Chapter 6. Mass immunisation campaigns for measles elimination: necessary and effective, but judicious timing essential

6.1. Chapter Overview

Mass immunisation campaigns have proven an invaluable tool in consolidating polio elimination in Mpumalanga Province, South Africa. More recently this strategy has been adopted for regional measles elimination in southern Africa. There has been criticism that the additional resources consumed by campaigns would be better spent on augmenting comprehensive primary health care services, and that this alone would accomplish measles elimination.

Results from the only cross-sectional immunisation coverage survey ever conducted in a South African province that included all sub-districts, provided valuable information for improving routine immunisation services in Mpumalanga. The survey confirmed that even where acceptable routine immunisation services existed in a rural African province, these were insufficient alone for achieving the high coverage levels demanded for successfully eliminating measles with its remarkably high basic reproductive rate.

An evaluation, by statutory notification and on-site hospital admission review, of the supplemental measles vaccination campaign targeting all children aged 9 months - 14 years attests to the profound impact of the campaign on measles epidemiology. In Mpumalanga, 4,498 measles cases and six deaths were reported by statutory notification during the period 1992-1996, and 182 cases and no deaths following the 1996 mass campaigns, during 1997-1998. Measles accounted for 1,647 hospitalisations and 11 deaths in the pre-campaign period (1992-1996), compared to 60 hospitalisations and no deaths post-campaign, until April 1999.

Examination of costs associated with mass immunisation campaigns has focused almost exclusively on direct health service expenditure. However, other costs including the opportunity cost of deploying skilled health professionals in immunisation teams are

equally important. The psychophysical fatigue that attends exacting field deployment, and waning political and parental interest associated with regular repeated campaigns can negatively impact on coverage. Analysis of coverage levels achieved during recent immunisation campaigns in South Africa supports the contention that injudicious timing of campaigns negatively impacts on coverage.

Mpumalanga data indicates that mass immunisation campaigns will remain a core strategy for eliminating measles, but future campaigns must be judiciously timed and spaced.

6.2. Peer-reviewed publications arising from research summarised in this chapter

* Durrheim, D.N. & Ogunbanjo, G.A. (2000) Measles elimination – is it achievable? Lessons from an immunisation coverage survey. *South African Medical Journal*, 90, 130-135.
* Durrheim, D.N., Ogunbanjo, G.A., Webb, E. & Lee, C.K. (2001) Mass immunisation campaigns in South Africa - The case for judicious timing and spacing. *South African Medical Journal*, 91, 829 - 830.

6.3. Introduction

The eradication of smallpox during the late 1970s has been hailed as the greatest public health achievement to date (Henderson, 1994). This success provided the impetus for the current global poliomyelitis eradication effort. In addition it fuelled speculation that regional progress towards measles elimination might prove the forerunner of global measles eradication.

This optimistic buoyancy resulted in a Southern African Measles Elimination Meeting hosted in Pretoria, South Africa from 2-4 December 1997 and the publication of a measles elimination plan for South Africa (Department of Health, 1998). Recommended strategies adopted were to:

(1) achieve and sustain routine immunisation coverage of ≥95% with one dose of measles vaccine administered at nine months of age;
(2) implement a one-time nationwide "catch-up" measles vaccination campaign targeting all children, aged 9 months - 14 years, regardless of history of measles disease or vaccination;
(3) implement periodic national "follow-up" vaccination campaigns every two to five years targeting all children born after the "catch-up" campaign, aged 9 months - 4 years; and
(4) establish case-based measles surveillance with laboratory confirmation (Centers for Disease Control and Prevention, 1999).

Although the goal of measles elimination enjoys broad support in South Africa, the mass immunisation campaign strategy has galvanised controversy within the public health fraternity. This culminated in a tempestuous reception for the national measles catch-up campaigns conducted during 1996 and 1997 (Thomas & Kibel, 1990; Schoub *et al.*, 1996; Wigton *et al.*, 1996). The potential for mass campaigns to divert resources away from routine services was cited as the principal argument against this approach, with critics arguing that a targeted approach focused on areas of low coverage and attendant epidemic risk or investment of additional campaign resources into primary health care services alone would be more appropriate strategies for South Africa.

Mpumalanga Province is a predominantly rural agricultural area in the northeast of the country flanked by Mozambique in the east and Swaziland in the south. The population of approximately 3 million inhabitants is largely concentrated in a number of urban areas and two former "homelands", Kangwane in the east and Kwandebele in the west. Routine measles immunisation was introduced in 1975, and two doses of measles vaccine (Schwartz strain) are offered to all children at 9 and 18 months of age through the public health system, consisting of 227 fixed clinics, 21 mobile services and 22 hospitals.

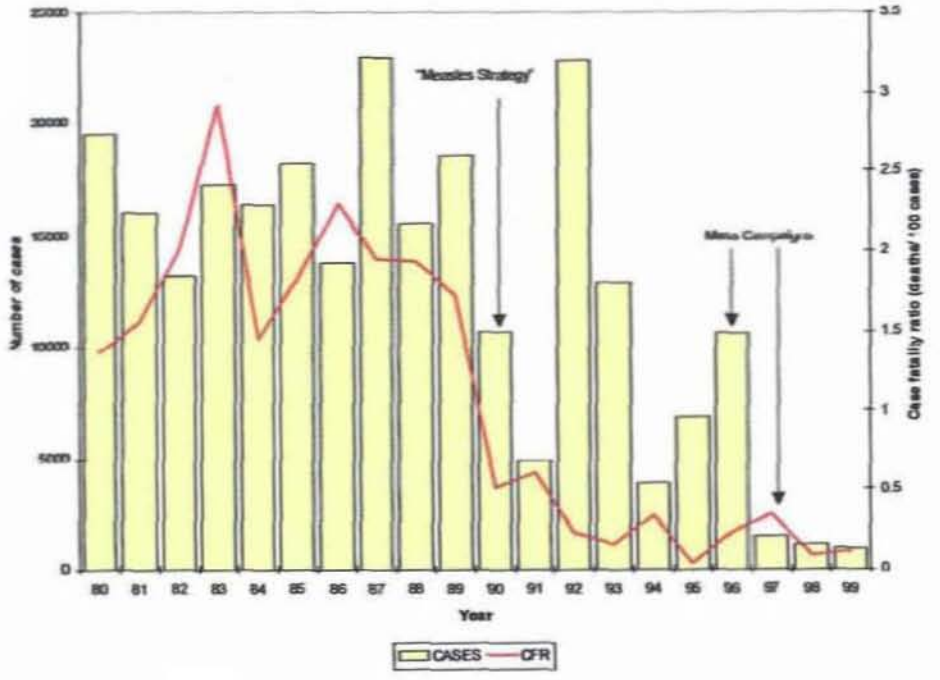
Measles has been a notifiable disease in South Africa since 1979. During the 1980s, 15,000 to 20,000 measles cases and 250-500 deaths were reported each year [Figure 6.1].

In 1990, a nation-wide effort called "The Measles Strategy" was launched to vaccinate previously unimmunised children under 5 years of age against all six Expanded Programme on Immunisation (EPI) target diseases (tuberculosis, diphtheria, tetanus, pertussis, polio, and measles), primarily by increasing availability of vaccinations and by raising public awareness. Following implementation of this strategy, routine measles vaccination coverage rose from 63% in 1989 to 71% in 1990, and measles-related admissions in provincial hospitals declined by 85% (Department of Health, 1995a). Measles, however, remained endemic and epidemics continued to occur periodically during the 1990s, but the case fatality ratio declined sharply in the beginning of the decade and remained at low levels. In contrast to the 1980s when 60% to 70% of reported measles cases were among children aged less than five years, most cases reported during the 1990s occurred among school-aged children and young adults.

Vaccination coverage data were not available for South Africa prior to 1994. In 1994, the first national vaccination coverage survey was performed at provincial level, with a cluster survey technique, sampling 210 children per province, utilised to estimate measles vaccination coverage with at least one dose of measles vaccine in children aged 12-23 months (Department of Health, 1995a). This was estimated at 85% for the country, ranging from 72% to 95% in the nine provinces. Unfortunately, reliable data required for defining vulnerable areas of low immunisation coverage within provinces are not routinely available (Department of Health, 1997).

In 1996-1997, supplemental measles vaccination campaigns were implemented in all nine South African provinces. All children aged 9 months through 14 years were targeted during the campaigns, regardless of previous vaccination or disease history. Overall coverage achieved during the 1996-1997 campaigns in South Africa was estimated at 90% (Department of Health, 1998).

Figure 6.1. Annual measles notifications and case fatality ratio, South Africa, 1980-1999.



Three separate studies were undertaken in Mpumalanga to investigate the value and appropriateness of mass campaigns for measles elimination in a rural South African province. A cross-sectional coverage survey was conducted in each of Mpumalanga's 21 health sub-districts during November 1997. This allowed determination of routine measles coverage, and an insight into the pattern and reasons for immunisation failure. In addition it allowed assessment of whether the levels of routine vaccine delivery required to ensure measles elimination were feasible in a predominantly rural province. Secondly, to evaluate the impact of the 1996 measles mass campaign in Mpumalanga, routine measles surveillance data was analysed and hospital admission registers reviewed to determine measles admission and morbidity trends. Finally, coverage figures at national and provincial level of recent polio and measles mass campaigns conducted in South Africa were scrutinized to detect any important trends for future planning.

6.4. Measles elimination – is it achievable through routine immunisation services in Mpumalanga Province?

6.4.1. Methods

The CDCC in each of the 21 health sub-districts responsible for district Expanded Programme on Immunisation (EPI) activities, was trained on locally adapted WHO coverage survey material during a one-week residential training block just prior to conducting the survey (World Health Organization, 1991). This well-established survey method makes use of a simplified cluster sampling methodology to allow estimation of vaccination status within 10% confidence limits (Henderson & Sundaresan, 1982). The CDCC determined their total district populations using projections from the 1991 national census, validated and adjusted where necessary from other credible sources of demographic information, including tribal or elected municipal authorities, and agricultural unions. The comprehensive community listing with defined population sizes thus constructed was then used to select 30 clusters in each sub-district with probability proportional to estimated size, with a total of 630 clusters selected in the Province.

After simple maps were prepared for each cluster, a starting household was randomly selected using standard approaches specific for urban and rural clusters. Seven individuals in the age group 12-23 months were then selected beginning at the starting household and continuing to the next nearest household. All individuals of the appropriate age group living in the last household were included. The survey was completed within six weeks. On average, 214 children were included per sub-district, with a maximum of 224 in Tonga sub-district. The number of households visited per district ranged from 375 to 3,480, with an average of 1,160 households or 39 per cluster.

Three additional training sessions were conducted with district CDCC at critical points in the survey process to ensure uniformity and correctness of technique. Standard forms were completed for each identified cluster. One form was used to collect demographic details of sampled children and their immunisation history transcribed from child health cards. Antigen administered (BCG, DPT, HepB, OPV, measles), date of administration, dose of antigen where appropriate (DPT, OPV, HepB), and source of immunisation (permanent clinic, mobile clinic, hospital, private practitioner) were all recorded. Where a child health card was not available, the mother or guardian's recollection of immunisation history was recorded and clearly marked "by history" for separate analysis. Sampled children present were examined for a BCG scar.

If one or more immunisations had not been administered, then a second standardised form was completed during the visit. The mother was asked to provide the most important reason why the child failed to receive all immunisations (open-ended). The interviewer categorised reasons according to the most relevant of 20 predetermined "reasons for failure", the major categories being lack of information, lack of motivation or obstacles to immunisation (World Health Organization, 1991). Immunisations were only considered valid during analysis if they were administered in accordance with the provincial EPI schedule (i.e. BCG - as soon as possible after birth; OPV, DPT, HepB - the first dose at six weeks of age with second and third doses at least four weeks apart; and measles - a dose after nine months of age) and recorded on the child health card.

Data was processed and entered into a customised Excel for Windows 97 spreadsheet. Statistical analysis was performed using the SSPS for Windows 95 software package (Norusis, 1992). Weighted provincial coverage was calculated by summation of each district's coverage weighted by the proportion of the Province's population resident in that district. The Pearson correlation coefficient was used to calculate the strength of linear association between measles coverage at district level and other variables of interest, while Spearman's correlation coefficient was used to assess linear association between district ranks for routine measles coverage (1997) and ranks for campaign coverage (1996). Multiple regression, the forward stepwise method with probability of F to enter <=0.50 and probability of F to remove >=0.10, was used to explore the independent contribution of different factors, for example coverage of other antigens and sources of vaccination, to district measles coverage.

6.4.2. Results

The valid weighted population coverage with measles vaccine for children aged 12-23 months in Mpumalanga Province was 71.1% (95% CI = 64.9% - 78.5%). Coverage by card plus history was considerably higher at 83.4% (95% CI = 77.8% - 89.1%). The difference between coverage by card alone and by card plus history was greatest for measles (13% compared to 6-9% for the remaining antigens), due at least in part to a practice of ticking the dose of measles administered on the immunisation card without recording the date. Measles coverage was the lowest of all antigens [Table 6.1].

Table 6.1. Immunisation coverage (%) with EPI antigens - children aged 12-23 months, Mpumalanga Province, 1997.

District	BCG[1]	DPT1[2]	DPT2	DPT3	HepB1[3]	HepB2	HepB3	OPV1[4]	OPV2	OPV3	Measles
Barberton	86	83	83	83	83	83	83	83	83	83	82
	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(97)
Bethal	91	87	86	86	86	86	84	86	86	86	73
	(99)	(99)	(96)	(95)	(96)	(95)	(93)	(97)	(95)	(94)	(91)
Delmas	63	57	57	56	57	57	56	58	57	56	52
	(100)	(96)	(95)	(93)	(95)	(94)	(93)	(95)	(94)	(93)	(87)
Eerstehoek	91	94	93	92	94	93	91	94	94	92	88
	(100)	(100)	(100)	(99)	(100)	(99)	(98)	(100)	(100)	(99)	(94)
Ermelo	81	74	67	60	73	67	59	74	67	60	51
	(94)	(85)	(77)	(69)	(83)	(77)	(69)	(85)	(77)	(69)	(60)
Groblersdal	79	66	64	60	56	54	50	67	65	58	57
	(96)	(94)	(92)	(90)	(86)	(83)	(79)	(94)	(92)	(87)	(80)
Highveld Ridge	96	96	95	92	95	93	90	96	95	92	87
	(98)	(98)	(97)	(94)	(97)	(95)	(92)	(98)	(97)	(94)	(98)
Kabokweni	96	95	95	90	95	95	90	95	95	90	87
	(100)	(100)	(100)	(97)	(100)	(100)	(100)	(100)	(100)	(97)	(91)
KwaMhalanga	81	81	80	80	77	69	62	81	80	80	72
	(100)	(99)	(98)	(97)	(89)	(81)	(71)	(99)	(98)	(97)	(90)
Lydenburg	51	56	48	40	48	43	33	56	48	39	29
	(77)	(76)	(64)	(52)	(62)	(55)	(43)	(74)	(64)	(51)	(40)
Middelburg	84	83	82	82	83	82	82	82	82	82	73
	(95)	(96)	(95)	(94)	(95)	(94)	(94)	(95)	(94)	(93)	(86)
Mmamethlake	99	98	96	91	79	63	51	97	93	88	76
	(99)	(99)	(97)	(91)	(80)	(64)	(51)	(97)	(94)	(89)	(76)
Nelspruit	94	87	86	86	87	86	86	87	86	86	72
	(100)	(99)	(97)	(96)	(99)	(97)	(96)	(99)	(97)	(96)	(83)
Philadelphia	96	96	90	86	90	86	86	90	90	83	84
	(96)	(97)	(90)	(83)	(90)	(86)	(86)	(90)	(90)	(84)	(87)
Piet Retief	65	65	59	56	65	59	56	65	59	56	50
	(91)	(91)	(83)	(73)	(91)	(83)	(73)	(91)	(83)	(73)	(65)
Sabie	78	77	76	74	76	75	73	76	76	74	63
	(99)	(95)	(94)	(93)	(94)	(94)	(92)	(95)	(94)	(93)	(81)
Shongwe	94	93	93	93	93	93	93	93	93	93	82
	(99)	(98)	(98)	(97)	(98)	(97)	(97)	(97)	(97)	(97)	(85)
Standerton	96	87	83	82	86	83	82	87	84	82	84
	(100)	(100)	(98)	(100)	(100)	(98)	(99)	(100)	(98)	(100)	(93)
Tonga	100	97	97	94	97	97	94	98	97	95	87
	(100)	(97)	(97)	(94)	(97)	(97)	(94)	(98)	(97)	(95)	(87)
Volksrust	71	71	67	63	67	59	54	71	67	63	57
	(99)	(99)	(93)	(87)	(93)	(84)	(77)	(99)	(93)	(87)	(79)
Witbank	75	75	75	75	75	75	75	75	75	75	68
	(97)	(100)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(91)
Province	85	83	81	78	81	77	74	83	81	78	72
	(97)	(96)	(94)	(91)	(93)	(90)	(86)	(96)	(94)	(90)	(83)

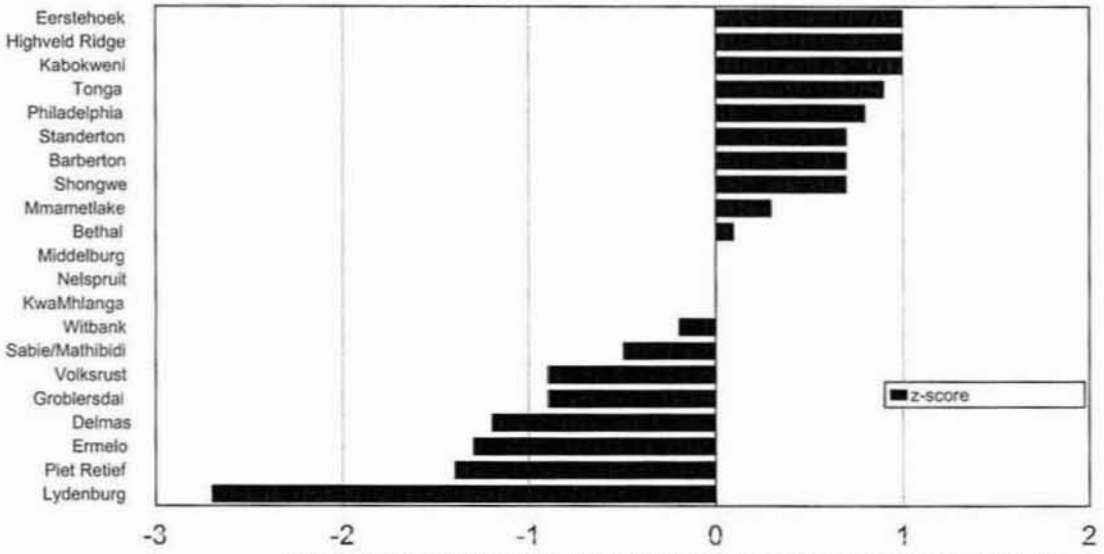
Note: numbers not in parenthesis ( ) are percentage coverage according to child health card alone while numbers in parenthesis ( ) are percentage coverage according to child health card and/or history.

[1] BCG – Bacillus Calmette Guerin; [2] DPT – Diphtheria, pertussis, tetanus; [3] Hep B – Hepatitis B; [4] OPV – trivalent oral polio vaccine.

There was however marked variation in measles coverage across the Province. The z-score varied from -2.7 (Lydenburg) to 1 (Eerstehoek, Highveld Ridge and Kabokweni) (Figure 6.2). The coefficient of variation for district measles coverage was 22.2%. Similarly sub-district measles "drop-out" rates displayed conspicuous variation ranging from 0% in Standerton to 27% in Lydenburg [Figure 6.3]. Of note was the geographical distribution of low coverage sub-districts with the lowest coverage sub-districts generally sharing borders with neighbouring provinces, namely Northern Province in the north and KwaZulu-Natal in the south.

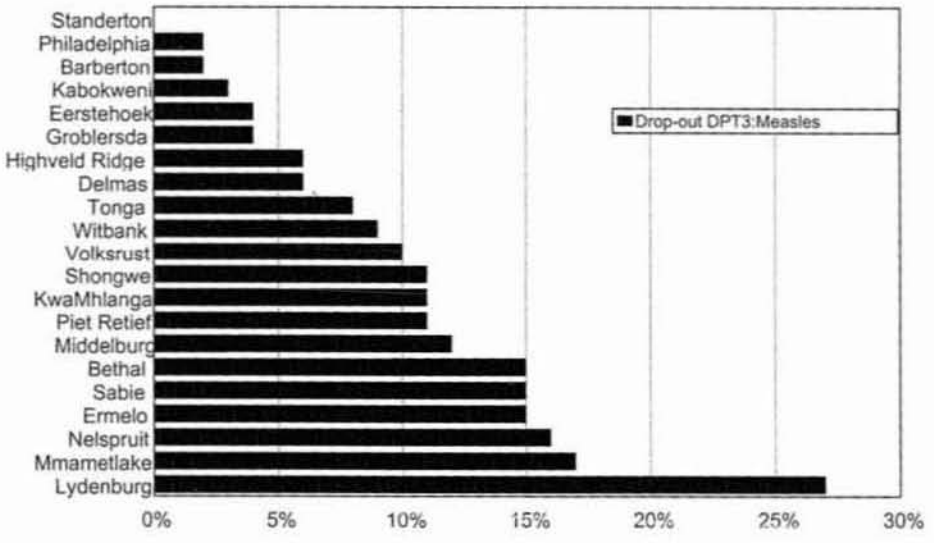
The most important sources of measles vaccine were permanent clinics and mobile clinics, and these accounted for 71.6% and 26.4% of doses recorded, respectively. Hospitals and private practitioners were the source of only 1.4% and 1.1% of measles immunisations recorded, respectively. The immunisation source pattern was heterogeneous [Figure 6.4]. Although the median hospital contribution was 0%, Philadelphia Hospital provided 19% of immunisations in that sub-district. In five predominantly rural sub-districts, fixed clinics were the source of more than 90% of measles immunisations and in 15 sub-districts less than one percent of children received immunisations from private practitioners.

Figure 6.2. Variation in district measles coverage, Mpumalanga Province, 1997.



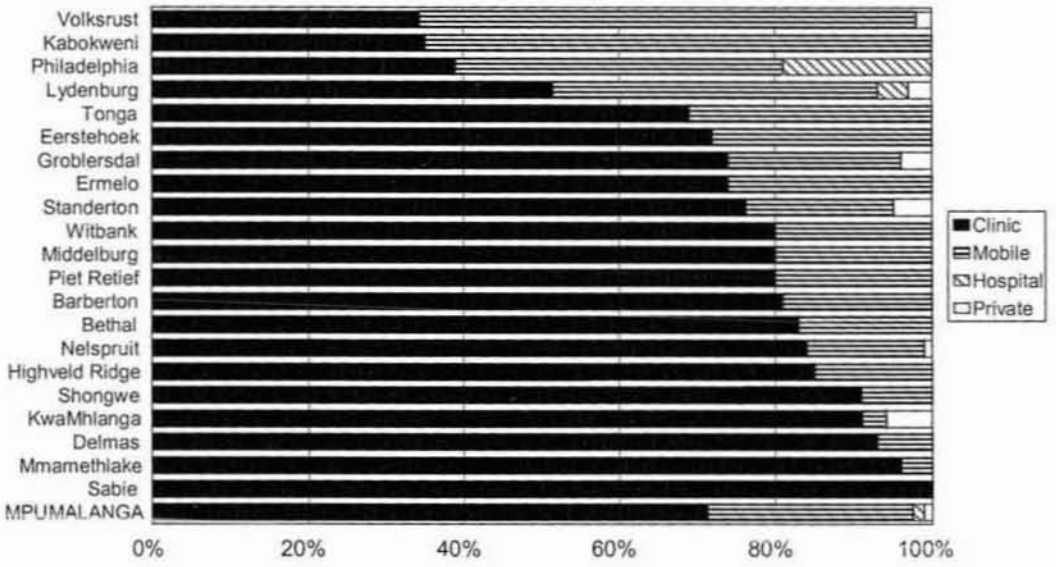
z-score = district coverage represented as standard deviations above or below mean coverage or (district coverage - average district coverage) divided by standard deviation

Figure 6.3. Drop-out rates (DPT3 to measles) by district, Mpumalanga Province, 1997.



Drop out = (Number who received DPT3 - Number who received measles) divided by the number who received DPT3 * 100

Figure 6.4. Source of measles immunisation, Mpumalanga Province, 1997.



"Obstacles to immunisation" accounted for nearly half (49%) of all reasons provided for immunisation failure, while "lack of information" and "lack of motivation" accounted for 30% and 21%, respectively. The most important "obstacles" mentioned were the non-availability of vaccine (9%), place of immunisation being too far (7%) or illness in the child (6%). Important reasons provided in the "lack of information" category were a lack of awareness of the need for immunisation (8%) or timing of immunisation (9%). Under "lack of motivation" the most common reason provided was that immunisation was postponed until a more convenient time (18%).

Sub-district measles coverage was highly positively correlated with DPT3 coverage ($r = 0.960$, $p = 0.000$). The adjusted coefficient of determination (R^2) was 0.917 and only DPT3 coverage remained in the forward stepwise regression model constructed from all variables associated with district measles coverage.

Figure 6.5 depicts notified measles cases in Mpumalanga Province from 1980 to 1997, inclusive. If an epidemic threshold of 220 measles notifications in a single quarter is used, then there were four epidemics in Mpumalanga prior to 1996, viz. fourth quarter of 1980, and the third quarters of 1983, 1987 and 1992, the latter three after an increase in cases during the second quarter. In 1996 there was a marked increase in measles notifications during the second quarter prior to the provincial mass immunisation campaign.

Sub-district measles coverage figures from the present survey were compared to sub-district coverage achieved during the 1996 mass measles campaigns. A strong negative correlation was found between sub-districts ranked routine measles coverage and ranked campaign coverage (Spearman's rho = -0.695, $p = 0.000$) [Figure 6.6].

Figure 6.5. Notified measles cases by quarter, 1980-1997, Mpumalanga Province.

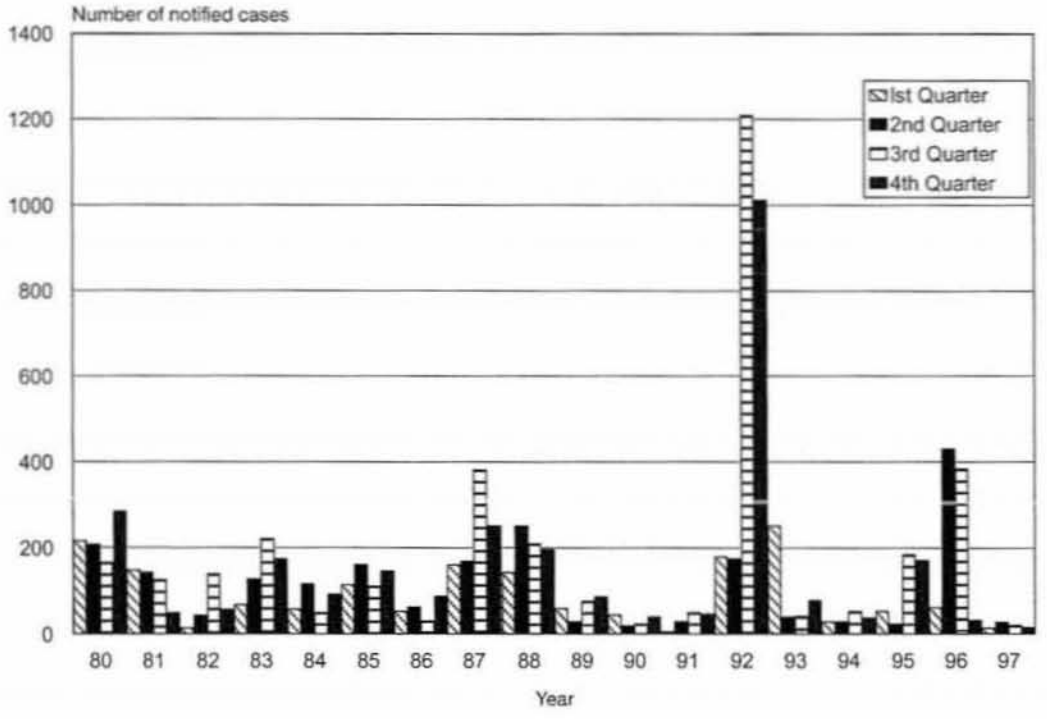
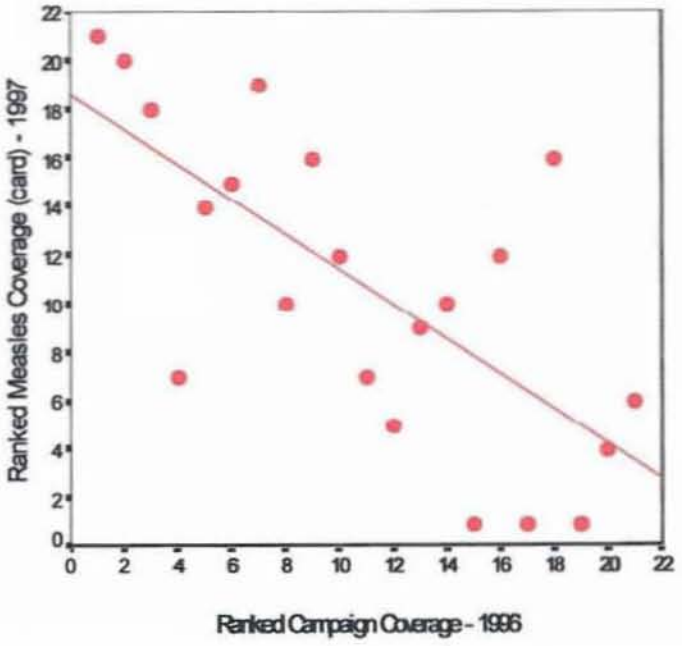


Figure 6.6. **Scatter diagram depicting the relationship between recorded district measles coverage by survey (1997) and district measles campaign coverage (1996).**



6.5. Impact of measles mass immunisation campaigns on measles occurrence and morbidity in Mpumalanga

6.5.1. Methods

Measles surveillance in South Africa involves reporting of physician-diagnosed measles cases and deaths on a statutory notification form to the national Department of Health in Pretoria by the respective Provincial Departments of Health. Reported data include the ICD-9 code of the disease, age, sex, race, date of disease onset, magisterial district, province, and patient outcome (alive or died). Routine measles surveillance data for 1980-1998 gathered through the disease notification system were available as an EpiInfo summary file, and were used to analyse demographic characteristics and plot the time series of reported measles cases.

All hospitals that could have hospitalised patients with measles during 1992-1998 were identified. A questionnaire was sent by fax to all hospitals to request their participation in the study and to obtain baseline information about the availability of hospital records for the study period, annual number of measles hospitalisations, and hospital policy on admitting suspected measles cases. Hospitals that had a policy not to admit suspected measles cases and those without admission registers available for review were excluded from the study. Measles-related hospitalisation was defined as "a patient diagnosed with measles on admission and/or on discharge from January 1, 1992 through to the date of the admission register review (March - April 1999)". Hospital infection control nurses were trained to review the admission registers and compile a line list of case-patients on a standard form. The following patient information was abstracted: age, gender, ethnicity, admission and discharge dates, diagnoses, and the outcome of hospitalisation (died or discharged). Admission and discharge diagnoses were abstracted exactly as they appeared in the hospital admission registers, and in the same temporal order.

To estimate the rate of measles-related complications patients for whom one or more of the following diagnoses were recorded on hospital admission and/or on discharge were

included. Diagnoses included: pneumonia, gastrointestinal complications (diarrhoea and vomiting), otitis media, and neurological complications (convulsions, meningitis and encephalitis). Hospitalised measles patients for whom the outcome in the admission register was recorded as "died" were considered measles-related deaths. The accuracy of the clinical diagnosis of measles could not be determined, as serologic confirmation was not routinely performed in South African hospitals prior to October 1998, nor was it possible to assess the appropriateness of the other recorded diagnoses and the accuracy of the recorded outcome. Data were entered in a customised EpiInfo database and analysis of pre- and post-campaign variables was performed using chi-square and Kruskal-Wallis tests for comparing proportions and median tests for evaluating differences between medians (Dean *et al.*, 1996; SAS Institute, 1997).

6.5.2. Results

During the period 1980-1998, 10,371 measles cases and 101 deaths were reported through the routine surveillance system in Mpumalanga Province; the lowest number of measles cases was notified in 1990 and 1991 (135 cases in both years) and the highest in 1992 (2,583 cases). During the five-year pre-campaign period (1992-1996), a total of 4,498 measles cases were notified with an annual average of 900 cases [Table 6.2]. After the 1996 campaign, no measles deaths and record low numbers of measles cases were reported in 1997 and 1998 (92 and 90, respectively). Both before and after the 1996 campaign, most notified cases occurred among Black Africans; after the campaign, the proportion of reported measles cases that occurred in this population group increased.

Table 6.2. Characteristics of notified measles cases, Mpumalanga Province, South Africa, 1992-1998.

	Before the campaign (1992-1996)	After the campaign (1997-1998)	p
Notified measles cases	4,498	182	
Average annual number of notifications	900	91	
Age distribution[1]			
<1 year	190 (4%)	6 (3%)	0.51
1-4 years	1,067 (24%)	50 (28%)	0.28
5-9 years	1,938 (45%)	87 (49%)	0.43
10-14 years	867 (20%)	26 (15%)	0.08
≥15 years	289 (7%)	9 (5%)	0.42
Black African	3,701 (83%)	172 (95%)	<0.0001
Female Gender	2,225 (50%)	93 (51%)	0.65
Died	6	0	

[1] Data on age was available for 4,529 notified measles cases.

Sixteen of 22 public hospitals in Mpumalanga participated in the hospital study, representing a total of 3,512 (82%) acute-care hospital beds. One of 10 private hospitals participated. From January 1992 to April 1999, a total of 1,707 measles-related hospitalisations occurred in the participating hospitals [Figure 6.7]. The average annual number of measles-related admissions declined by 91%, from 329 during the five-year pre-campaign period to 29 in the first two post-campaign years [Table 6.3].

Table 6.3. Characteristics of patients hospitalised with measles in Mpumalanga Province, Jan 1992 - Apr 1999.

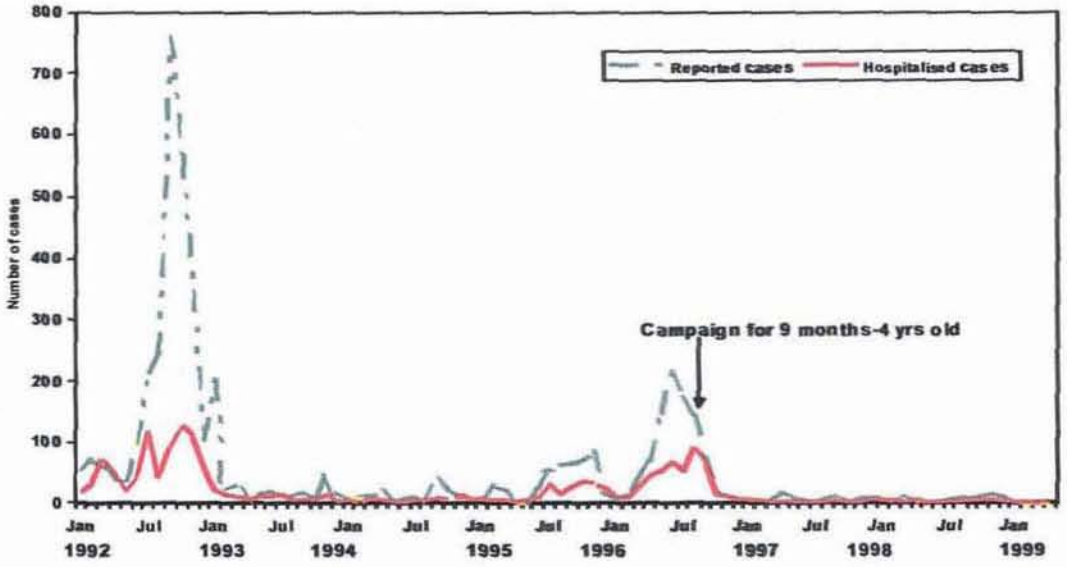
	Before the campaign (1992-1996)	After the campaign (1997- Apr 1998)	P
Number of hospitalizations	1,647	60	
Average annual number of hospitalizations	329	29[1]	
Age distribution[2]			
<1 year	156 (10%)	7 (13%)	0.48
1-4 years	533 (33%)	21 (39%)	0.37
5-9 years	622 (39%)	21 (39%)	0.99
10-14 years	221 (14%)	2 (4%)	0.03
≥15 years	64 (4%)	3 (5%)	0.83
Mean age in months (Standard Deviation)	70.7 (52.7)	59.1 (57.4)	0.03
Median age in months	60	48.5	0.02
Female gender	48%	41%	0.31
Hospital located in a former homeland[3]	1,240 (75%)	44 (73%)	0.77
At least 1 recorded complication	224 (22%)	3 (6%)	<0.01
Diagnosed with pneumonia on admission and/or discharge	161 (16%)	3 (6%)	<0.05
Diagnosed with measles both on hospital admission and on discharge[4]	561/606 (93%)	20/31 (65%)	<0.0001
Mean hospital stay in days (SD)	6.9 (7.5)	5.5 (3.5)	0.09
Median hospital stay in days	6	5	0.28
Died in the hospital	11	0	

[1] Average annual number of hospitalisations for 1997-1998. [2] Information on age was available for 1,650 patients.

[3] Hospitals: Themba, Embhuleni, Shongwe and Philadelphia.

[4] Patients diagnosed with measles on the admission with one or more recorded diagnosis on discharge (n=637).

Figure 6.7. Measles-related hospital admissions and notified measles cases, Mpumalanga Province, Jan 1992 – Apr 1999.



Both before and after the campaign, most hospitalisations occurred in four hospitals located in former "homeland" areas. Compared to the pre-campaign 5-year period, declines were observed during 1997-1998 in the mean age of hospitalised patients, the proportion of patients with ≥1 measles-associated complication, the proportion of patients diagnosed with pneumonia, and the mean duration of the hospitalisation. None of the patients hospitalised with measles was recorded as HIV positive. All 11 measles-associated deaths occurred among patients admitted during the pre-campaign period (1992-1996), for a pre-campaign case fatality ratio of 1.1 deaths per 100 measles-related hospital admissions.

6.6. Trends in mass immunisation campaign coverage in South Africa

6.6.1. Methods

The coverage data gathered through collation of vaccinator completed tally-sheets during campaigns at provincial and national level of all mass immunisation campaigns conducted in South Africa were investigated to determine differences in coverage by time, province, antigen (measles and polio vaccine) and between the two rounds of polio immunisation, two doses of vaccine four weeks apart during polio campaigns.

The Chi-square test for trend was used to analyse differences in coverage over time (Dean *et al.*, 1996).

6.6.2. Results

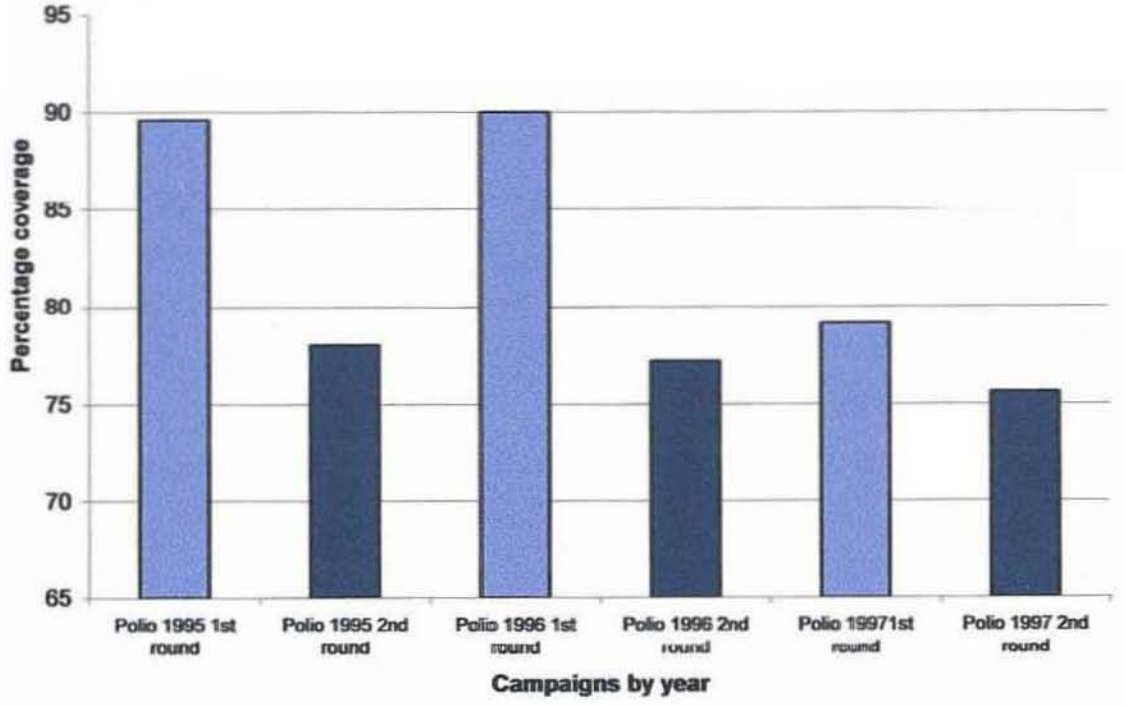
There were marked declines in coverage during subsequent polio mass campaigns over time [Figure 6.8]. The decreasing national polio campaign coverage trend is initially concealed in 1996 as the Western Cape conducted their only polio campaign in 1996. When 1996 Western Cape data is excluded to allow comparison over the three years for the remaining eight provinces, it is found that the annual polio mass campaign coverage

declined monotonically by 7.7% between 1995 and 1997, a highly statistically significant trend (Chi-square test for trend = 7465.3, DF = 1, $p < 0.001$).

The decline in coverage was particularly acute within polio campaigns. The decrease in second-round national coverage was 11.7% in 1995, 12.8% in 1996 and 3.5% in 1997. The majority of provinces mirrored this trend, with a decrease in second round coverage in six of eight provinces in 1995, eight of nine provinces in 1996 and seven of eight provinces in 1997.

There was no significant decline in measles campaign coverage between the mass campaigns conducted in 1996 (91.1%) and 2000 (91%). However three provinces conducted campaigns from nine months to under 15 years in 1996 and it is not possible to disaggregate the under six years coverage for these provinces. Therefore to ensure comparability of coverage it is useful to compare the coverage achieved by the six provinces (Eastern Cape, Northern Province, KwaZulu-Natal, Northern Cape, Gauteng and Western Cape) that conducted campaigns targeting children aged 9-59 months in both 1996 and 2000. This was again similar, being 89.6 % in 1996 and 91% in 2000.

Figure 6.8. Coverage during mass polio immunisation campaigns, South Africa, 1995 –1997.



Note truncated vertical axis.

6.7. Discussion

Immunisation against measles demonstrates some of the greatest strengths and weaknesses of public health programmes. The discrepancy between the availability of an efficacious and cost-effective measure and the relatively poor record in routinely realising its full potential is highlighted by the findings of the province-wide coverage survey. Nearly 30% of children surveyed in Mpumalanga did not have a record of measles immunisation and were therefore potentially at risk for the complications associated with measles infection in developing settings (World Health Organization, 1995; Hussey, 1997). Nevertheless these results represent a marked improvement on previous coverage surveys conducted within the borders of Mpumalanga Province. Measles coverage recorded by card was found to be 59% in 1991 and 69.5% in 1994 (Verburgh & Crisp, 1992; South African Vitamin A Consultative Group, 1994). The latter included 20.7% of measles doses administered before nine months of age, doses considered invalid in the present analysis. This increase is due, at least in part, to the restructuring of health services in the Province, with a commitment to delivering immunisation on each clinic day and extension of clinic services to previously under-served areas.

It is important that Mpumalanga should continue to optimise routine delivery of measles vaccine (Lambert & Siegrist, 1997). However, when present coverage is considered in the light of measles epidemiology, it becomes evident that Mpumalanga will not achieve measles eradication by routine immunisation alone (Expanded Programme on Immunisation, 1996). Measles is a remarkably contagious disease with a basic reproductive rate (R_o) of 15-17 in developing settings, like sub-Saharan Africa (Schoub, 1989; Anderson & May, 1992; McLean, 1992). As a result, the critical level of population vaccination immunity necessary for interrupting transmission is 92-95%.

Although a number of antagonists remain sceptical that measles can be eradicated, there is a burgeoning belief that the goal is feasible, cost-effective and worth pursuing (Evans, 1985; Tamblyn, 1995; Cutts & Steinglass, 1998; Durrheim & Ogunbanjo, 2000). Factors

favouring measles eradication include the successful eradication of smallpox, the anticipated success of polio eradication and the success of measles elimination in the Americas and Finland (Risi *et al.*, 1985; Peltola *et al.*, 1994; Peltola *et al.*, 1997; Watson *et al.*, 1998; Hersh *et al.*, 2000). It is notable that much of the success achieved in South America has been accredited to well-organised single-dose mass campaigns (Expanded Programme on Immunization, 1994).

Concerns have been expressed that campaigns may be unsustainable and divert critical resources from routine health services. However it is clear from routine sub-district coverage figures that if Mpumalanga Province is to achieve the goal of measles elimination, supplementary immunisation will be required (Barron *et al.*, 1987; Global Programme for Vaccines of the World Health Organization, 1994; Wigton *et al.*, 1996).

The initial experience with a mass measles campaign in Mpumalanga was positive with unprecedented political, community and health worker support. The expected epidemic in 1990/1991 did not materialise because of the accelerated immunisation campaigns and the measles campaign in Mpumalanga during the third quarter of 1996 averted a large-scale epidemic predicted by mathematical modelling (McLean, 1995; Department of Health, 1998). Coverage was 104.3% in the latter campaign, with more children immunised than initially targeted due to flows across provincial and international borders, in particular from the Northern Province of South Africa and Swaziland (Department of Health, 1998).

The need for repeated campaigns to avert measles epidemics that occur despite high routine coverage, due to the accumulation of susceptible individuals and waning immunity, has been appreciated both in South Africa and countries where interruption of indigenous measles transmission has been accomplished (Abdool Karim *et al.*, 1993; Cutts & Markowitz, 1994; Centers for Disease Control and Prevention, 1998; Cox *et al.*, 1998).

We found profound variation in sub-district measles coverage, a finding also previously documented in South Africa at local level and explained largely by fragmentation of health service delivery and vast socio-economic differentials in the population (Byarugaba, 1991; Schoub & Martin, 1993). Of considerable interest was the strong negative association between measles campaign coverage (1996) and routine coverage (12-23 months) found at sub-district level. Although numerous factors may have contributed to this finding, it provides support for a blend of routine permanent clinic-based and outreach services, supplemented by mass immunisation activities in low coverage areas, as this strategy appears effective in reaching children who missed their routine immunisations (Miller, 1994; Edelson, 1995).

In addition to rapidly increasing immunisation coverage, campaigns have been accredited with effectively mobilising additional political, human and financial resources, and improving logistical systems for vaccine delivery (Shepard *et al.*, 1989; De Quadros, 1996) .

The experience of one sub-district, Philadelphia, where the large public hospital has conducted a sustained campaign to minimise missed opportunities for childhood immunisation, contrasts with the proportional contribution of hospitals in other sub-districts. Attempts to address health service missed opportunities in South African hospitals previously have had little impact, with one study in the Western Cape recording missed opportunities at a hospital exceeding 50% despite an attempt to eliminate missed opportunities (Metcalf *et al.*, 1994). This should however not deter Mpumalanga facilities from making every attempt to minimise missed opportunities for immunisation by using all contacts with children to screen their immunisation cards and provide immunisations immediately where indicated (Cutts *et al.*, 1991; Hutchins *et al.*, 1993; Bachmann & Barron, 1996).

When investigating reasons for immunisation failure many of the factors emphasised by previous studies were in evidence, viz. the proximity of health facilities, district of residence, mother's awareness of disease and importance of immunisation, and false

beliefs of mothers regarding contra-indications to immunisation, in particular fever (Cutts *et al.*, 1989; Limtragool *et al.*, 1992; Begg & Nicoll, 1994; Bhuiya *et al.*, 1995; Brugha & Kevany, 1995). Many of these factors are difficult to address but the finding of non-availability of vaccine at health facilities cannot be condoned.

False contra-indications to measles immunisation, particularly among health professionals, are recognised as an important barrier to routine measles coverage (Lakhani *et al.*, 1987). During a survey conducted prior to the WHO sponsored EPI Review in South Africa during 1997 to explore vaccinators' knowledge, attitudes and practices at 20 randomly selected clinics in Mpumalanga, vaccinators were presented with a number of vignettes and asked to provide their usual response (Department of Health, 1997). Only 55% of vaccinators interviewed indicated that they would provide measles immunisation to a nine-month old child with a mild fever (38°C) despite this being a false contra-indication (Galazka *et al.*, 1984; Hull, 1987; Expanded Programme on Immunization, 1988; Clements, 1996).

The EPI coverage survey technique has been maligned by purists because of its susceptibility to non-homogenous clustering but field-based public health practitioners have noted the direct and indirect benefits of properly conducted EPI surveys coupled with appropriate feedback (Harris & Lemeshow, 1991). These include, an increase in the provision of outreach services, targeting of socially marginalized communities, appointment of additional community health workers, improvement in supervision and marked increases in immunisation coverage (Joseph *et al.*, 1988; Brugha & Kevany, 1996; LeBaron *et al.*, 1997). In this regard, the experience of Eerstehoek sub-district in Mpumalanga should be mentioned. Three immunisation coverage surveys, making use of the standard EPI technique, have been conducted in recent years in this sub-district. Measles coverage by card in the age-group 12-23 months increased from 48.0% in 1992, to 86.6% in 1994, to 88.1% in the present survey.

Following implementation of the 1996 measles mass vaccination campaigns, the number of measles cases and deaths reported through the routine surveillance system in all nine

provinces of South Africa declined to record low levels. In Mpumalanga Province, the routine measles surveillance system documented a 90% post-campaign reduction in the annual number of measles notifications. Review of the 1992-1999 hospital admission registers documented a 91% post-campaign reduction in the annual number of measles-related hospitalisations. The admission register review identified more measles-related deaths among hospitalised patients (11) than were notified through routine surveillance (6). Following the campaign, during 1997-1999 no measles-related deaths were notified or identified through the review of hospital admission registers until the end of the hospital admission record review (March 30, 1999).

In interpreting these findings it is important to note that diagnosis of measles in Mpumalanga hospitals during 1992-1998 was entirely clinical as little laboratory confirmation was performed. Hospital admission registers were incomplete in certain participating hospitals, and alternative patient information sources, including nursing records, measles record books and infection control registers, were used to supplement admission registers where available. However, most participating hospitals had complete admission records for recent years (1996-1999), providing a more precise assessment of the measles-associated hospitalisations in the post-campaign period. The 1996 mass measles vaccination campaign coincided with an increase in reported measles incidence and it is not possible to separate the effect on immunity resulting from the campaign from that of the 1995-1996 measles epidemic on the subsequent reduction in measles morbidity and mortality. The relatively short post-campaign observation time limits inferences about the duration of the reduction in measles disease burden.

Approximately 80% of the South African population have little or no access to the private sector and relies mainly on the public sector for their health care needs and this proportion is even higher in rural areas (McIntyre *et al.*, 1995). Thus it is unlikely that the post-campaign reduction of measles-related hospitalisations and hospital-based deaths was overestimated given the high participation rate of public hospitals and availability of generally complete admission registers for post-campaign years in the participating hospitals. Moreover, it is likely that the proportion of patients incorrectly diagnosed with

measles on hospital admission may have increased following the 1996/1997 campaigns compared to the pre-campaign period, due to a decreased positive predictive value of the clinical diagnosis of measles in the presence of reduced disease incidence (Brown *et al.*, 1994; Ferson *et al.*, 1995; Durrheim & Speare, 2000).

Until the introduction of enhanced case-based measles surveillance in late 1998, that includes epidemiological investigation and laboratory confirmation of suspected cases, notifications of measles cases and deaths have been the only tool for monitoring disease trends in South Africa. Measles notification in South Africa is incomplete, with multiple deficiencies in the passive routine surveillance system (Durrheim *et al.*, 2001c). Thus in the absence of a fully functional case-based surveillance system with laboratory confirmation of all suspected measles cases, the review of hospital admission registers in Mpumalanga was useful in verifying the reduction in measles morbidity and mortality observed in the routine surveillance system. In October 1998, a new case-based measles surveillance system that requires laboratory confirmation and epidemiological investigation of all suspected measles cases was introduced in South Africa. Although this new system is not yet fully functional in all parts of the country, available data suggest that measles virus does not cause the majority of clinically diagnosed and reported measles cases in South Africa. Of 220 sera collected from suspected measles cases tested at the National Institute of Virology in Sandringham, South Africa, only 12 (5.5%) were measles IgM positive, but 106 (48%) were rubella IgM positive and 28 (13%) were IgM positive for human herpes virus 6 (Blackburn *et al.*, 2000).

During the 1990s, South Africa experienced one of the worst HIV/AIDS epidemics in Africa (Williams & Campbell, 1998). In the 1998 National HIV Seroprevalence Survey, the estimated rate of HIV-positive women attending public antenatal clinics in Western Cape was lowest in the country (5%), but in Mpumalanga it was 30% (Department of Health, 1999). Implications of the ongoing HIV/AIDS pandemic on measles control have not yet been fully elucidated, but a recent publication suggests that the HIV/AIDS epidemic might impede measles elimination efforts in several ways (Moss *et al.*, 1999). The available post-campaign routine measles surveillance data from South Africa, as well

as the data collected through the hospital study in Mpumalanga indicate that transmission can be markedly reduced and possibly interrupted even in areas with high HIV prevalence. Since our study was not specifically designed to investigate the interaction between the HIV/AIDS epidemic and the measles elimination efforts in South Africa, further research is needed to evaluate this important issue.

Mass immunisation campaigns have proven to be an invaluable tool in the drive towards polio eradication, providing adequate levels of protection in the youthful portion of the population who are at greatest risk of infection and contribute most to poliovirus transmission (Hull *et al.*, 1994). Mass immunisation campaigns will continue to be an essential component of the measles elimination drive because the remarkably high basic reproductive rate, R_0, of measles defies elimination by routine coverage alone and differential global progress will inevitably result in repeated introduction of measles virus into countries that have achieved interruption of wild measles virus circulation (Fenner, 1998; McLean & Anderson, 1988; Durrheim & Ogunbanjo, 2000).

The euphoria accompanying disease eradication or imminent extinction appears to cloud thorough examination of costs associated with mass immunisation campaigns. Elaborate economic analyses guaranteeing eventual societal savings, focus almost exclusively on direct health service expenditure, including the costs of vaccine and consumables, campaign waste disposal and marketing. Although these costs themselves have been recognised as a constraint to sustained pulsed campaigns, less visible costs may prove a greater impediment to achieving high coverage in follow-up campaigns (Global Programme for Vaccines of the World Health Organization, 1994). Most prominent amongst the latter are the opportunity costs resulting from the deployment of skilled health professionals in immunisation teams, as demanded by statute.

A commonly discounted campaign consequence is the psychophysical fatigue amongst health care workers that attends exacting field deployment. Waning political interests associated with decreased novelty of repeated campaigns are also to be expected. Maintaining a perception of campaign value amongst parents is also a challenge to the

health system. These factors detrimentally affect campaign coverage and this effect appears amplified by close spacing of mass immunisation campaigns.

Scrutiny of coverage achieved during recent mass immunisation campaigns in South Africa supports this contention. The decline in coverage appears particularly acute within polio campaigns as it is necessary to provide each child with two doses of vaccine four weeks apart. The decline in national coverage achieved in subsequent polio vaccination campaigns is further evidence of this trend. The absence of a significant decline in measles campaign coverage between the 1996 and 2000 campaigns provides support for an approach that spaces campaigns further apart, in this case at a four year interval for measles compared to the one year interval for polio.

Appropriate mathematical modelling of the accumulation of susceptibles may prove valuable for limiting the potential epidemic risk of extended inter-campaign intervals and research into optimal timing of campaigns is clearly necessary (Durrheim *et al.*, 2001f).

6.8. Conclusions

The goal of measles elimination in South Africa and the southern African region has altruistic and economic appeal if it is indeed achievable. Although there is documented improvement in routine coverage with measles immunisation in Mpumalanga Province over time and the cross-sectional district survey demonstrated some scope for further enhancing routine immunisation services, coverage levels found make elimination highly improbable by routine vaccination alone. The strong negative correlation between routine and campaign coverage at district level provides support for the complimentary approach of combining routine and supplementary immunisation for measles elimination in areas similar to Mpumalanga Province.

The measles disease burden, notably deaths and hospital admissions, was considerably reduced after a mass measles immunisation campaign, compared to the pre-campaign period. Although longer observation is needed to estimate the long-term impact of the

campaign, this finding adds encouraging evidence that measles elimination may be achievable in southern Africa, when two-dose routine measles immunisation is coupled with mass immunisation campaigns.

However, the South African data suggests that repeated and closely spaced mass immunisation campaigns are associated with declining coverage, and health care system fatigue. In order to achieve coverage levels that justify the commitment of considerable scarce resources it is essential that future campaigns be judiciously timed and spaced.

Chapter 7. Optimising leprosy control after achieving the elimination target

7.1. Chapter Overview

In South Africa, leprosy has been a notifiable condition since 1921. Although the WHO elimination target of less than one case per 10,000 population has been achieved at country-level, the distribution of leprosy in the country is distinctly heterogeneous, with a prominent "leprosy belt" of greater prevalence stretching across Mpumalanga Province into northern KwaZulu-Natal. The highest prevalence in this "belt" has historically been Ermelo Magisterial District. Recently few newly detected leprosy patients in this district raised concerns that health system changes may have resulted in failure to detect leprosy cases. Thus a large-scale community awareness campaign was conducted followed by an intensively advertised screening programme of three-month duration at schools and central gathering points in villages and farms from 1 June to 31 August 2000. One thousand one hundred and seventy seven people presented for clinical screening at designated points, while 790 scholars were screened at schools and an additional 1,433 people were screened at their homes by the field team. Forty four people with skin or nervous system lesions compatible with leprosy were referred for specialized assessment and biopsy where indicated. Four new leprosy patients were diagnosed, including an elderly lady with pronounced disability. Two of these patients had prior contact with the health service due to dermatological manifestations of leprosy without diagnosis being made. All four patients provided a history of close prolonged contact with known leprosy patients. Ongoing intense tracing and follow-up of close contacts of proven leprosy cases may be a more efficient method of detecting leprosy cases in areas that have accomplished "leprosy elimination", than resource intensive community surveys.

7.2. Peer-reviewed publication arising from research summarised in this chapter

* Durrheim, D.N., Fourie, A., Balt, E., le Roux, M., Harris, B.N., Matebula, M., de Villiers, M. & Speare, R. (2002) Leprosy in Mpumalanga Province, South Africa – Eliminated or hidden? *Leprosy Review, in press.*

7.3. Introduction

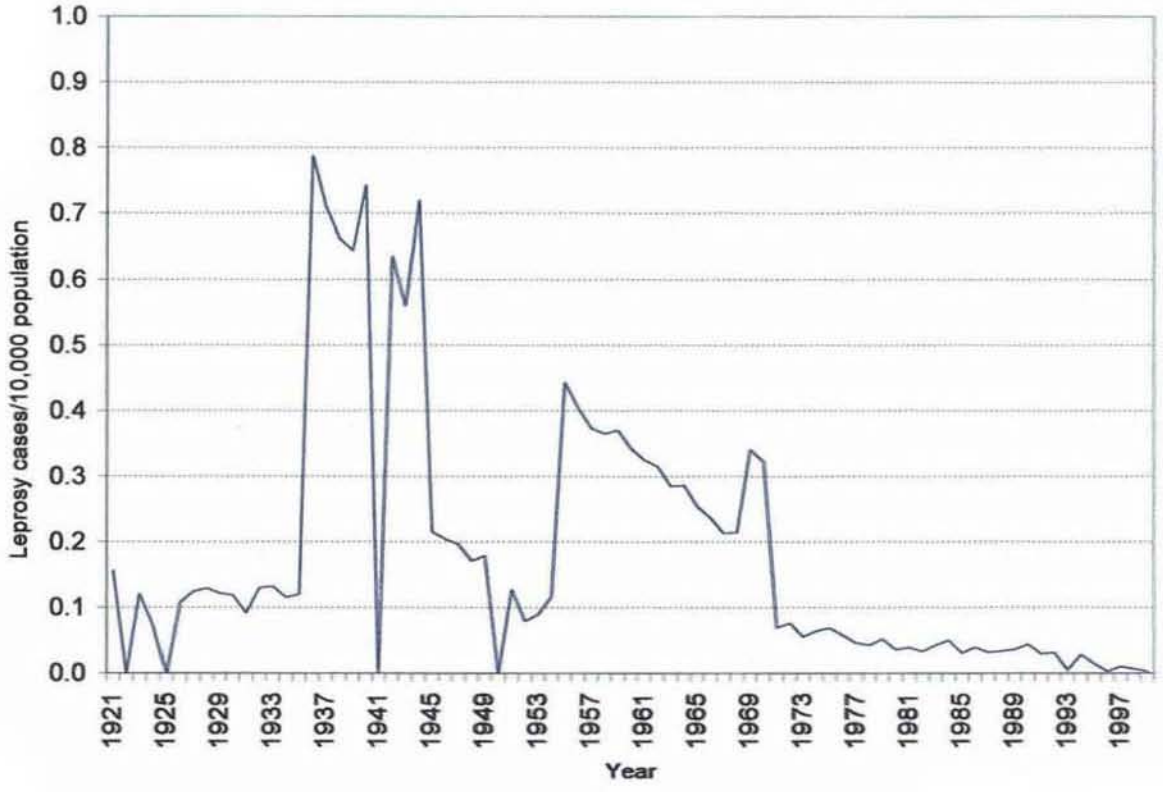
The target of eliminating leprosy as a public health problem in all countries by 2000 has proven elusive despite the availability, during the past two decades, of safe and effective fixed-duration multidrug treatment (MDT) (World Health Organization, 1992; World Health Organization, 1994c). However progress towards the elimination goal of attaining a prevalence level below one case per 10,000 population has been heartening with a 86% reduction in global prevalence since 1985 (Noorden, 1993; World Health Organization, 2000a). Of the 122 countries considered endemic in 1985, 98 have since achieved the elimination target.

Control efforts are now concentrated on the 11 countries that contribute 89% of global prevalence and 92% of new leprosy cases detected (World Health Organization, 2001). Although this is clearly appropriate, it is equally important to sustain gains achieved in formerly endemic areas. Proof of long-term carriage of *Mycobacterium leprae* DNA in the nose, suggests that carriers without frank disease may be an important reservoir for ongoing transmission (Jacob John, 1998). Thus diminishing public health control efforts, a phenomenon that has often followed highly successful disease control programs, could result in re-emergence of leprosy.

Although leprosy is endemic in South Africa and has been notifiable since 1921, official Ministry of Health notification data indicate that the WHO elimination target was already achieved at country-level prior to the initiation of leprosy notification [Figure 7.1]. However the distribution of leprosy in South Africa is distinctly heterogeneous. A prominent "leprosy belt" of greater prevalence stretches across Mpumalanga Province into northern KwaZulu-Natal [Figure 7.2] (Department of Health, 1976). Although the figure only provides numbers of cases detected and not a rate, the rural areas with the highest number of cases also have amongst the lowest district populations. Surprisingly, the heart of this affected area does not border Mozambique, a country where leprosy is prevalent, but is located in the Eastvaal Region of Mpumalanga Province, where the population is relatively stable and Mozambican migrants have not historically settled.

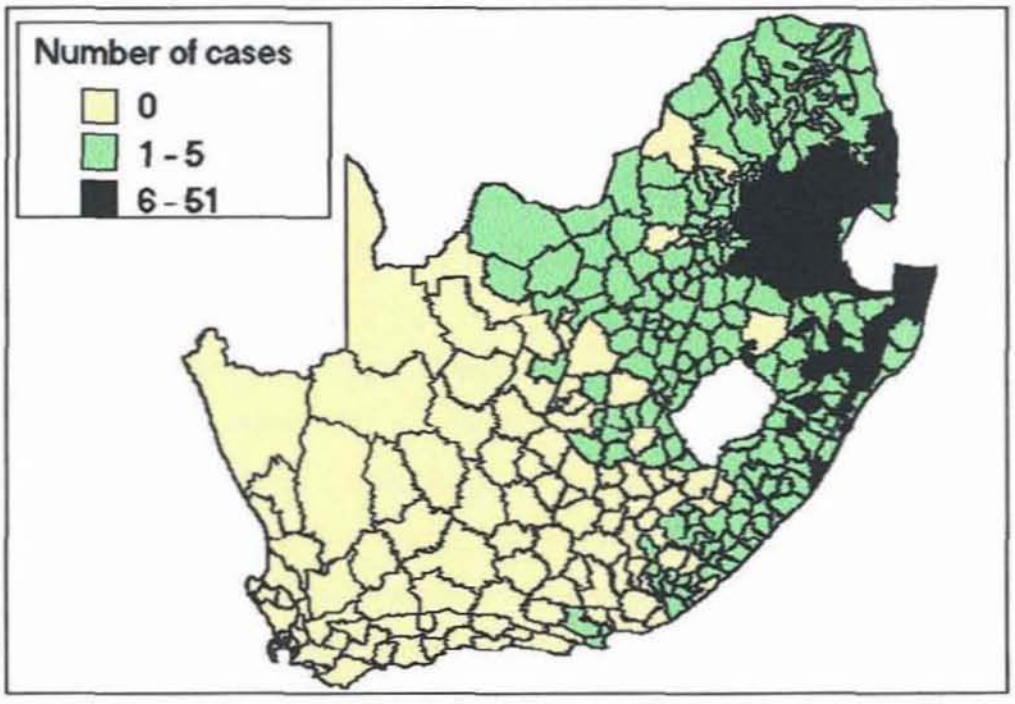
Mean incidence in this area is the highest in the country, and the last formal review, covering the 11 year period 1981-1991, found a prevalence rate in this Region of 0.68 per 100,000 compared to a national average of 0.37 per 100,000 (Department of Health, 1993). One magisterial district within this region, Ermelo, has consistently experienced the highest leprosy prevalence and detection of new cases despite no additional dedicated leprosy services or focus in this particular district.

Figure 7.1. Annual leprosy case notification rate, South Africa, 1921–2000.



Source: South African National Notification Database

Figure 7.2. Leprosy cases per magisterial district, South Africa, 1981–1991.

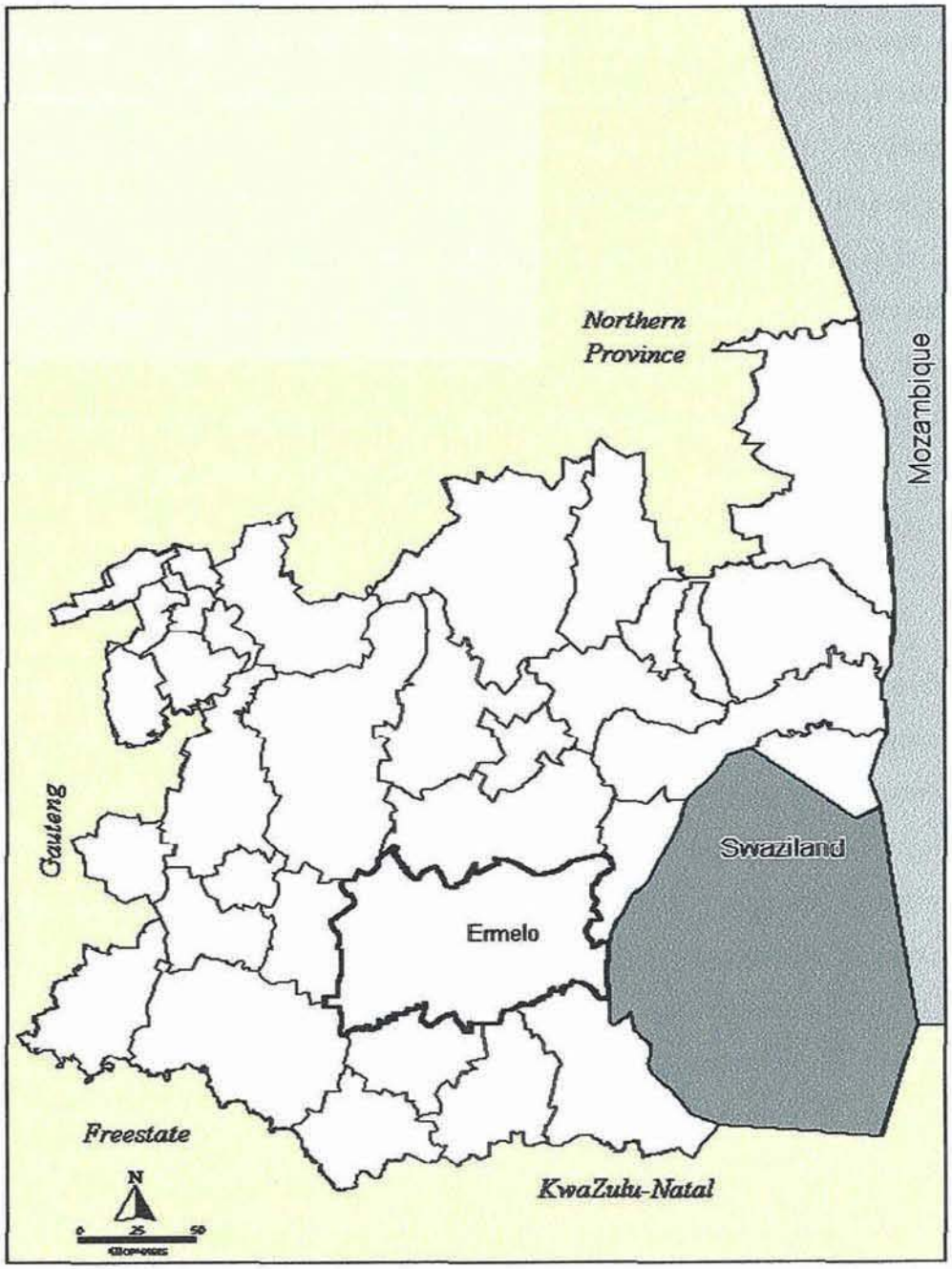


Source: South African National Notification Database

Ermelo is a predominantly agricultural area of 7,254 km^2 with a population estimated at 131,603 [Figure 7.3]. Ermelo Town, including the peripheral formal townships of Wesselton and Cassim Park, is the hub of the District with a population of 91,427. Most district health facilities are sited within the town's boundaries, and include a 242 bed government hospital, a 40 bed private hospital, a 60 bed tuberculosis hospital and five permanent clinics. The remainder of the district's population is relatively stable, residing on 291 farms, predominantly maize and cattle, and in 10 villages. These outlying communities are served by three permanent and four mobile clinics, with the latter providing the bulk of health services for the rural farm and village communities at 143 scheduled stopping points that are visited on average once every four weeks.

Leprosy services throughout Mpumalanga have been provided in a decentralised form by primary care clinics since 1995. Prior to this, all leprosy patients from the four northern South African provinces, Mpumalanga, Northern, North-West and Gauteng, were admitted at Westfort Leprosy Hospital in Pretoria in Gauteng Province, usually for the duration of therapy. Specialised leprosy clinics are conducted every three months for all leprosy patients currently on treatment at 10 Mpumalanga hospitals by nursing staff from the Leprosy Mission-South Africa and specially trained provincial doctors. One of these clinics is conducted at the government district hospital in Ermelo. The Leprosy Mission-South Africa has a contract with the Mpumalanga Department of Health to provide this service. In addition this non-governmental organisation is responsible for training provincial health staff in the recognition of leprosy, community awareness and has a field officer who traces any patient defaulting on treatment.

Figure 7.3. Ermelo District, Mpumalanga Province, South Africa.



During the period 1985-1996, of 306 new leprosy patients diagnosed in Mpumalanga, 68% (n=209) were from the Eastvaal Region, while Ermelo Magisterial District contributed 33% (68) of these cases, although it only represents 18% of the Eastvaal population. However from 1997-1999, of 64 new cases of leprosy diagnosed in Mpumalanga, only 14 (21%) were from Ermelo and only one (6%) of the 17 cases diagnosed in 1999 was from this magisterial district. It was unclear whether this phenomenon was a chance finding, or due to changes in health service accessibility for leprosy diagnosis or sustained reduction in disease transmission. A disturbing feature was that 30% (19/64) and 29% (4/14) of the new leprosy patients diagnosed during this period in Mpumalanga Province and Ermelo, respectively, had Grade 2 disabilities (World Health Organization, 1998). The provincial Leprosy Management Team, with representation from the Mpumalanga Health Department and Leprosy Mission decided that a survey was indicated to investigate whether reduced case detection was an accurate indication of reduced incidence.

7.4. Methods

To accurately determine leprosy prevalence in a low-incidence area, a carefully designed community survey is necessary, but financial and human resource constraints made a classical cross-sectional survey untenable owing to the large number of people that would have to be screened. It was thus decided to conduct a large-scale community awareness campaign in Ermelo Magisterial District focusing on leprosy symptoms/signs and conveying the message that leprosy has a good prognosis if correctly treated. Concurrently specific dates and venues for screening were advertised. This campaign began in May 2000 through a variety of modalities, including the local radio station, posters prominently displayed at clinics and other public buildings, active marketing by mobile and permanent clinic staff to patient populations while encouraging peer dissemination, and through traditional community channels, including religious and other societal structures. Personal or telephonic contact was made with farmers to inform them of the campaign and to identify the specific farms chosen to serve as gathering points for screening. Head teachers of rural primary schools were contacted for permission to visit

their schools. The assistance of farmers and head teachers was also enlisted for marketing the screening campaign. These marketing efforts continued throughout the duration of the campaign.

A professional nurse and a leprosy fieldworker, both experienced in clinical dermatological and neurological screening techniques, conducted the intensive screening campaign from 1 June to 31 August 2000. They offered this service at the 31 designated and highly publicized screening points on farms and eight central points in villages, while eight primary schools were also visited. Primary education is compulsory in Mpumalanga and head teachers of these schools have a successful record of securing parental consent for health-related activities. Clinical findings suggestive of leprosy or a history elicited of a community or family member with suspicious symptoms prompted follow-up at the specific household. Simple demographic details, including residential address, were collected from all people examined.

The provincial Medical Officer responsible for the Leprosy and Tuberculosis Control Programs and the professional nurse from the Leprosy Mission conducted pre-arranged clinics at Ermelo district hospital biweekly for the duration of the screening campaign. Any person detected by the field team with a clinical picture remotely suspicious of leprosy was referred to this clinic for careful clinical examination and biopsy of suspicious lesions when indicated. As the purpose of the survey was to confirm true elimination, a high sensitivity approach was adopted for detecting any possible leprosy cases during screening. The Leprosy Mission traced the three suspects who failed to present to the clinic before the end of the study period. Skin biopsy specimens were taken from the active, erythematous part of lesions and fixed in buffered 10% formalin before being sent to the South African Institute of Medical Research for histological and microbiological examination, and independently reviewed by an experienced histopathologist with the National Center for Communicable Diseases, Johannesburg, South Africa.

7.5. Results

One thousand one hundred and seventy seven people presented for clinical screening at the designated points while 790 scholars were screened at primary schools. An additional 1,433 people were clinically screened at their homes by the field team. Forty-four people, 20 resident on farms and 24 from villages, with skin or nervous system lesions compatible with leprosy were detected during this screening survey and referred to the special clinic at Ermelo district hospital. After clinical assessment by the Provincial Tuberculosis and Leprosy Coordinator and Leprosy Mission professional nurse, biopsies were taken from suspicious lesions of 19 patients.

Two adult females and one adult male were histologically confirmed as leprosy and acid fast bacilli (AFB) were found in the dermatological specimens [Table 7.1].

Table 7.1. Leprosy patients detected by intensive community survey, Ermelo District, 2000.

Name	Village/Farm	Sex	Age	Consulted [1]	Known contacts[2]	Histological classification[3]	Disability grading		
							Eye	Upper limb	Lower limb
TM	Village	F	22	Yes	Yes	BB	0	0	0
LN	Farm	F	71	Yes	Yes	BB	2	2	2
TS	Farm	M	27	No	Yes	TT	0	0	0
LN	Farm	F	65	No	Yes	[4]	0	0	0

[1] Patient had consulted health service for symptoms or signs related to leprosy.

[2] Patient had close prolonged contact (family or friend) with a person previously diagnosed and treated for leprosy.

[3] Ridley-Jopling classification: BB = borderline leprosy; TT = typical tuberculoid leprosy.

[4] Granulomatous dermatitis, consistent with tuberculoid or borderline tuberculoid leprosy, despite the absence of demonstrable *M. leprae* by special stain or polymerase chain reaction.

Treatment was initiated for one additional female patient although no AFB were found in the biopsy specimen. The 71 year-old female had extensive classical dermatological and neurological involvement that had been present for approximately five years. Although she had consulted a government clinic and private general practitioner, only a topical ointment had been prescribed and leprosy had not been diagnosed. The younger lady had a three-year history of skin involvement and on examination had multiple hypopigmented skin lesions and thickened nerves. She too had only received a topical ointment when she consulted a government clinic. The male farm-worker had not been aware of the single skin lesion over his left calf and accompanying thickened peroneal nerve. One additional female patient, aged 65 years, with a histological picture of granulomatous dermatitis, was considered clinically to be a leprosy case on the basis of highly suggestive skin lesions on her lower limbs for about eight years.

All confirmed patients offered a history of close prolonged contact with known leprosy patients prior to the onset of disease. The male patient's sister is a leprosy patient who is currently on MDT. Results for the remaining 15 patients biopsied included lupus erythematosus (1), subacute psoriasiform seborrhoeic dermatitis (5), lichenoid reaction pattern (3), Kaposi sarcoma (1), tinea versicolor (1), eczema (1) and no significant pathological changes (3).

7.6. Discussion

Complacency after achieving the goal of leprosy elimination at national level may result in its return as a re-emergent disease (Morse, 1995). In countries where the elimination goal has been achieved, efforts will need to be made to identify areas requiring sustained efforts to interrupt transmission and finally achieve eradication. Target areas include districts where late diagnosis with disability in new cases is common and/or where the elimination target has not been achieved (Gil Suarez & Lombardi, 2000; Neira & Daumerie, 2000). In low prevalence sites, the focus must become the detection of hidden leprosy cases, which was the motivation for the Ermelo survey.

The detection of only four "new" leprosy cases during this survey supports the impression that leprosy transmission is approaching very low levels in the former leprosy nucleus of South Africa. However, the relatively young age of two patients precludes definitive statements on the status of transmission. The present survey technique may be criticised, as despite the concerted community awareness and screening efforts, individual leprosy patients, particularly those with early disease, may have been missed. Unfortunately, traditional cross-sectional surveys to establish the burden of uncommon diseases demand very large sample sizes to achieve an acceptable degree of precision. For example, if the true leprosy prevalence in Ermelo Magisterial District excluding the urban area (population of approximately 40,000) was 1/10,000, a simple random sample of 29,956 people would be required to detect this rate with 95% confidence. In rural areas, like Ermelo, where a comprehensive community census is not available, cluster sampling would be required with a resulting further increase in the required sample size. The resource requirements to conduct such a survey could not be justified given competing health priorities in this area.

Reports by two patients of previous self-presentation to public and private sector health staff for their dermatological condition resulting only in non-specific topical treatment, were disconcerting. Unfortunately, as a medical condition becomes increasingly rare, recognition by health workers is impaired by lack of diagnostic experience and a decreased index of suspicion (Durrheim & Speare, 2000). Clinical diagnosis is made more complex by the increasing prevalence of HIV-associated dermatological conditions that may mimic leprosy. There thus exists a need for regular training of primary health care staff working in this area and similar regions in sub-Saharan Africa on how to detect leprosy against a background of highly prevalent dermatological presentations of AIDS. Where possible referral clinics with staff able to assess complicated dermatological presentations should also be provided on a regular basis.

Traditional leprosy survey methods appear to have restricted application in sub-national areas with low endemicity (Kumaresan *et al.*, 1993; World Health Organization, 1994b). Our experience is similar to that of Botswana, where the resource commitment required

did not appear justified by the low yield (Revankar *et al.*, 1997). The transition from the national "sprint" towards leprosy elimination to the sub-national elimination "marathon", will require new tools and strategies (Croft, 1999). Our findings suggest that ongoing intense tracing and follow-up of close contacts of proven leprosy cases may be a more efficient means of detecting leprosy cases. Efforts should be made to educate close contacts of proven leprosy cases on the symptoms and signs of leprosy, curable nature of promptly detected and treated disease, and appropriate referral screening sites should they suspect symptoms. In addition governmental and non-governmental agencies responsible for leprosy elimination at sub-national level, should keep a register of all close contacts of proven leprosy cases, and initiate a follow-up visit to offer active annual screening.

7.7. Conclusions

The community prevalence survey in Ermelo Magisterial District confirmed achievement of leprosy elimination levels in this historically high-prevalence area. However, four leprosy patients were detected, including one lady with considerable disability. The survey highlighted the importance of ongoing efforts to raise the awareness of community members and health workers in former leprosy endemic areas. Traditional leprosy survey methods, which are resource intensive and logistically complex, appear to have restricted application in sub-national areas with low endemicity. The finding that all new patients detected during this survey had close contact with proven leprosy patients deserves study in similar sub-national areas that have achieved elimination targets as this might allow more efficient surveillance for undiagnosed leprosy patients.

Chapter 8. Using a telephonic survey as a rapid operational research tool

8.1. Chapter Overview

Rabies is an important disease in rural South Africa, and vaccine and immunoglobulin are provided, at the State's expense, to humans following suspected exposure to rabies virus by bite, scratch or mucosal splash. Health facilities where post-exposure treatment is available are listed, with contact telephone numbers, in national rabies guidelines. To verify the accuracy of this recently updated information, members of the national Rabies Advisory Group were tasked to conduct a rapid survey. A simple standardized telephone interview technique was used. This revealed startling deficiencies in the availability of vaccine and immunoglobulin at the indicated sites, and led to decisive corrective action. This "quick and dirty" survey technique provided valuable information for improving an important public health program, and should be considered when auditing other health programs, particularly where a means for validating responses is readily available.

8.2. Peer-reviewed publication arising from research summarised in this chapter

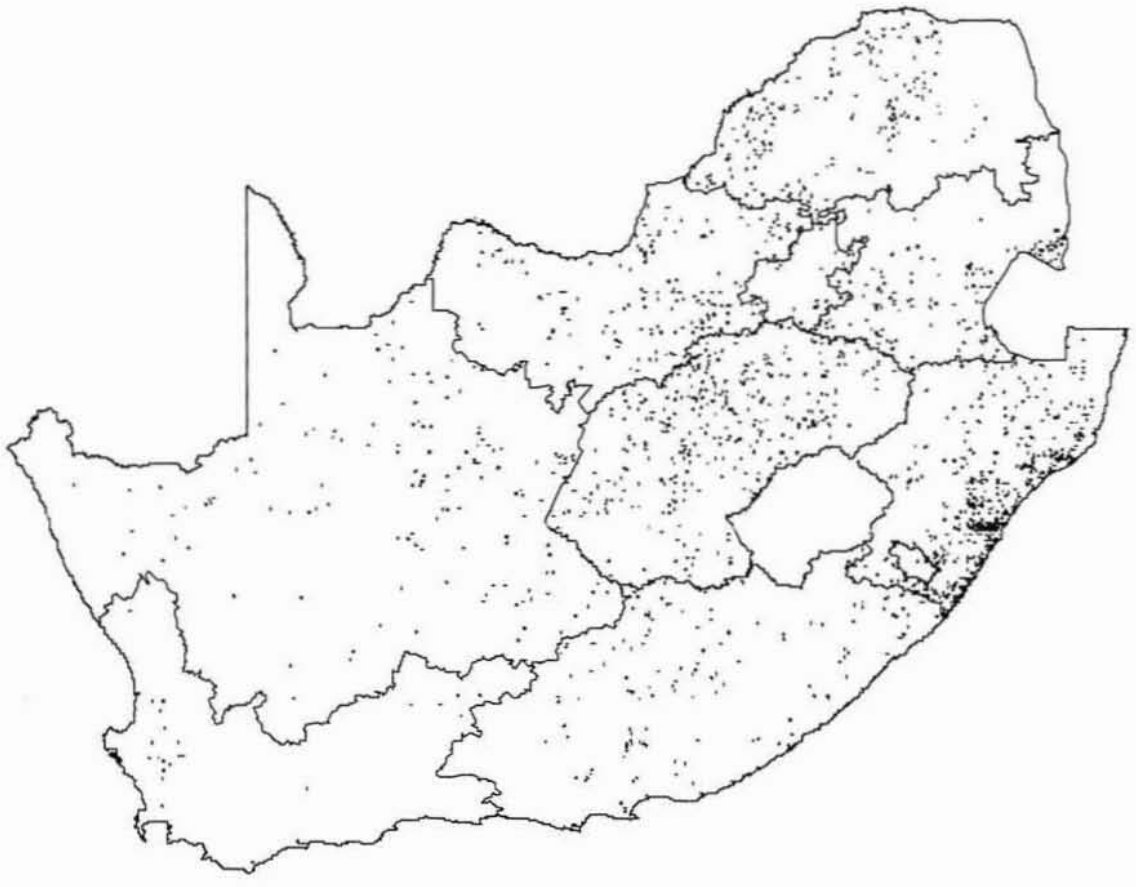
* Durrheim, D.N., Speare, R. & Petzer, M. (2002) Rabies post-exposure management in South Africa: a telephonic survey used as a rapid tool for operational research. *Tropical Medicine and International Health*, 7, 459-461.

8.3. Introduction

The double-blind randomised control trial or meta-analyses of the same are considered the benchmark for health sciences research (Sackett *et al.*, 1991). This approach is sensible when the most effective and least harmful therapy for a human disease is being sought or risk factors underlying a health condition are being elucidated. However, in the public health arena, "lesser" study designs can provide equally valuable data, particularly when research resources are limited. We used a "quick and dirty" study method to explore an important aspect of a rabies management programme.

South Africa is endemic for rabies [Figure 8.1]. Herpestid rabies circulates amongst mongoose, particularly yellow mongoose (*Cynicitis penicillata)*, on the central plateau, while canine rabies is maintained among stray dog populations, and to a lesser extent black-backed jackal (*Canis mesomelas*), in the eastern coastal and northern regions of the country. The onset of clinical neurological rabies disease in mammals is the precursor of inevitable death. However, currently available vaccines and immunoglobulin, when administered to humans in schedules recommended by the World Health Organization, have proven safe and highly efficacious in preventing rabies in human victims of rabid animal bites (Dreesen & Hanlon, 1998).

Figure 8.1. Geographical locations of animal rabies cases diagnosed in South Africa over the five-year period, 1995 – 1999.



Source: Allerton Veterinary Laboratory, Pietermaritzburg, South Africa

8.4. Methods

A simple Excel for Windows 98™ spreadsheet was prepared for systematic data entry and one of the researchers conducted standardized telephonic interviews of pharmacists at listed telephone numbers. The number of facilities listed ranged from six in the Free State to 60 in the Eastern Cape. A 50% random sample of facilities from each of the three provinces with the largest number of sites, KwaZulu-Natal, Eastern Cape and Northern, were selected, while all facilities in the remaining six provinces were included. As a quality control measure to ensure standardisation, the interviewer's technique was observed during a small number of interviews by a second investigator.

Interviews were brief, consisting of a greeting and an introduction to indicate that the survey was being conducted under the auspices of the RAG. The responding pharmacist was then asked to indicate whether rabies vaccine and rabies immunoglobulin were available, and if stock was available, to provide the batch numbers and expiry dates. The latter information served a dual purpose, providing an indication of stock rotation and control, but also allowing validation of the information supplied against batch numbers and expiry dates provided by vaccine and immunoglobulin manufacturers. All telephone calls were made during office hours and not over the midday lunch period. Where telephone calls were not answered, two further calls were made on subsequent days, before the attempt was abandoned. The survey was completed on a part-time basis within seven working days during March 2001 and only one pharmacist refused to assist with the survey.

8.5. Results

The results of this audit were disconcerting [Table 8.1]. Many facilities (n = 24, 16%) could not be contacted despite three protracted attempts. The telephone numbers of 22 (15%) facilities were incorrect or did not exist. No facilities had expired vaccine stock but five facilities (two in North-West, two in Western Cape and one in Eastern Cape) had vaccine stock that would expire at the end of the survey month. One facility in KwaZulu-

Natal had expired rabies immunoglobulin in stock. Of the 99 (68%) sites that were contactable, 41 (41%) had both vaccine and immunoglobulin, 32 (32%) had only vaccine, five (5%) had only immunoglobulin and 21 (21%) had neither vaccine nor immunoglobulin available.

Table 8.1. Results of a telephonic survey [n (%)] to determine the availability of rabies vaccine and rabies immunoglobulin (RIG) at listed sites in South Africa, March 2001.

Province	Total facilities[1]	Facilities surveyed	No answer[2]	Refusal to participate	Faulty number[3]	No vaccine available	Vaccine expired	No RIG available	RIG expired
Eastern Cape	60	30 (50)	9 (30)	1 (3)	4 (22)	6 (20)	0 (0)	13 (43)	0 (0)
Free State	6	6 (100)	1 (17)	0 (0)	0 (0)	1 (17)	0 (0)	3 (50)	0 (0)
Gauteng	9	9 (100)	3 (33)	0 (0)	0 (0)	1 (11)	0 (0)	3 (33)	0 (0)
KwaZulu-Natal	49	25 (51)	3 (12)	0 (0)	4 (16)	2 (8)	0 (0)	9 (36)	1 (4)
Mpumalanga	14	14 (100)	2 (14)	0 (0)	2 (14)	1 (7)	0 (0)	4 (29)	0 (0)
Northern Cape	17	17 (100)	2 (12)	0 (0)	8 (47)	3 (18)	0 (0)	3 (18)	0 (0)
Northern	41	21 (51)	0 (0)	0 (0)	3 (14)	6 (29)	0 (0)	9 (43)	0 (0)
North-West	10	10 (100)	1 (10)	0 (0)	1 (10)	0 (0)	0 (0)	3 (30)	0 (0)
Western Cape	14	14 (100)	3 (21)	0 (0)	0 (0)	6 (43)	0 (0)	6 (43)	0 (0)
SOUTH AFRICA	220	146 (66)	24 (16)	1 (1)	22 (15)	26 (18)	0 (0)	53 (36)	1 (1)

[1] Where Provincial Chief Pharmacist indicated that vaccine and rabies immunoglobulin were available.

[2] Despite three determined attempts.

[3] Telephone number provided either incorrect or invalid.

8.6. Discussion

Survey findings may be criticised because of the relatively poor response rate. However, the inability to elicit a response due to an invalid telephone number or despite three separate protracted attempts would have been the experience of a community member or health worker at a remote clinic or hospital attempting to gain access to post-exposure treatment on the days of the survey. This translates into a non-availability of vaccine and immunoglobulin at 50% and 68% of sites, respectively, reflecting gross inaccessibility of treatment. The availability of either vaccine or immunoglobulin alone at many sites could result in incomplete post-exposure treatment with attendant rabies risk to patients. Pharmacists were not asked whether they ever had rabies treatment in stock or to provide reasons why stock was unavailable, as this would have increased the duration of the survey and may have negatively influenced the willingness of pharmacists to cooperate.

A focus on collecting verifiable stock data meant that errors, which commonly attend structured interviews, particularly the tendency of respondents to provide socially desirable responses, were not an issue (Fontana & Frey, 1994).

The response by the national Department of Health on receipt of survey results was immediate and decisive with feedback of results to provincial chief pharmacists with a demand for an accurate depot list, and training of pharmacists on the importance of correct rabies post-exposure treatment and the implications of incorrect treatment. The RAG donated a copy of an educational rabies video, "Rabies in Humans and Animals" to each Chief Provincial Pharmacist.

A review of failed post-exposure treatment in Thailand indicated that many rabies deaths could be prevented (Wilde *et al.*, 1989). The present study emphasizes the importance of ensuring reliable sources of rabies vaccine and immunoglobulin supplies, while previous studies in South Africa and Thailand have highlighted deficiencies in health workers' knowledge on managing suspected rabies exposures (Durrheim *et al.*, 1998b; Kositprapa *et al.*, 1998). The South African study also made use of a telephonic survey technique.

The health worker primarily responsible for managing a victim of an animal bite at all hospitals in Mpumalanga Province was presented with a series of short vignettes to explore the usual management practices of the respondent's institution in a non-threatening manner.

8.7. Conclusions

This simple telephonic survey provided invaluable information on the quality of an important aspect of a public health program. The structured set of simple questions was systematically presented to all respondents in an extremely cost-effective fashion.

Similar rapid survey designs may have great utility in auditing other public health programs, particularly where a means for validation is readily available.

The value of a study method should always be judged on its ability to provide answers to important questions within available resources. This study was "quick and dirty", yet very useful.

Chapter 9. The case for evidence-based public health policy

9.1. Chapter Overview

Much communicable disease control research has had little impact on local control program policy and practice for want of an operational component. The operational research model, the systematic search for knowledge on interventions, tools or strategies that enhance program effectiveness, is being recognised as useful for addressing perplexing questions at public health program level. A series of operational research studies were conducted between 1995 and 1999 to refine malaria diagnosis in Mpumalanga, South Africa. To explore positive and negative attributes of operational research that impact on its value for influencing communicable disease control policy and practice, the grounded theory approach was used with groups of experienced Masters of Public Health students in South Africa and Australia to analyse a compilation of these six studies.

The analysis suggests that the operational research approach effectively influences disease control policy and practice, and accelerates the inclusion of effective measures into local communicable disease control efforts. Operational research not only provides resource-sensitive answers to locally relevant questions but also effectively engages policy-makers. This analysis also endorsed the value of equipping health program staff with the knowledge and skills to efficiently conduct essential operational research at control program level.

9.2. Peer-reviewed publication arising from research summarised in this chapter

* Durrheim, D.N., Speare, R. & Harries, A.D. (2002) Research that influences policy and practice – characteristics of operational research to improve malaria control in Mpumalanga Province, South Africa (2002). *Malaria Journal, in press.*

9.3. Introduction

"We have at our disposal the tools necessary for achieving control – elimination - eradication of a particular disease", is a common refrain of public health bodies and practitioners. Vaccination programmes have had a major impact on a few key diseases, even in developing countries, but it remains puzzling that there are relatively few examples of successful disease control programs, particularly of non-vaccine preventable endemic diseases, in developing settings. The inequitable global distribution of resources available for health care is certainly an important contributory factor. However, even interventions deemed cost-effective for developing environments often fail to match expectations. Apology, justification or condemnation is customary, and a recommendation for further research commonly suggested as the way forward. Although this suggestion occasionally stimulates complaints that available resources should be channelled into service delivery rather than research, there is generally an acknowledgement that immediate problem-solving should not be at the expense of discovering sustainable longer-term solutions (Morris *et al.*, 1998). However, research per se is not a panacea for an ineffectual health program. The research conducted must produce locally applicable answers to be relevant and ethical (World Health Organization, 2000c).

The operational research model is becoming increasingly popular for addressing perplexing questions at public health program level. It has even been suggested that success in combating communicable diseases in Africa depends upon each country having the ability to conduct appropriate operational research (Foster *et al.*, 1990; World Health Organization, 2000c). Optimal use of operational research for improving communicable disease control is contingent on an appreciation of its inherent strengths and potential weaknesses.

In the Lowveld Region of Mpumalanga Province in the rural northeast of South Africa (population approximately 850,000), malaria is an important seasonal public health problem, with approximately 5,000 malaria patients notified per annum between 1995

and 1998 (Durrheim *et al.*, 1999c). *P. falciparum* parasites account for more than 90% of infections. Traditionally, detection of parasites in the peripheral blood by Giemsa stained thick blood films (GTF) preceded the initiation of therapy, as rickettsial and viral febrile illnesses that commonly occur in the area mimic malaria. In 1995, only two of the 72 clinics in the Region had an on-site microscopist skilled in malaria diagnosis. The remaining clinics depended on four centralized laboratories for examining GTF, as adequate facilities and technically skilled laboratory personnel were not available in more remote areas.

A series of operational research studies were conducted between 1995 and 1999 to assess the accuracy and appropriateness of the GTF diagnostic approach, and explore alternative diagnostic methods. These studies are presented in Chapter 4 but a summary is provided here. The first study, a random survey of 40% (30/72) of Lowveld clinics, found that only 20 clinics were still preparing thick blood films and of these, only three clinics received microscopy results within 24 hours, while 11 clinics never received results (Durrheim *et al.*, 1997b). Of nine clinics that had blood slides available for scrutiny, only four had prepared slides of acceptable quality. The second study assessed the diagnostic accuracy of the four laboratories responsible for examining malaria blood films in the Province. Marked diagnostic disagreement was found. Kappa, the measure classically used for summarizing agreement beyond chance, had a value of only 0.11 (95% confidence interval of 0.0-0.23) for a series of quality assurance GTF (Durrheim *et al.*, 1997a). This value signified only minimal agreement amongst the laboratories, as kappa has a value ranging from 0 to 1, where 0 represents no agreement beyond chance and 1 perfect agreement.

A marked escalation in *P. falciparum* malaria cases resulted in demands for action from local politicians and senior health officials, and provided an opportunity for evaluating novel approaches to early definitive diagnosis. The third study considered a new diagnostic approach, with two rapid malaria card tests compared at a number of pilot clinics in the malaria area (Lee *et al.*, 1996). Participating nurses indicated a clear preference for the ICT Malaria Pf™ test, with short time to diagnosis and ease of use

being the reasons cited for this choice. A fourth study demonstrated excellent field accuracy of the ICT Malaria Pf™ test and as a result the rapid card test was introduced for first-line malaria diagnosis in all Lowveld Region clinics during 1996 (Durrheim *et al.*, 1998c). The fifth study was a confidential inquiry into malaria deaths. The utility of this approach documented during this study for identifying important public health programme deficiencies requiring remedial action is discussed in detail in Chapter 2. An important finding was that delays in accessing GTF results in hospitals, particularly after-hours and during weekends, may have contributed to fatal outcomes among hospitalised malaria patients (Durrheim *et al.*, 1999a). This finding provided the impetus for deploying ICT Malaria Pf™ tests in hospital accident and emergency units throughout the Mpumalanga malaria area. The sixth study, a field evaluation of a multiple *Plasmodium* species immunochromatographic test, established that the multiple species test shared equivalent sensitivity and specificity with the ICT Malaria Pf™, but resulted in difficult interpretation (la Grange *et al.*, 1999). In addition, therapy for non-*falciparum* malaria is not available at clinic level due to the predominance of *P. falciparum* malaria in Mpumalanga. This prompted a policy decision to continue using the older rapid test. Quantitative and qualitative field evaluation of new-generation rapid tests is now routinely conducted in Mpumalanga to provide the information necessary for procurement of affordable and accurate tests.

We provided a compilation of these six studies to experienced students on Masters-level public health courses in two countries for formal qualitative assessment. The students used this case-study to explore the role of operational research in influencing policy and practice.

9.4. Methods

A synopsis of the six studies mentioned above, including their rationale, methodology, results and outcomes, were compiled for a case-study used in a half-day session entitled "Strengths and Weaknesses of Operational Research". This module is a component of the Masters of Public Health subject "Introduction to Communicable Disease Control"

offered by the Thusano School of Public Health, South Africa and the "Disease Control" subject of the Masters of Public Health and Tropical Medicine offered by James Cook University, Australia. These subjects are currently presented by attendance mode once per annum in Pretoria, South Africa and Townsville, Australia, respectively.

This material was provided as pre-reading the evening before the session. At the session's commencement the principles of grounded theory, the inductive process of identifying analytical categories from data, were briefly reviewed. The students were then introduced to their task, which was to apply the basic steps of the grounded theory approach for analysing the material provided to derive positive and negative attributes of operational research for influencing communicable disease policy and practice in southern Africa. This exercise was initially tackled as individuals, and then small groups of three to four students discussed and synthesised their themes. Finally, a plenary session was facilitated during which students had the opportunity of listing the positive and negative attributes that emerged during the qualitative exercise, providing clarification where required, and discussing the impact of operational research on public health policy and practice. This method was successfully piloted in July 2000 at the Townsville Disease Control course, and then employed in Pretoria during October 2000 and Townsville in May 2001.

The majority of the 12 female and 7 male participants on the Thusano 2000 course were experienced professional nurses (n = 11), with the remainder being doctors or medical specialists. Most of these students (n = 15) were actively involved in managing disease control programs in South Africa, either at national (n = 3), provincial (n = 6) or district level (n = 6). The James Cook University students were predominantly medical doctors (n = 15), although there were also 2 nurses and 3 allied health professionals. Seventeen of these students were employed in rural settings in Australia and five in developing countries. Twelve Townsville students were female and four students were employed in public health positions directly involving control of communicable diseases.

Thematic analysis was used to analyse the data generated during this exercise and catalogue strengths and weaknesses of operational research from the perspective of these students.

9.5. Results

9.5.1. *Positive attributes of operational research*

The "high relevance of operational research" was the most prominent theme that emerged, mentioned and discussed extensively by both Thusano School of Public Health and James Cook University Masters students. Codes, or analytical categories, derived by the Pretoria students supporting this theme included "research driven by real problems", "allowed in-depth exploration of real reasons for problems" and "set in actual context, therefore provides specific answers". The Townsville students concluded that operational research was "real world research", "research that addresses real problems", and "draws on local knowledge". In addition, the Australian students mentioned that operational research had the advantage of "detecting locally unanticipated factors".

Both groups cited "high relevance" as a major reason why "operational research successfully affects policy and practice". The Australian analysts found that operational research "provides an evidence base for policy and procedures", while the South Africans concluded that operational research "leads to improved policy that is based on evidence." A number of additional benefits were derived from the case-study [Table 9.1].

Table 9.1. Positive attributes of operational research for influencing policy and practice derived from Mpumalanga malaria diagnosis case- study.

Operational research feature	Supportive codes	Students
Effectively engages and convinces policy-makers and programme staff	"a focus on impact" "involvement of implementers in the research process" "decreased resistance to change, as policy based on operational research findings is seen (by policy-makers) to provide an opportunity to improve services" "more likely to positively affect attitudes about the necessity to alter control measures - rather than just knowledge" "as senior management are aware that field personnel know the research outcomes, there is pressure on them to actively implement findings" "less suspicion because the research question, process and outcomes are open to local observers" "every manager enjoys success and being seen as proactive"	Pretoria
	"operational research by a health program creates immediate demand, by highlighting problems and demanding intervention" "resistance to change may be less, as local health department management are more closely involved in the research"	Townsville
Relatively short period between generation of research findings and implementation of resulting recommendations	"immediate benefit" "fast application, even simultaneous, of lessons learned"	Pretoria
	"short lead-time to implementing findings" "changes occur in real-time"	Townsville
Economic benefits	"cost-effective, as existing resources are used" "high quality research would attract additional resources from outside"	Pretoria
	"led to better use of resources" "focus of staff and management shift to areas where operational research occurs with additional resources"	Townsville
Establishes a commitment to ongoing research for evidence-based policy	"once perceived to have positively influenced service delivery, the buy-in from management for investing in future research and continued interest in the particular program area was more likely" "incremental" "continues into the future" "ongoing" "identified new problems setting a relevant research agenda"	Pretoria
	"highly adaptable agenda"	Townsville
Personal benefit accrue to health programme staff involved in planning and implementing research	"capacity to conduct research is being built" "improving research ability" "opportunity for collaboration with respected individuals and research organizations" "scientific credibility and publications"	Pretoria
	"people in field get research skills" "acquire excellence in report-writing skills" "opportunity for interacting with external bodies"	Townsville

9.5.2. *Negative attributes of operational research*

The major concerns expressed by the Townsville students were that operational research, "may be of poor quality if there is a lack of local research skills" and that "poor quality research may have more weight as evidence and lead to inappropriate changes to practice and policy". The Pretoria students noted that there was an attendant "opportunity cost – other functions of field staff may be compromised". They expressed disquiet that routine program evaluation may be compromised, "may lead to down-scaling of routine service evaluation because of a perception that service evaluation was also research, needing researchers, budget and ethics approval". They also indicated a reservation that "approval (to conduct operational research) may not be granted by senior management if they predict unflattering outcomes of research". Both groups mentioned the potential vulnerability of program staff participating in operational research. Codes included, "vulnerable if practices that have been long entrenched are found to be wasteful or useless" (Pretoria), and "researcher more vulnerable to unfavourable outcomes" and "field staff may feel threatened by results" (Townsville).

At a practical level, Townsville respondents were concerned that "resources, money and interest are diverted from other areas where no operational research was happening", and "field staff may object to additional work associated with conducting research".

9.6. Discussion

Experienced health policymakers have noted a widening gap between scientific knowledge and health policy, and also between theoretical health policy and actual practice (Mills, 1998; Chopra & Sanders, 2000; Bedregal & Ferlie, 2001). Many public health tools and strategies with proven laboratory or field trial efficacy do not produce tangible benefits in terms of disease control. Unfortunately there is a dearth of research on how to successfully translate the results of field efficacy trials into field effectiveness (Feenstra, 1996; Lengeler *et al.*, 1996; Sharma *et al.*, 1997).

For the purposes of this study we defined operational research as the systematic search for knowledge on interventions, tools or strategies that enhance program effectiveness, with the rider that the research should be planned and conducted by or in equal partnership with the local control program. A distinction should be made between operational research as we define it and operations or health systems research, which traditionally involves an incursion of external analysts, usually from a university environment, into a field setting. The latter approach focuses, almost exclusively, on developing information systems and technology to support planning, and has elicited criticism of "pursuing theory at the expense of practice" (Boldy & O'Kane, 1982; Cooper, 1999; McCarthy & White, 2000).

Specific features of operational research increase the likelihood that research-derived recommendations will successfully influence local control program policy and practice. The principal feature highlighted by this study is the extraordinary relevance of local operational research. Public health interventions studied in the setting in which they will be applied, are more likely to take account of the vagaries of local disease epidemiology, and available material and human resources. Local studies are also ideally suited to consider native context (biological, political, socio-economic and technological), a key determinant of the success of communicable disease control and eradication strategies (Najera, 1984; Kumar, 1990; Murray, 1991; Harries *et al.*, 1998; Varkevisser *et al.*, 2001; Zimmermann *et al.*, 2001).

High relevance is assured by forging a close link between researchers and local control program management, or by equipping the control program to conduct its own research (Druilhe, 2000). A seamless research-control interface increases the value of research topics chosen for enhancing program effectiveness (Haines & Jones, 1994; Pearce, 1996). The chasm between the agendas of research organizations and consumers of research findings is well documented (Tallon *et al.*, 2000). Considerable disparity exists between the volume of work published on specific interventions, and their inherent interest to health program managers (Flisher *et al.*, 2000). Intimate involvement of field staff in setting the research agenda appears to address this incongruence.

Efficient use of available resources emerged as a dominant theme. The number of instances where operational research has generated practical affordable local solutions, in stark contrast with the extravagantly expensive and impractical measures more generally recommended, continues to grow (Harries *et al.*, 1997; Durrheim & Govere, 2002b). It should come as little surprise that analysis of local problems by informed stakeholders generates locally appropriate solutions consistent with available resources (Guyatt *et al.*, 2000; Kelly, 2001).

An interesting feature elucidated was the utility of the operational research approach for studying locally occurring aberrations that follow adoption of guidelines and policy developed elsewhere. A prominent example of this aberration is the strikingly divergent impact on HIV transmission observed when a similar approach to controlling sexually transmitted infections was implemented in two African countries (Grosskurth *et al.*, 1995; Wawer *et al.*, 1999). Even the central doctrine of tuberculosis control, directly observed short-course chemotherapy, has come under the spotlight, with the publication of conflicting results from the only randomised controlled evaluations conducted at program level, in different geographical and social settings (Zwarenstein *et al.*, 1998; Kamolratanakul *et al.*, 1999; Walley *et al.*, 2001). Policy-makers should fastidiously guard against automatically extrapolating positive findings from control strategy evaluations in one environment to other settings. Increasingly complex and disparate contexts around the world demand context-specific solutions. Local operational research should inform adaptation and precede wide-scale implementation (Mayaud *et al.*, 1998).

Inherent attributes of the operational research approach facilitate implementation of findings at senior health management and policy-making level. A candid research agenda and involvement of local health staff, averts senior management suspicion of "research", provides greater credibility to research findings and recommendations, and diminishes the inevitable resistance to change (Madhok, 1999). This is important as the human factor in organisations has a major influence on the nature of policy and its implementation, with political factors often carrying more weight than formal evidence

(Bedregal & Ferlie, 2001). Outside researchers are often viewed with suspicion by government officials charged with policy making, as it is perceived that academic research fails to address priority issues (Flisher *et al.*, 2000). Differences between consumers and researchers in values and life experience, understanding of science and access to decision-making structures, fuel the perception that the researchers primarily have a selfish agenda (Tallon *et al.*, 2000). This perception is fostered by the common failure of academic and research institutions in developing countries to communicate research findings with local policymakers, practicing health professionals, and the public (Kitua *et al.*, 2000). Many researchers may be led to believe that they have no direct role to play in improving health, that such involvement may devalue the independence of their research, and optimistically assume that key decision makers will source relevant publications, understand the research language and results, and then apply these for improving local health programs. Delays in publication of research results in professional journals or even exclusion by print journals owing to competition for space may effectively preclude results from influencing policy decisions (Caelleigh, 2000). Even when outside researchers do present research results to local decision-makers, there is little compulsion for health management to implement recommended changes, as the researchers will soon depart. In contrast, where research is conducted by, or in partnership with the local health program, then results are usually immediately available and decision-makers more accountable (Ham *et al.*, 1995; Falshaw *et al.*, 2000). The rapid, even simultaneous, introduction of research findings into practice was a noted benefit of operational research. Shorter turn-around may reflect natural geographical expansion by the control program of patently effective measures beyond a restricted field research site when marginal additional resources are required. Program management also usually shares the language of local policy-makers (Kitua *et al.*, 2000).

The respondents identified operational research as a dynamic process, setting a continuously evolving agenda. The rapid generation of new knowledge and technology with potential benefits for the local population makes a dynamic research approach obligatory. Environmental vicissitude, and demographic and epidemiological changes demand continuous review of disease control policy and an unrelenting search for better

control strategies. The success of this incremental research agenda should be measured by its ability to introduce appropriate control program policy and practice changes (Trigg & Kondrachine, 1998; Kwanjana *et al.*, 2000).

A manifest benefit that emerged from the data was the development of a research culture within the health program conducting operational research. Encouraging a healthy inquisitiveness in program leaders will ensure that the right questions are posed and answered. Investing in providing programme managers with the research design and analytical tools necessary for framing and answering these questions, addresses the concern raised that poor quality results may engender false credibility and inappropriate program modifications (Mayaud *et al.*, 1998).

The potential weaknesses of the operational research approach highlighted by this study deserve close scrutiny. Firstly, although operational research and routine program evaluation are part of the same spectrum of public health methodologies, program evaluation may be viewed as ongoing audit of routine service delivery, while operational research aims to solve operational problems identified, and to develop and evaluate pilot interventions (Cutts *et al.*, 1992). Thus when operational research findings lead to changes in communicable disease control policy, then routine evaluation must be built in to properly monitor the impact of the changes (Harries *et al.*, 1996; Zwarenstein *et al.*, 1998). Secondly, unlike routine program evaluation, operational research requires preparation and submission of research protocols for technical and ethical review. This rigorous process should assist in preventing inexperienced researchers from reaching invalid conclusions and making inappropriate policy decisions. Field-dominated partnerships between research or academic institutions and health programs should be encouraged as these will serve as an additional safeguard against unrealistic policy.

An adaptation of the "grounded theory" approach was used during this study (Strauss & Corbin, 1994). "Grounded theory" is the term used to describe the inductive process of identifying analytical categories from data, the data being read and then re-read to allow data-immersion by the researchers, who then identify and index themes and categories.

The approach promotes the development of theoretical accounts and explanations that conform closely to the data. Constant comparison allows key themes to be selected (Glaser & Strauss, 1967). Similar themes emerged in two different geographical regions, amongst two discrete groups of Public Health Masters students with diverse life experiences. This triangulation provided support for the validity of the thematic analysis (Turner 1981; Giacomini & Cook, 2000). These informant-analysts were "information rich" in the area of interest, thus maximising the potential for identifying pertinent themes. In addition, a comprehensive review of published literature on operational research in communicable disease control detected themes similar to those derived by the two groups of analysts from the case study of published operational research literature on definitive diagnosis of malaria in Mpumalanga, South Africa. However, caution should be exercised to avoid exceeding the bounds of the data and further research in other programs and settings is encouraged to test the integrity and credibility of this analysis.

9.7. Conclusions

Efficacy is only one prerequisite for a public health intervention to be successful (De Zoysa *et al.*, 1998). Selection of appropriate public health measures should be based on an assessment of their effectiveness and feasibility in a specific local setting. This will ensure that their impact, measured in another environment and context, is locally reproducible (Maher *et al.*, 1997). Local research at operational level is essential for optimising the delivery of effective public health interventions (Cutts, 1991). The analysis of operational research conducted into definitive malaria diagnosis in Mpumalanga Province, South Africa, suggests that the operational research approach can influence disease control policy and practice, and accelerate the inclusion of effective measures into local communicable disease control efforts. This analysis also endorses the value of equipping health program staff with the knowledge and skills to efficiently conduct essential operational research at control program level.

Chapter 10. Conclusions

The widening gap between scientific knowledge, health policy and actual practice has elicited consternation amongst public health practitioners, particularly those working in developing countries. A key determinant of this failure in much communicable disease control research appears to be the lack of an operational component. This thesis presents a collation of operational research studies that demonstrate the approach's utility for influencing communicable disease policy, public health practice and patient management in Mpumalanga Province, South Africa.

Operational research is defined as the systematic search for knowledge on interventions, tools or strategies that enhance program effectiveness. An important rider emanating from the Mpumalanga studies is that the research be planned and conducted in equal partnership with local control program staff. This has resulted in skills transfer with an ongoing operational research agenda, with programme staff using the skills gained to ensure sustainable pursuit of evidence-based approaches to disease control and patient management.

The communicable disease examples presented include those where statutory notification confirmed a high relative burden in Mpumalanga compared to other South African provinces. The diseases chosen, malaria, measles, leprosy and cholera, have markedly different epidemiology and transmission dynamics, thus permitting a broad spectrum of operational research investigations into interrupting different components of infection cycles. Effective control or elimination of these diseases in southern Africa also poses a challenge to traditional approaches, available resources and current knowledge.

Confidential inquiries, the thorough investigation to establish the cause of death, identify any possible contributory health system related factors, and recommend corrective action necessary to prevent any future deaths, proved immensely valuable in the Mpumalanga experience for identifying remediable causes of death in malaria and cholera control programmes. This operational research tool, seldom utilised in developing settings,

provided solid data to guide the design of strategies for eliminating avoidable deaths, with evidence of a positive impact on malaria case-fatality ratios.

Operational research studies into the behaviour of *An. arabiensis*, the foremost malaria vector in South Africa, conducted at Malahlapanga, a unique wilderness site in the north of the Kruger National Park, provided practical and affordable measures for targeted vector control. Research results have directly influenced national guidelines, directed larviciding around residential camps in nature reserves, been employed for effective malaria outbreak response in a rural village and offer great potential for cost-effective personal protection against *An. arabiensis* in low incidence malaria areas.

A series of operational research studies documented the shortcomings of microscopic malaria diagnosis and led to the introduction of rapid card tests for primary diagnosis of *P. falciparum* malaria throughout the Mpumalanga malaria area. Subsequent operational research confirmed the local appropriateness of this diagnostic modality. The Mpumalanga results have contributed to providing an appreciation of the potential value of simple, accurate and rapid non-microscopic diagnosis as a means for "Rolling Back Malaria" in selected areas and the expertise developed in evaluating new rapid malaria tests has resulted in Mpumalanga Province providing an expert reference function for the national pharmaceutical tender.

The first sentinel surveillance site for determining malaria treatment efficacy in South Africa was established in Mpumalanga Province. The *in vivo* SP resistance studies conducted at this site are unique, as they are the first successful 42-day SP *in vivo* studies conducted under field conditions in Africa. The sentinel site has thus allowed a more comprehensive understanding of drug resistance, investigation of the differential resolution of clinical symptoms and peripheral parasitaemia, an initial evaluation of the adequacy of the recommended SP dosage for adults exceeding 60kgs, and determination of gametocyte levels at different stages following therapy. Mpumalanga Malaria Control Programme management are so convinced of the value of the sentinel site that they have taken over primary responsibility for conducting follow-up evaluations of first-line

malaria therapy efficacy every two years. The recognised success of the Mpumalanga sentinel surveillance site in providing high-quality drug efficacy information for policy-making has resulted in the establishment of a fledgling sentinel surveillance network for epidemiological research and malaria policy planning in South Africa.

The goal of measles elimination in South Africa and the southern African region has altruistic and economic appeal if it is indeed achievable. The first cross-sectional district-based survey of immunisation coverage throughout Mpumalanga provided evidence of improvement in routine coverage with measles immunisation over time. Although the district survey indicated some scope for further improving routine immunisation services, existing coverage levels make elimination highly improbable by routine vaccination alone. A strong negative correlation between routine and campaign coverage at district level provided support for the complimentary approach of combining routine and supplementary immunisation for measles elimination in Mpumalanga Province. Through an initial investigation following a mass measles immunisation campaign, the measles disease burden, reflected by deaths and hospital admissions, was shown to be considerably reduced compared to the pre-campaign period. However, comparison of South African data on mass campaigns for measles and poliomyelitis suggests that repeated and closely spaced mass immunisation campaigns are associated with declining coverage. Thus, to achieve coverage levels that justify the commitment of considerable scarce resources it is essential that future campaigns be judiciously timed and spaced.

A simple telephonic survey was used to verify the accuracy of information on pharmaceutical products essential for appropriate patient management following high-risk exposure to a potentially rabid animal. This survey revealed startling deficiencies in the availability of vaccine and immunoglobulin at the sites designated by Provincial Health Department's in South Africa, and led to decisive corrective action. The rapid telephonic survey technique provided valuable information for improving an important public health program, where a means for validating responses was readily available.

This study confirms that the research method chosen should always be judged on its ability to provide answers to important questions within available resources.

The "grounded theory" approach was used to explore the attributes of operational research that impact on its ability to influence communicable disease control policy and practice. Specific features that increase the likelihood that research-derived recommendations will influence policy and practice, include the extraordinary relevance of local operational research, which takes account of the vagaries of local disease epidemiology, available material and human resources, and the local biological, political, socio-economic and technological environment. High relevance is assured by forging a close link between researchers and local control program management, and this relationship also facilitates accelerated implementation of research recommendations, with program management usually sharing the language of local policy-makers. The analysis suggested that the operational research approach can influence disease control policy and practice, accelerate the inclusion of effective measures into local communicable disease control efforts and endorsed the value of equipping health program staff with the knowledge and skills to efficiently conduct essential operational research at control program level.

The series of operational research projects reported in this thesis document application of a variety of operational research methods available to improve the evidence base of communicable disease control policy and practice. The ongoing application of this approach in the study area and adoption in new environments provides evidence of the value of this method. Thus, Mpumalanga's groundbreaking evaluation of rapid tests for malaria diagnosis resulted in implementation of this diagnostic method throughout South Africa's malaria-endemic area. The sentinel malaria surveillance site in Mpumalanga routinely evaluates new malaria diagnostic technology for the national Ministry of Health. The 42-day *in vivo* studies conducted at the sentinel site, with the most recent study currently underway, have provided the most comprehensive understanding of the evolution of sulfadoxine-pyrimethamine resistance in a seasonal malaria area. An appreciation of the value of this tactic has lead to successful establishment of similar

sentinel surveillance sites in all of South Africa's malaria-affected provinces and neighbouring Mozambique. A similar system is planned for Swaziland.

Confidential inquires into all deaths suspected to be due to malaria or associated with malaria treatment have been incorporated in the core set of adverse event monitoring tools that will accompany the introduction of combination antimalarial treatment in all SEACAT sites. Recently the national Rabies Advisory Group decided to pilot the confidential inquiry method in KwaZulu-Natal for any deaths suspected to be due to rabies, in an attempt to improve case management and prevent future fatalities. If this is successful, implementation will be expanded to the three South African provinces affected by canine rabies.

Evidence from Mpumalanga of the value of mass measles immunisation campaigns has provided impetus for adopting this approach in other southern and east African countries (personal communication, Dr. Rudi Egger, WHO AFRO). The analysis we conducted into appropriate timing of campaigns has resulted in the national Ministry of Health making use of epidemiological modelling in the planning of forthcoming campaigns.

The vector behavioural research agenda at Malahlapanga into cost-effective mosquito avoidance measures is ongoing. Currently we are investigating the impact that a number of measures, including varying the height of sleeping surfaces, modifying bed supports, tucking in bed linen and altering bed placement relative to walls and other solid surfaces, has on the biting behaviour of *An. arabiensis*. In addition, a detailed study is in progress exploring the resting habits of endophilic mosquitoes within two experimental huts erected at Malahlapanga, and a promising natural plant repellent *Lippia javanica* is being evaluated under field conditions against feral mosquitoes at Malahlapanga.

Operational research can be conducted while maintaining academic credibility. Successful publication of 18 peer reviewed scientific articles and a chapter in a monograph from the research presented in this thesis supports this contention. The articles included 11 original articles, five short reports, an editorial and a scientific letter.

Ten were published in African journals and eight were published in high profile international scientific and public health journals. The decision of which journal to target was made on the basis of probable maximum public health impact and relevance.

Operational research, in partnership with heath programs, has effectively bridged the gap between scientific evidence and communicable disease control policy and practice in Mpumalanga, South Africa. Evidence of the value of this research model is also emerging from its application in other settings and disease control programs. The profound benefits offered for developing novel effective control program strategies and improving service delivery should be realised in additional settings.

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Appendix A

Peer-reviewed publications arising from research summarised in Chapter 2

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