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Original Article

Why Do Neonates Die in Rural Gadchiroli, India? (Part I): Primary Causes of Death Assigned by Neonatologist Based on Prospectively Observed Records

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OBJECTIVE:

To determine the primary causes of death in home-cared rural neonates by using prospectively kept health records of neonates and a neonatologist's clinical judgment.

STUDY DESIGN:

In the first year (1995 to 1996) of the field trial in Gadchiroli, India, trained village health workers observed neonates in 39 villages by attending home deliveries and making eight home visits during days 0 to 28. The recorded data were validated in the field by a physician. An independent neonatologist assigned the most probable single primary cause of death based on these recorded data.

FINDINGS:

A total of 763 neonates were observed, of whom 40 died (NMR 52.4/1000). The primary causes of death were sepsis/pneumonia 21 (52.5%), asphyxia 8 (20%), prematurity <32 weeks 6 (15%), hypothermia 1 (2.5%), and other/not known 4 (10%). Most of the prematurity or asphyxia deaths occurred during the first 3 days of life. All 21 sepsis/pneumonia deaths occurred during days 4 to 28. A similar picture existed in England before the antibiotic era.

CONCLUSION:

Sepsis/pneumonia is the primary cause in half the deaths in rural neonates cared for at home in Gadchiroli, followed by asphyxia and prematurity. Infections cause a larger proportion of deaths in neonates in the community compared to the reported proportion in hospital-based studies.

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INTRODUCTION

Although the causal analysis can be extended far beyond medical factors, we shall limit this inquiry into ''Why do neonates die in rural homes?'' only to medical causes of death. The purpose is to estimate the contribution of the main diseases in causing neonatal deaths, and, thereby, to estimate the potential for preventing deaths by preventing or treating these diseases and finally, to select the correct priorities for action. We do this in two parts:

Part I. Primary causes of death, assigned by a neonatologist.

Part II. We find that most often, death results not due to a single morbidity but due to multiple morbidities. Hence, using a multicausal analysis, we estimate the population attributable fractions of six major causes of death, and also identity different combinations of morbidities causing neonatal deaths. We estimate the proportion of deaths that would be prevented by addressing some of the main causes. We finally identify priorities based on this analysis. We also propose a hypothesis on how neonatal mortality can be reduced.

In the absence of access to hospital care, most neonatal births and deaths in rural areas in developing countries occur at home.[1] Hence, for selecting the appropriate interventions to reduce neonatal mortality, it is essential to know the causes of neonatal deaths in rural homes. However, most available studies are hospital based.[2–4] The situation of neonatal health in rural homes cannot be extrapolated from the hospital-based studies because the conditions are radically different. Besides, only selected neonates reach hospitals. Therefore, we need information from population-based studies.

Population-based studies have invariably used retrospective inquiry or ''verbal autopsy'' to determine the cause of death.[5–7] However, this method has not been validated for neonatal deaths, except for neonatal tetanus.[8] The diagnosis of birth asphyxia as the cause of death, based on history alone, may be invalid, since

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mothers may not be able to correctly report the condition of the baby at birth. Determining that low birth weight (LBW), sepsis or hypothermia is the cause of death needs ante-mortem clinical observations and measurements, which are not available in verbal autopsy. Thus, the currently available community-based information on causes of neonatal deaths is of questionable validity.

This lack of valid information may affect the choice of interventions. To determine causes of death, the neonates in rural homes need to be prospectively observed, their medical data recorded, and the causes of death determined from such medical record review. Prior to the field trial in Gadchiroli, India,[9,10] such studies have not been conducted because of absence of any observer and of prospectively recorded data on neonates in rural homes.

During the first year of our field trial of Home-based Neonatal Care in rural Gadchiroli, we prospectively observed the neonates in 39 villages.[9–11] This study was conducted to answer the question: ''What are the primary causes of deaths in home-cared neonates in a rural community?''

METHODS

The first year of the intervention (1995 to 1996) in the field trial was devoted primarily to observing neonatal health with few interventions. The present study is an outcome of this observation period. The study design, area, and the methods of data collection have been extensively reported.[9–11] Therefore, their presentation here is brief.

After appropriate training, female village health workers (VHWs), one each in 39 villages, collected data on mothers during pregnancy by making three home visits. Most women in the area delivered at home, attended by traditional birth attendants (TBAs). The VHWs were also present at the home deliveries and made observations, including assessment of neonates at 1 and 5 minutes after birth. Subsequently, they visited mothers and neonates on eight fixed days (1, 2, 3, 5, 7, 15, 21, and 28) during the neonatal period, taking history, examining the baby, and recording the findings. They made additional visits on other days if the baby was sick and they were informed.

The record filled by VHWs included four sections:

(a) information during pregnancy,
(b) information during labor,
(c) first examination of newborn within 6 hours after birth, and
(d) information about mother and newborn, collected during eight or more postnatal home visits.

Altogether, information on 18 maternal and 28 neonatal variables was recorded.

In the first year of intervention, VHWs were not trained in the treatment of sick neonates. The newborns received care from the family and TBA and, if invited by the family, also from a government nurse or private doctor. The VHWs recorded the findings until the baby reached 28 days, or left the village, or died. In case of death, VHWs made efforts to collect information from the family about the circumstances before death, symptoms in the neonate, and the treatment provided. The data collection started on April 1, 1995, and continued for 1 year, until March 31, 1996.

A supervisory physician from the study team (S.B.B.) visited each neonate at home once in 2 weeks, verified the data recorded by the VHW, and noted any other observations. If a newborn was found to be sick, the family was advised to hospitalize the baby; SEARCH offered free ambulance service for transporting the sick baby; but the final decision was left to the family, who most often decided not to go to hospital. The care seeking behavior has been described earlier.[10,11]

Records of the 40 neonates who died during 1 year of the study period were reviewed by a neonatologist (V.K.P.) at the All India Institute of Medical Sciences, New Delhi, who assigned the most probable cause of death. The primary cause of death was defined as ''the disease or injury which initiated the train of morbid events leading directly to death''.[12] Although many conditions/complications contribute to death, in view of the difficulties and uncertainty involved in assigning the cause of death in neonates, we selected a limited number of principal entities as the primary causes of neonatal death: (i) prematurity, (ii) birth asphyxia, (iii) sepsis/pneumonia, (iv) tetanus neonatorum, (v) hypothermia, and (vi) others. LBW per se was not considered as the primary cause of death.

The neonatologist carefully evaluated the information in the case record. The assignment of the primary cause was based on the answer to the following question: ''Which of the six categories of primary causes of death fits best with the clinical course of the baby?'' In spite of the overlapping clinical features of various primary causes, the evolution of the clinical picture and the course of events allowed assigning a primary cause to most of the deaths. Since we were determining the primary cause as against the contributory causes, prematurity was considered only if the period of gestation was less than 32 weeks, and hypothermia (skin temperature $<95^{\circ}$F) only if it was persistent (recorded more than once) in the absence of any other major cause. Tetanus neonatorum was diagnosed if the baby of an unimmunized mother died at any time from the fourth day onwards because of inability to feed, trismus, and spasms. Sepsis was diagnosed if the baby died with features suggestive of systemic bacterial infections manifesting as septicemia, meningitis, or pneumonia. Birth asphyxia was diagnosed if the baby had failed to establish breathing at birth with subsequent features suggestive of hypoxemic ischemic encephalopathy or hypoxic damage to other

organ systems. ''Others'' included congenital malformations or any other cause, or where a definite cause could not be established.

A vital statistics surveillance system involving male village health workers and supervisors independently recorded births and deaths in the study area. This system was earlier evaluated to be 98% complete.[9,10]

The ethical clearance for the study was granted by an external committee.[9]

RESULTS

The vital statistics surveillance system recorded a total of 1016 live births in the 39 villages during the 1-year of study, and 52 of these babies died during the neonatal period. Out of the total live births, 763 neonates (75.1%) were studied by female VHWs, and 253 were not studied. A total of 40 neonates died from among the 763 studied; and 12 died from among the 253 not studied. The neonatal mortality rate in the two groups was 52.4 and 47.4, respectively ($p>0.5$). The still birth rate (SBR) in the births observed was 24/1000 births and 25/1000 in the unobserved births ($p>0.5$). Hereafter, the 763 observed neonates constitute the study population. Socio-demographic characteristics of the population in the 39 villages, the completeness of recording births and deaths, and the lack of selection bias in the neonates included in this study population have been published.[10,11,13]

Nearly 95% of mothers delivered at home and 81% were delivered by TBAs. VHWs were present during labor (74.7%) and within 6 hours of the birth (92.4%). Data on maternal and labor characteristics and the incidence of various neonatal morbidities and the associated case fatality have been published.[10,13] In all, 42% neonates were LBW (<2500 g), 75 (9.8%) were preterm (<37 weeks), 130 (17%) had clinical features suggestive of infection, and 26 (4.6%) had severe asphyxia at birth. Only three (0.4%) neonates were hospitalized for sickness. None of them died.

A total of 40 neonatal deaths occurred in the 763 study neonates, giving the neonatal mortality rate of 52.4 per 1000 live births (95% CI: 36.6 to 68.2). Of this, early NMR (during days 1 to 7) was 30.1 per 1000 live births (23/763), and late NMR (during days 8 to 28) was 22.3 per 1000 live births (17/763).

The primary causes of death are shown in Figure 1. Sepsis 21 deaths (52.5%, 95% CI 37.0 to 69.0), asphyxia 8 deaths (20%, 95% CI 7.6 to 32.4), and prematurity <32 weeks 6 deaths (15%, 95% CI 3.9 to 26.1) were the most common primary causes. The temporal distribution of neonatal deaths by the primary cause is presented in Table 1. Almost all deaths due to asphyxia and prematurity occurred in the first 3 days, while all sepsis deaths occurred after 3 days of life. Out of the 17 deaths in the late neonatal period, 16 occurred due to sepsis. The mean day of death due to sepsis was 12.5.

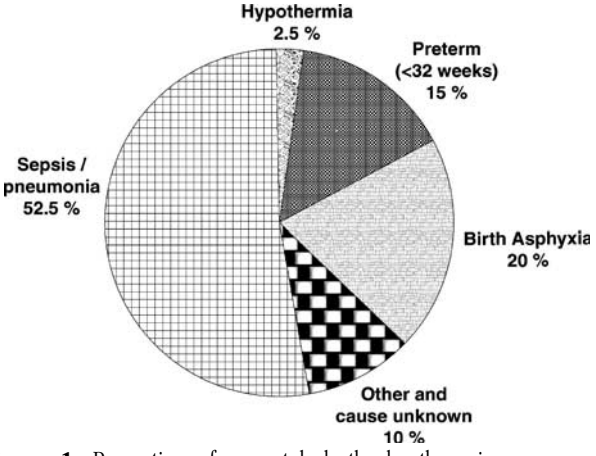

Figure 1. Proportion of neonatal deaths by the primary cause of death.

Table 1 Primary Causes of Neonatal Deaths and the Day of Death ($n=40$ Deaths)

Primary cause	Day of death					% Deaths (95% CI)	Mean age at death (days)	CSNMR/1000 live births*
	1–3	4–7	8–14	15–28	Total			
Preterm <32 weeks	6	—	—	—	6	15.0 (3.9–26.1)	2.0	7.9
Birth asphyxia	7	1	—	—	8	20.0 (7.6–32.4)	1.8	10.5
Sepsis/pneumonia	—	5	11	5	21	52.5 (37.0–69.0)	12.5	27.5
Tetanus neonatorum	—	—	—	—	—	—	—	—
Hypothermia	—	1	—	—	1	2.5 (−2.3–7.3)	5.0	1.3
Other and cause not known	1	2	—	1	4	10.0 (0.7–19.3)	8.5	5.2
Total	14	9	11	6	40	100.0	7.9	—

*Cause specific neonatal mortality rate/1000 live births.

DISCUSSION

This is the first study in which the neonates in rural homes were prospectively observed, including during home-delivery and at birth, and the causes of death determined from these ante-mortem records. It revealed that sepsis was the primary cause in half of the deaths, with most of the sepsis deaths occurring during 4 to 28 days of life. This picture is quite different from the one gained from hospital-based studies. The primary causes of neonatal deaths reported in the hospital-based National Neonatal Perinatal Database, India (1996)[2] were prematurity (31.0%), birth asphyxia (26.0%), infections (22.0%), and malformations (9.6%). Similarly, the World Health Organization estimates (in 2001) that, globally, the causes of neonatal deaths are: birth asphyxia/injury 29%, complications of prematurity 24%, and infections: (sepsis + pneumonia) 26%, tetanus 7%; congenital malformations 11%. LBW was an important secondary factor in 40 to 80% of neonatal deaths.[1] The proportion of deaths due to sepsis observed in this study was twice these estimates.

Are Our Findings an Artifact?

The study area and the socio-demographic characteristics were similar to most villages in India.[9–11] The NMR of 52.4 in the study population during 1995 to 1996 was virtually identical to the 52.3 reported by the Sample Registration System of the Govt. of India in 1995.[7] The reporting of births and deaths in the study area was 98 to 99% complete.[9] Although not all neonates born in the 39 study villages could be studied, there was no apparent selection bias in the neonates studied and not studied,[10,13] and the quality of data collected was verified in the field by a physician and also validated by parallel observations.

The date of last menstrual period was recorded by VHWs during early pregnancy. Hence, the period of gestation could be estimated based on history. Only deaths in neonates <32 weeks were considered for prematurity as the primary cause of death. Therefore, prematurity as an associated cause of death in neonates >32 weeks is not represented in this analysis. (It is included in the next article, ''Why do neonates die in rural homes, part II''.)

As the VHWs were present at the time of home deliveries and recorded the cry and breathing at 1 and 5 minutes after birth, this cohort of neonates provides a reliable estimate of the incidence of birth asphyxia in home-delivered neonates. Of the 10 neonatal deaths that occurred in severely asphyxiated neonates, asphyxia was assigned as the primary cause in eight deaths. Thus, the estimated proportion of deaths due to asphyxia (20%) in this cohort seems reliable.

The diagnosis of sepsis in this study was based on data prospectively collected by the VHW as interpreted by a neonatologist. Some degree of inaccuracy is inherent in an approach that is based on clinical findings only and not on laboratory workup including bacterial cultures. Many conditions in neonates may mimic sepsis. We recognize this limitation of the study. However, radiological and bacteriological investigations are unlikely to be available in the near future to the population of interest, that is, home-cared rural neonates. Hence within these limitations, the method adopted in this study appears to be the best available.

In our study, sepsis/pneumonia was not identified as the cause of death for infants who died in the first 3 days of life. It is quite possible we misclassified these early deaths and hence missed some cases of early-onset sepsis. Based on the onset, it is customary to classify neonatal sepsis into early (onset within 3 days) or late (onset after 3 or more days) varieties. Early-onset sepsis may occur as pneumonia presenting as respiratory distress, which may be, quite often, indistinguishable from that due to lung immaturity (hyaline membrane disease), aspiration syndromes, or metabolic disease. Out of 14 deaths on days 1 to 3, 13 were assigned to prematurity and asphyxia (Table 1). Infection may have contributed to death in premature neonates, or may result in failure to establish breathing at birth mimicking asphyxia. Hence, early-onset sepsis may be a cause of death in some of the deaths occurring during 1 to 3 days of life. It is also possible that sepsis may have had an early onset, but it actually killed the infant after 3 days of life, and hence the death was included in the later time period.

How can the Finding of the High Proportion of Neonatal Deaths due to Sepsis be Explained?

A high proportion of LBW (42%) and preterm (10%) babies in the neonates exposed to unhygienic conditions and care, resulting in a large proportion acquiring infections (umbilical infection, skin infection, and clinically suspected sepsis), and lack of access to medical care seem to be the main reasons for such a high proportion of deaths due to infections.[10,11,13]

The study population being community-based may be another explanation for this observed difference. Since hospital-born neonates receive hygienic care and early treatment with antibiotics on the slightest suspicion of infection, the incidence of sepsis as well as deaths due to sepsis are expected to be low in them. Moreover, hospital-delivered neonates are very often discharged within a few days after birth,[14] but almost all sepsis deaths in this study occurred after 3 days of birth. Hence, it is likely that hospital-based information selectively underrepresents sepsis deaths. In a global review, the proportion of neonatal deaths attributed to infections (including tetanus) were reported to be 4 to 56% in hospital-based studies vs 8 to 85% in community-based studies.[15] This supports our contention.

This view is also supported by the causes of neonatal admissions to the peripheral hospitals. Sepsis is the most common indication for neonatal admissions to the district and subdistrict hospitals.[16] In a district hospital in Himachal Pradesh, India, 96% of neonates were admitted with the clinical diagnosis of septicemia or pneumonia.[17] Similarly, 82% neonates admitted to a subdistrict

hospital had septicemia, pneumonia, meningitis, or cellulitis as the main diagnosis.[18] Thus, it appears that if the study population is community-based or from peripheral hospitals, infections predominate as the cause of illness or death.

The probable reasons for such a high proportion of deaths due to infections in our study were poor hygiene in rural homes,[11,13] a high proportion of reproductive tract infections in mothers,[19] 42% of neonates being LBW, and the traditional custom of not breast feeding for the first 3 days, thus depriving the baby of colostrum. The observed incidence of umbilical infection was 19.8% and of skin infections was 11.5%. All these factors predispose the neonates to infections and could explain the high (17%) incidence of suspected sepsis in the 763 observed neonates.[11,13]

As many as 54.4% of the observed 763 home-cared neonates in this study had indications for medical attention. However, only 2.6% of neonates were seen by a doctor, most often an unqualified village doctor, and only 0.4% were hospitalized.[13] Parents were either unwilling or unable to hospitalize the sick neonates, and existing primary health care essentially did not provide neonatal care. The lack of medical care certainly contributed to deaths due to infection.

Most community-based studies used retrospective inquiry to determine the causes of death.[5–7] The clinical manifestations of systemic infections, except tetanus, may be subtle, varied, and insidious,[20] and hence missed in the retrospective inquiry. Our study, based on a detailed recording of prospective observations made at home, is more likely to detect infection as the cause of death. However, even a recent community-based study in rural Gambia, using retrospective inquiry, estimated that 57% deaths in neonates were due to infections.[21]

A recent global review of infections in neonates estimated that 30 to 40%, that is, approximately 1.2 to 1.6 million, neonatal deaths occur each year due to infections.[15] Our study supports this, and puts the proportion of deaths due to sepsis at nearly 50%. Yet, our estimate is not unique, and the reported proportion in community-based estimates has ranged from 8% to as high as 85%.[15]

A similar pattern existed in developed countries before the antibiotic era. The Royal College of Obstetricians and Gynaecologists and the British Paediatric Association appointed a Joint Committee to investigate the causes of the high infant mortality rate in England (47/1000 live births) in 1945. It reported on a large series of necropsies on neonates in 1943, which showed that 36.5% of dead neonates had infections, and this proportion was 73.6% in the neonatal deaths occurring during 8 to 28th days of life.[22]

The limitations of this study must be kept in mind. Nearly 25% of births and neonatal deaths in the area were not observed by VHWs and hence not included in the study. Moreover, this is a relatively small size study, in one area. Hence, the estimates have wide confidence intervals. Other prospective observational studies on home-cared neonates need to be conducted in other areas to confirm our findings. The pattern of cause of death seen in this study may vary with the different levels of NMR. The proportion of deaths due to infection may be smaller at the lower levels of NMR. However, the picture reported in this study may be relevant to a large number of developing countries, including the Indian subcontinent, where NMR remains high.

We have already mentioned the limitations of diagnosis based only on history and physical examination, without laboratory investigations. Attributing death to a single primary cause is convenient but arbitrary. In reality, most deaths were associated with multiple, overlapping morbidities and mean number of morbidities per 763 observed neonates was 2.2. Hence, although this analysis provides very useful information it does not provide the complete picture. In a subsequent analysis, we attempt to take into consideration multiple morbidities as the cause of death.

CONCLUSIONS

This prospective observational study of home-cared neonates in a poor, rural community suggests that infections are the most important cause of neonatal deaths. Infections contribute a larger proportion of neonatal deaths at a high level of NMR such as is prevalent in rural India, and in the community-based estimates. No death occurred due to tetanus — probably because 79% of mothers received tetanus toxoid[10] and because TBAs were trained and provided with clean blades and thread. Since all sepsis deaths occurred from day 4 onwards, we see an opportunity for reducing the incidence of acquired infection by providing health education, improving hygiene, and promoting early breast feeding. And finally, those who develop clinical features suggestive of sepsis need early treatment with antibiotics. Since the mean day of death due to sepsis was 12.5, most of these neonates are likely to be at home. If monitored for sepsis, it may be possible to detect and treat them in time.

References

1. Save the children. State of the World's Newborn: Save the Children. Washington DC; 2001.
2. National Neonatology Forum. National neonatal–perinatal database. Report for the year 1995, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi; 1996.
3. Singh M, Deorari AK, Khajuria RC, Paul VK. A four year study on neonatal morbidity in a New Delhi hospital. Indian J Med Res (B) 1991;94:186–92.
4. Bhakoo ON, Narang A, Kulkarni KN, et al. Neonatal morbidity and mortality in hospital-born babies. Indian Pediatr 1975;12:303–8.
5. Indian Council of Medical Research. A national collaborative study of identification of high-risk families, mothers and outcome of their off-springs with particular reference to the problem of maternal nutrition, low birth weight, perinatal and infant morbidity and mortality in rural and

urban slum communities An ICMR Task Force Study. Indian Council of Medical Research, New Delhi; 1990.
6. National Family Health Survey, India, 1992–93. International Institute for Population Sciences, Bombay (1994).
7. Registrar General, India. Sample registration system, fertility and mortality indicators, 1993. Government of India, New Delhi; 1995.
8. Kalter HD, Gray RH, Black RE, Gultino SA. Validation of postmortem interviews to ascertain selected causes of death in children. Int J Epidemol 1990;19:380–6.
9. Bang AT, Bang RA, Baitule SB, Deshmukh MD, Reddy MH. Effect of home-based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. Lancet 1999;354:1955–61.
10. Bang AT, Bang RA, Baitule SB, Deshmukh MD, Reddy MH. Burden of morbidities and the unmet need for health care in rural neonates: a prospective observational study in Gadchiroli, India. Indian Pediatr 2001;38:952–65.
11. Bang AT, Bang RA, Reddy MH, Deshmukh MD. Methods and the baseline situation in the field trial of home-based neonatal care in Gadchiroli, India. J Perinatol 2005;25:S11–7.
12. World Health Organization. International Classification of the Diseases. 9th round, Vol. 1. WHO: Geneva; 1977.
13. Bang AT, Reddy MH, Baitule SB, Deshmukh MD, Bang RA. The incidence of morbidities in a cohort of neonates in rural Gadchiroli, India. J Perinatol 2005;25:S18–28.
14. World Health Organization (1996). Essential newborn care: report of a technical working group, 1994. WHO/FRH/MSM/96.13 WHO, Geneva; 1996.
15. Stoll Barbara J. Neonatal infections: a global perspective. In: Remington JS, Klein JO, editors. Infectious Diseases of Fetus and Newborn Infant. Philadelphia: WB Saunders Co. (in press).
16. Paul VK, Ramani AV. Newborn care at peripheral health facilities. Indian J Pediatr 2000;67:378–82.
17. Sharma BB, Paul VK, Deorari AK, Padmalatha P, Rama G. Profile of sick neonates at a remote district hospital in Himachal Pradesh. Presented at the XVIII Annual Convention of National Neonatology Forum, Vellore, 1998.
18. Gulati S, Kapoor SK, Anand K, Goswami K, Paul VK. What morbidity is seen in outborn neonates admitted at a sub-district hospital? Presented at the XV Annual Convention of National Neonatology Forum, Patna, 1995.
19. Bang RA, Bang AT, Baitule M, et al. High prevalence of gynecological diseases in rural Indian women. Lancet 1989;i:85–8.
20. Klein JO, Marcy SM. Bacterial sepsis and meningitis. In: Remington JS, Klein JO, editors. Infectious Diseases of the Fetus and Newborn Infant. 3rd ed. Philadelphia: Saunders; 1990. p. 601–56.
21. Leach A, McArdle TF, Banya WAS, et al. Neonatal mortality in a rural area of The Gambia. Ann Trop Pediatr 1999;19:33–43.
22. Joint Committee of the Royal College of Obstericians and Gynaecologists and the British Paediatric Association. Neonatal Mortality and Morbidity. London: Her Majesty's Stationery Office; 1949.