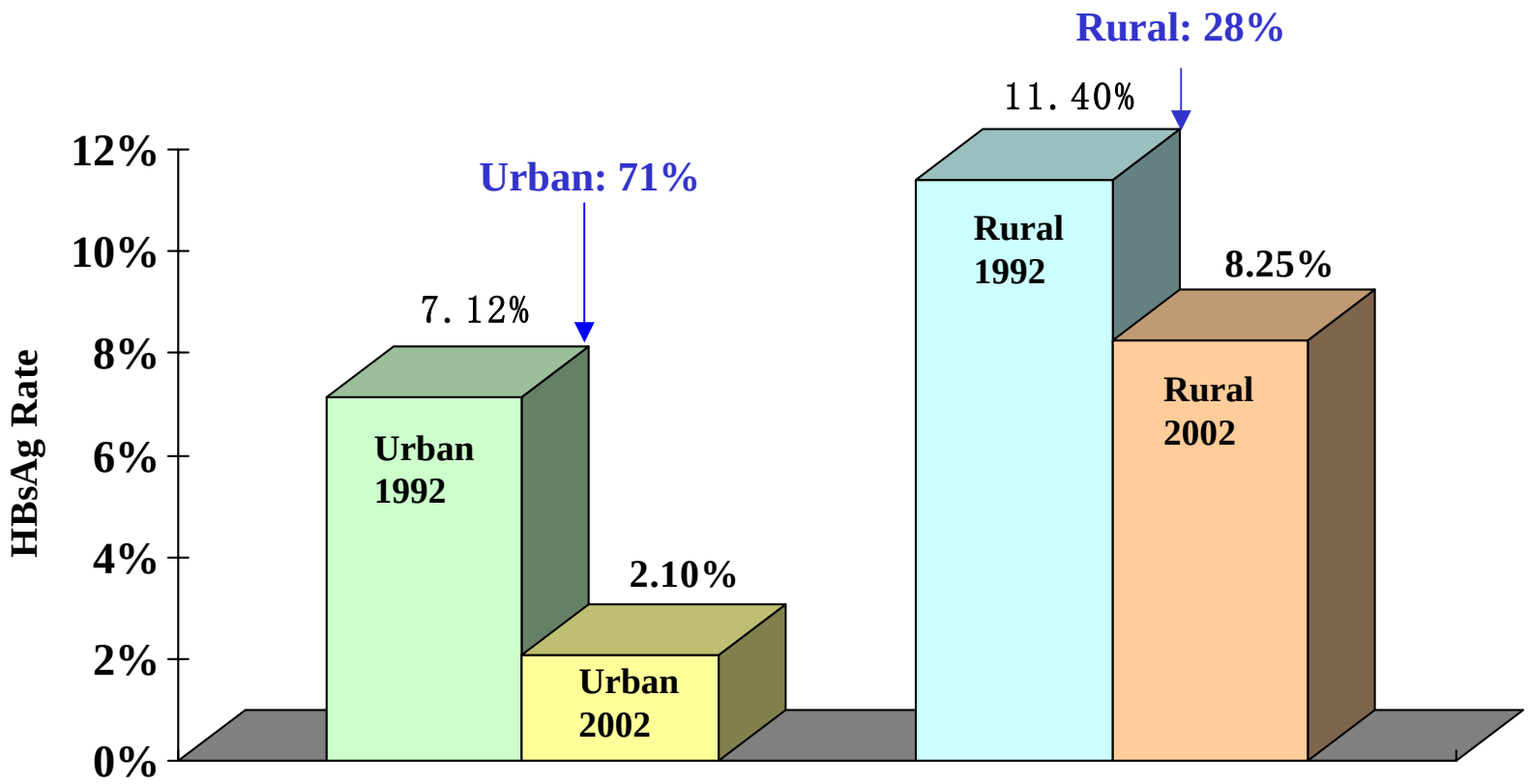
Hepatitis B in China

- Hepatitis B (HB) is one of the four major infectious diseases in China
- 120 million people are chronically infected with hepatitis B virus (HBV)—10% of the population
- An estimated 280,000 deaths annually
  - >33% of global deaths attributed to HB

Sources:

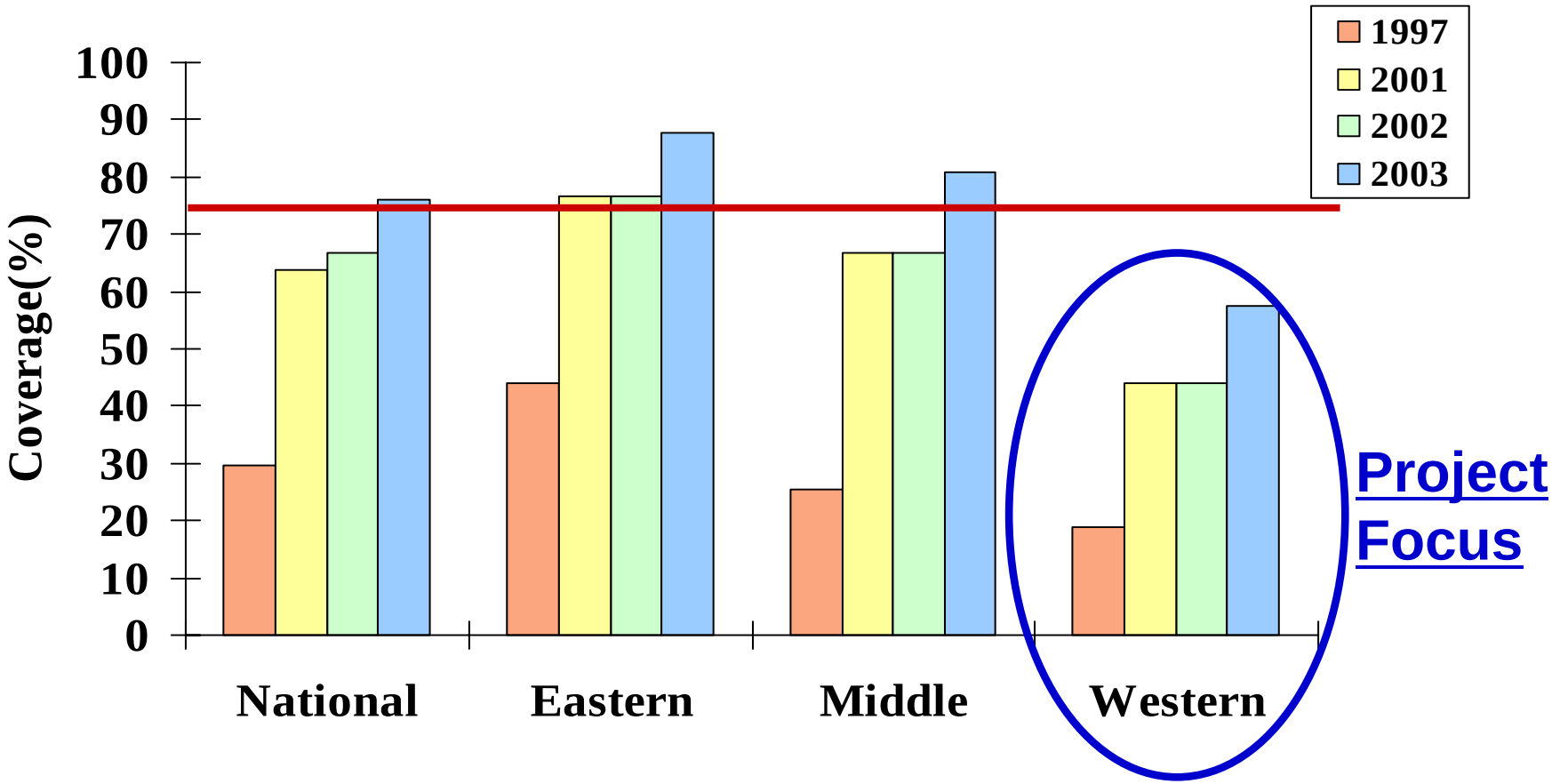
State of the World's Vaccines and Immunization. WHO, UNICEF, The World Bank. 2002.
The Global Alliance for Vaccines and Immunization. Progress Report. 2002.
1992 National Serosurvey. China.

HBV surface antigen rate among children



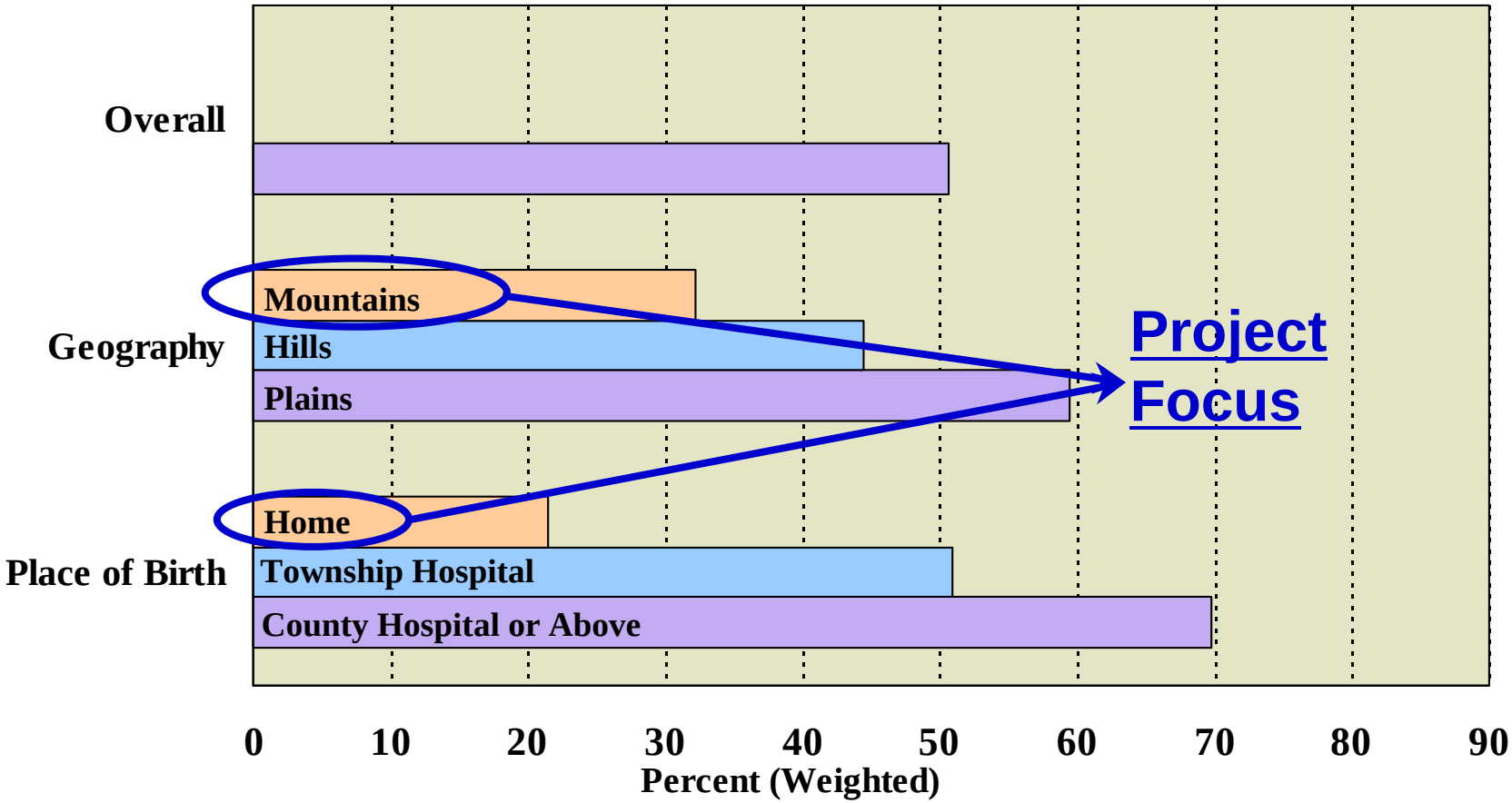
Source: Serosurvey adopting the samples from 2002 national nutrition survey (unpublished)

Increase in on-time administration of HB vaccine birth dose



Source: National EPI Coverage Survey. China. 1999 and 2004

Proportion of children receiving the HB vaccine birth dose on 1st or 2nd day of life



Source: National EPI Coverage Survey. China. 1999

Objective

To evaluate strategies for improving on-time delivery (within 24 hours) of the HB vaccine birth dose in remote areas of China, especially among children born at home.

Study design

- Townships situated at least 20 km from the county capital in three counties in Hunan Province were randomly divided into three groups:
  - Group 1: Ampoule inside the cold chain
  - Group 2: Ampoule outside the cold chain
  - Group 3: HB vaccine in Uniject™* (HB-Uniject) outside the cold chain
- All ampoules of HB vaccine and HB-Uniject packages were marked with vaccine vial monitors (VVMs)

*Uniject is a registered trademark of BD.

Hospital vaccination in the cold chain; home vaccination out of the cold chain

Group 1:

- HB vaccine delivered in township hospitals. Vaccine stored in the cold chain

Group 2 and Group 3:

- Village-based doctors and midwives trained as vaccine providers. Vaccine stored and delivered out of the cold chain

Preparations

- Held trainings with vaccine providers at township and village levels
- Conducted social mobilization to emphasize the importance of hepatitis B immunization and on-time delivery of the birth dose
- Monitored vaccine storage temperatures with data loggers

Evaluation methods

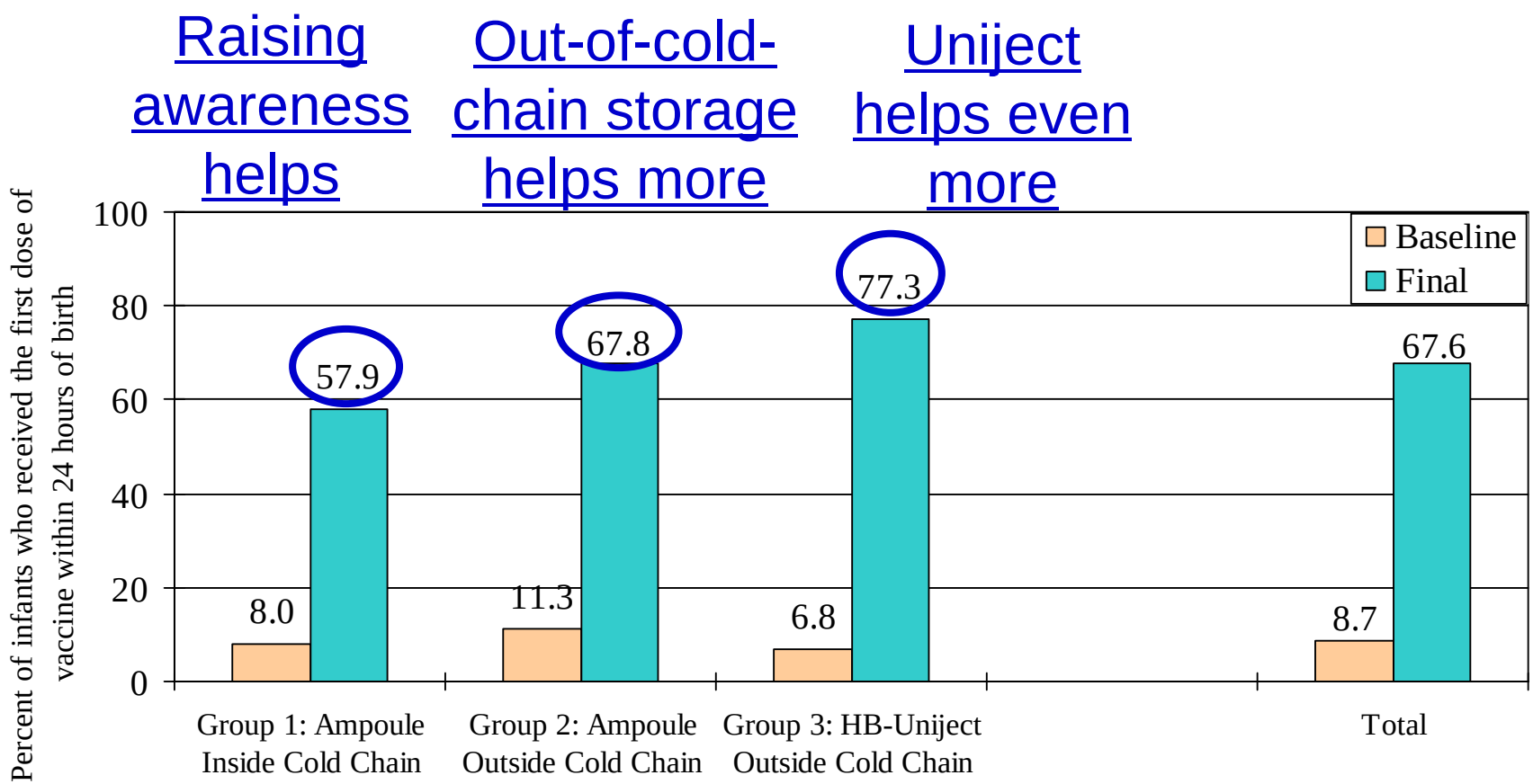
Baseline and final coverage survey

- Review of children's immunization cards
- Review of village/township immunization records

Immunologic response survey

- Radioimmunoassay for HBsAg, anti-HBs

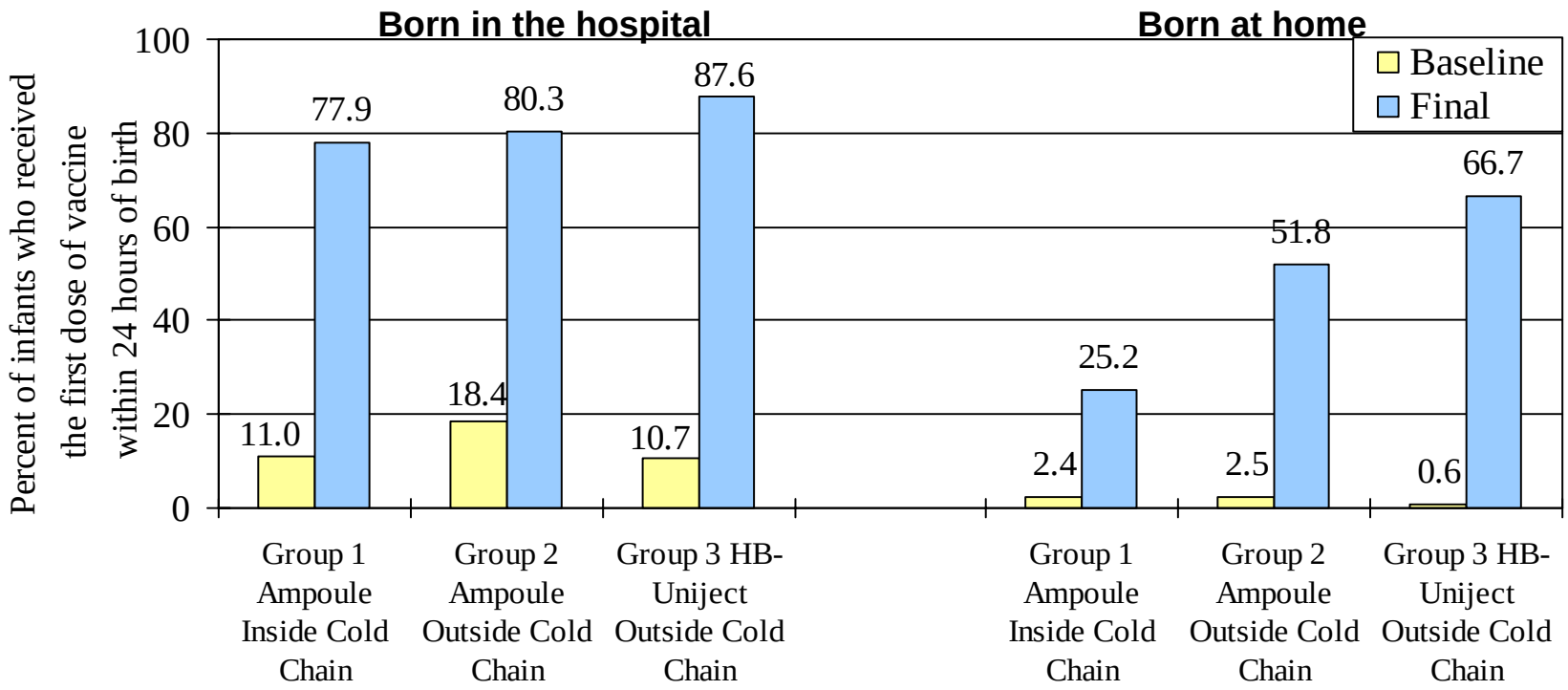
Results: Significant improvements in on-time vaccination



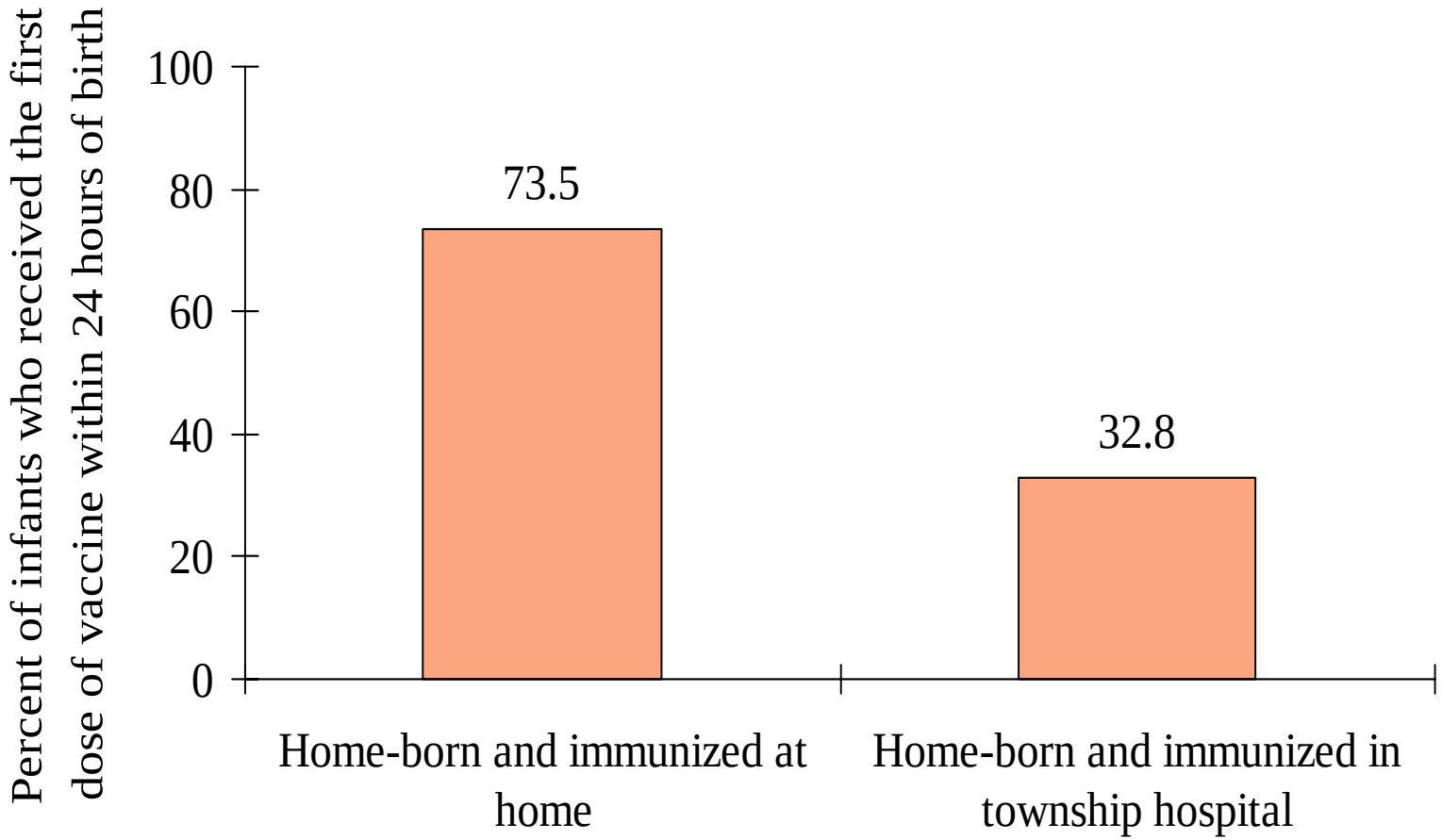
Results: Significant improvements in on-time vaccination

Hospital births—improved by raising awareness

Home births—improved by out-of-cold-chain strategy



Results: Home-born infants better served when vaccinated at home



Serology results: No difference between in-the-cold-chain and out-of-cold-chain groups

Groups	Children observed	Anti-HBs positive			HBsAg positive		
		Children	%	95%CI	Children	%	95%CI
Group 1	203	194	95.6	91.5-97.8	1	0.5	0.03－3.1
Group 2	203	195	96.1	92.1－98.2	1	0.5	0.03－3.1
Group 3	200	191	95.5	91.4－97.8	3	1.5	0.4－4.7
Total	606	580	96.0	93.7－97.1	5	0.8	0.3－2.0

Serology results: No difference between in-the-cold-chain and out-of-cold-chain groups

Groups	Children observed	Children with Anti-HBs +	Anti-HBs>=10 mIU/ml		GMT
			Among Anti-HBs positive (%)	Among children observed (%)	
Group 1	203	194	180 (92.8 %)	180 (88.7 %)	95.5
Group 2	203	195	184 (94.4 %)	184 (90.6 %)	93.3
Group 3	200	191	178 (93.2 %)	178 (89.0 %)	102.3
Inside cold chain	203	194	180 (92.8 %)	180 (88.7 %)	95.5
Outside cold chain	403	386	362 (93.8 %)	362 (89.8 %)	97.7
Total	606	580	542 (93.5 %)	542 (89.4 %)	97.7

Storage temperatures: freeze and heat exposure

- In the cold chain: 2/3 township refrigerators below 0 °C
- Out of the cold chain: temperatures 2°C–30°C
  - 0.2% vaccine was discarded due to heat exposure
  - VVMs effective in identifying heat exposure
- No serious adverse events following immunization were reported during the study

Acceptability of Uniject

- Among providers who had used the Uniject device:
  - 98% thought Uniject was easy to carry, transport, and use
  - 95% thought Uniject could administer a full dose of HB vaccine
  - 88% thought Uniject could save immunization time compared with standard syringes
- Almost all immunization providers thought that the village-based out-of-cold-chain strategy could improve the on-time delivery of the HB vaccine birth dose among children born at home

Conclusion 1

- In remote areas in China and other countries where many children are born at home, on-time administration of HB vaccine has been difficult to achieve through routine immunization service
- Village health workers using an out-of-cold chain immunization strategy can improve the on-time administration of the HB vaccine birth dose among infants born at home
- Training and monitoring of hospital health workers can improve on-time administration of the HB vaccine birth dose to children born in hospitals

Conclusion 2

- Simple tools such as VVMs and Uniject can ensure vaccine quality and injection safety when vaccines are administered by village health workers
- HB vaccine is sufficiently heat stable to withstand routine out-of-cold-chain storage in tropical conditions without loss of immunogenicity
- Taking vaccine out of the cold chain could potentially decrease the risk of vaccine damage due to inadvertent freezing

Next steps

- Improve awareness and coordination of the birth dose in hospital settings through increased supervision
- HB vaccine manufacturer will start application of licensure for use of HB-Uniject stored out of the cold chain
- Introduce VVMs on EPI vaccines, in accordance with UNICEF and WHO recommendations
- Adopt national policy of HB vaccine storage out of the cold chain, initially in warm areas among children born at home

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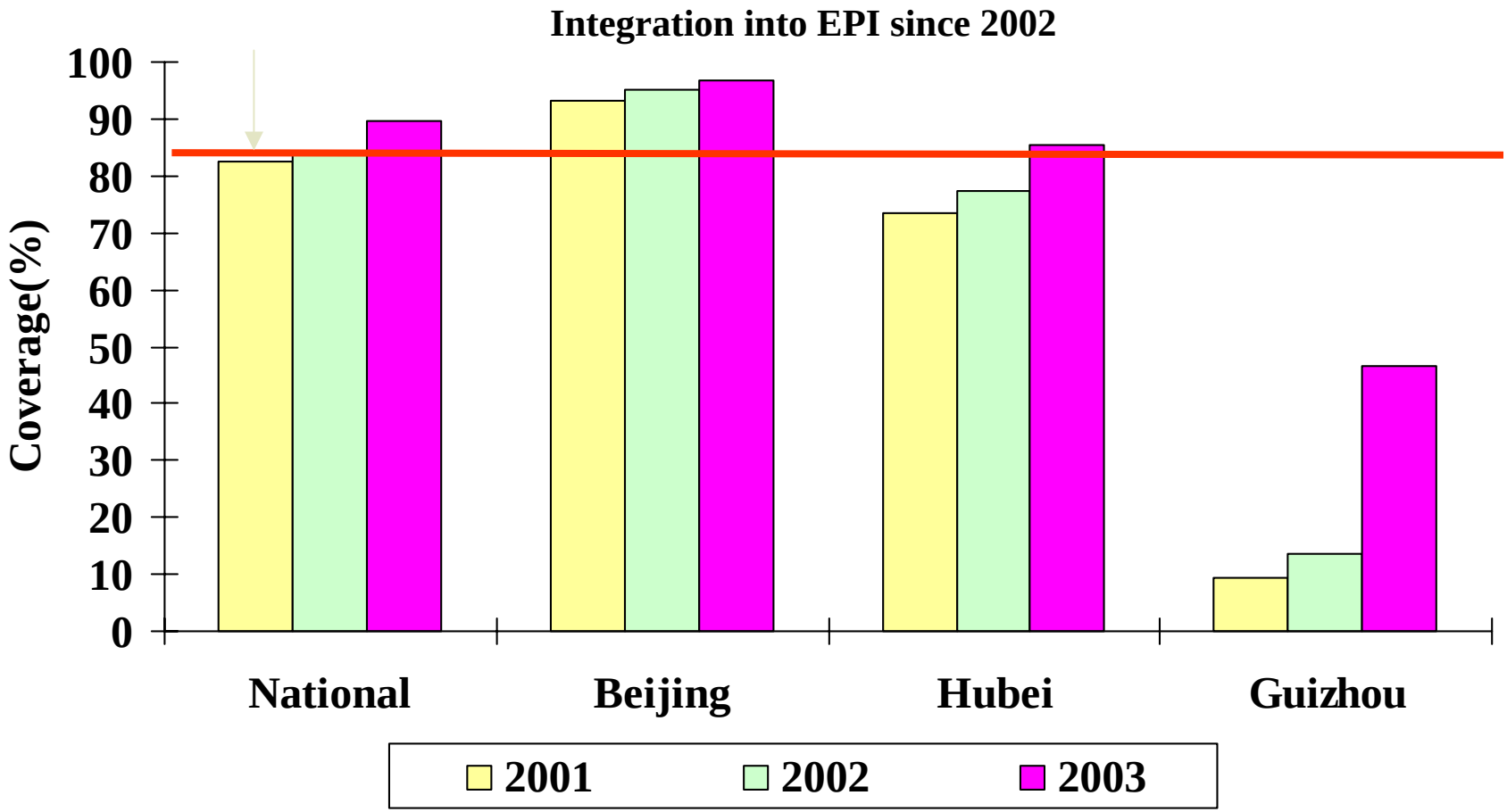
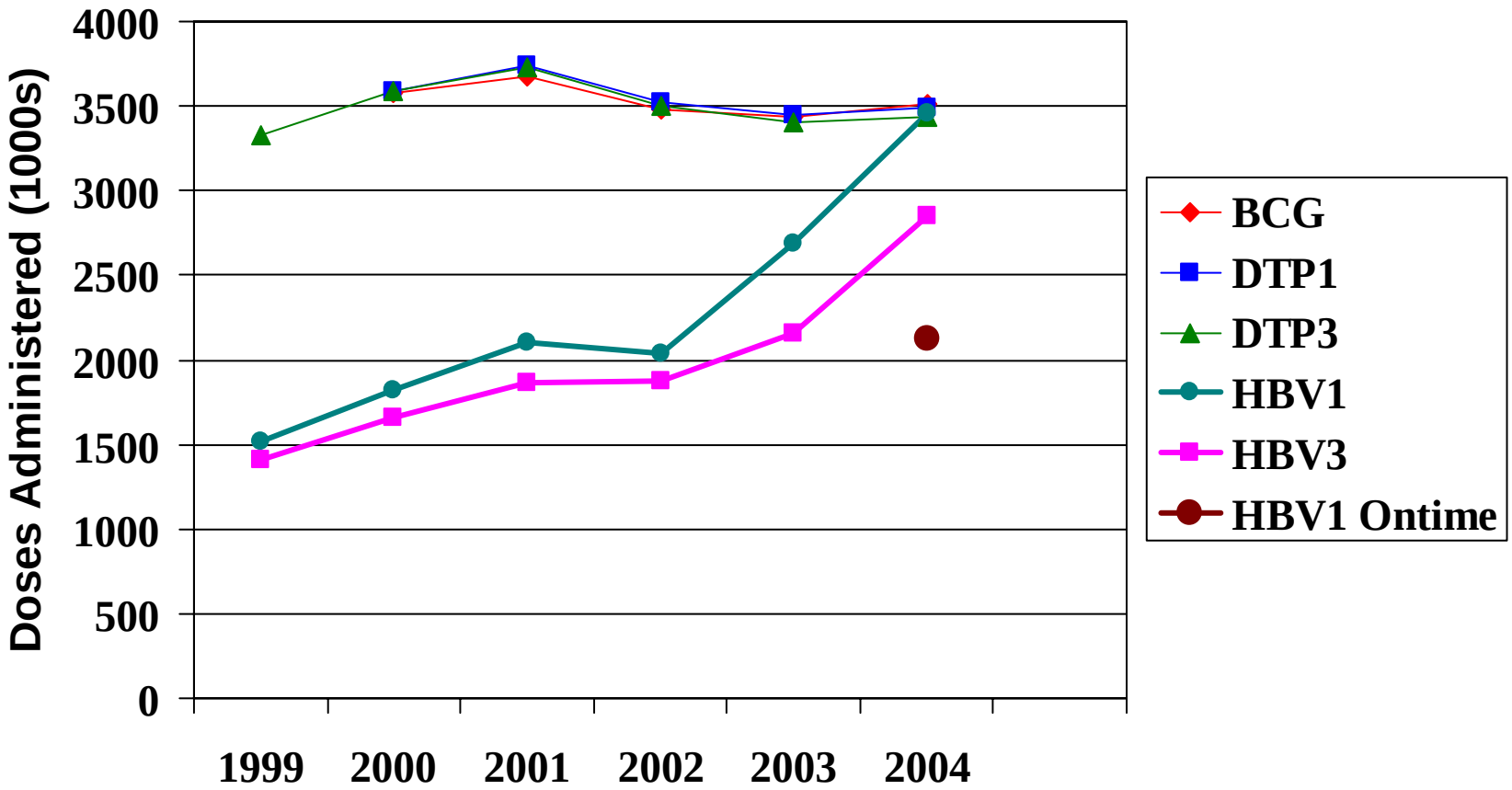
Increase in coverage of HB3



Source: National Coverage Survey, 2004

Progress in Hepatitis B Immunization Western Provinces 1999-2004 *



* Adjusted for corrected data Qinghai (2004), Xinjiang (2003-4)