Appendix 4: Acute Respiratory Infections (ARI)

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NOTE: The precise outcome and definition of acute respiratory infection (ARI) differs between studies. Studies report on incidences of pneumonia (defined in various ways e.g. radiologically or using Integrated Management of Childhood illness (IMCI) criteria), ARI and acute lower respiratory infection (ALRI). For the purpose of this report, in which a number of studies are reviewed, the terms will be used interchangeably; however the specific outcome reported by a study will be used when referring to that study.

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6) Integrated Serviced land Project (Cape Town)

LIST OF ABBREVIATIONS

ARI	Acute respiratory infection
HIV	Human Immunodeficiency Virus
ETS	Environmental tobacco smoke
SFU	Solid fuel use
ALRI	Acute lower respiratory infection
WHO	World Health Organisation
PGWC	Provincial Government of the Western Cape
OAP	Outdoor air pollution
LBW	Low birth weight
EPI	Expanded Programme of Immunisation
DPT	Diphtheria, Pertussis , Tetanus Vaccine
SES	Socio-economic status
NGO	Non-governmental organization
CO	Carbon monoxide
NO_2	Nitrogen dixide
SO_2	Sulphur dioxide
INP	Integrated Nutrition Programme
PEM	Protein-energy malnutrition
SD	Standard deviation
RR	Relative risk
OR	Odds ratio
CI	Confidence interval
WFA	Weight-for-age
CSG	Care Support Grant
CDG	Care Dependency Grant
IMCI	Integrated Management of Childhood Illness
iSLP	Integrated Serviced Land Project

INTRODUCTION

Childhood acute respiratory infection (ARI) especially pneumonia are a major cause of childhood morbidity and mortality in developing countries accounting for approximately 1.9 million (95% confidence interval 1.6 to 2.2 million) deaths globally in children under five each year (Black et al., 2003; Campbell, 1995; Mulholland, 1999; Williams et al., 2002) More than 90% of ARI-related deaths occur in the developing world (Black et al., 2003; Williams et al., 2002) . This has been exacerbated by the human immunodeficiency virus (HIV) epidemic especially in sub-Saharan Africa as pneumonia is the commonest causes of illness, hospitalisation and mortality in HIV-infected children (Zar, 2004).

There are multiple social and environmental factors associated with ARI morbidity and mortality in childhood. These include comorbid illnesses especially HIV, malnutrition, prematurity or measles, environmental determinants particularly passive smoke exposure, overcrowding or poor living conditions and social factors principally poverty and poor access to both preventative (including immunization) and curative health services.

IMPACT AND BURDEN OF DISEASE

Pneumonia constitutes a major proportion of the global burden of childhood disease responsible for around 20% of childhood deaths, especially in developing countries (Black et al., 2003; Campbell, 1995; Mulholland, 1999; Williams et al., 2002). Annually, almost half of the 1.9 million deaths due to acute respiratory tract infections in children under 5 years of age occur in Africa (WHO, 2005). In South Africa, childhood community acquired pneumonia accounts for between 30-40% of hospital admissions with associated case fatality rates of between 15-28% (Zwi et al., 1999; Graham, 2003).

Studies from South Africa have estimated the proportion of under-5 deaths due to pneumonia to range from 8% to 22% (Von Schirnding et al., 1991; Wyndham, 1970). These studies, done during the apartheid era, reported marked differences in pneumonia-specific mortality by ethnic group with the highest rates for black African children and the lowest rates for Caucasians. A study investigating childhood pneumonia deaths from 1968 to 1985 reported high rates in all population groups, ranging from 7 to 270 times those in developed countries and highlighted the large differences in rates by ethnic group (Von Schirnding et al., 1991). This is consistent with the observation that the proportion of children dying from pneumonia is related to the general under-5 mortality rate, declining as the under-5 mortality diminishes (Williams et al., 2002). In South Africa, under-5 mortality for 2003 was reported as 66 per 1000, representing a 1.3% increase from 1995-99 and a 1.6% increase from 2000-2003 (WHO, 2005). Moreover, in South Africa there is wide variation in under-5 mortality according to geographical and socioeconomic factors (Von Schirnding et al., 1991; Wyndham, 1970; Wyndham, 1977).

Besides directly causing childhood deaths, pneumonia is frequently an associated cause of mortality in children with other underlying conditions. Thus for every death directly attributable to pneumonia, 2 or 3 additional deaths associated with pneumonia may occur (Williams, 2002). Co-morbid conditions especially malnutrition, measles or immunosuppression such as HIV increase the severity and risk of mortality from pneumonia (Black et al., 2003; Zar, 2004; Duke et al., 2003).

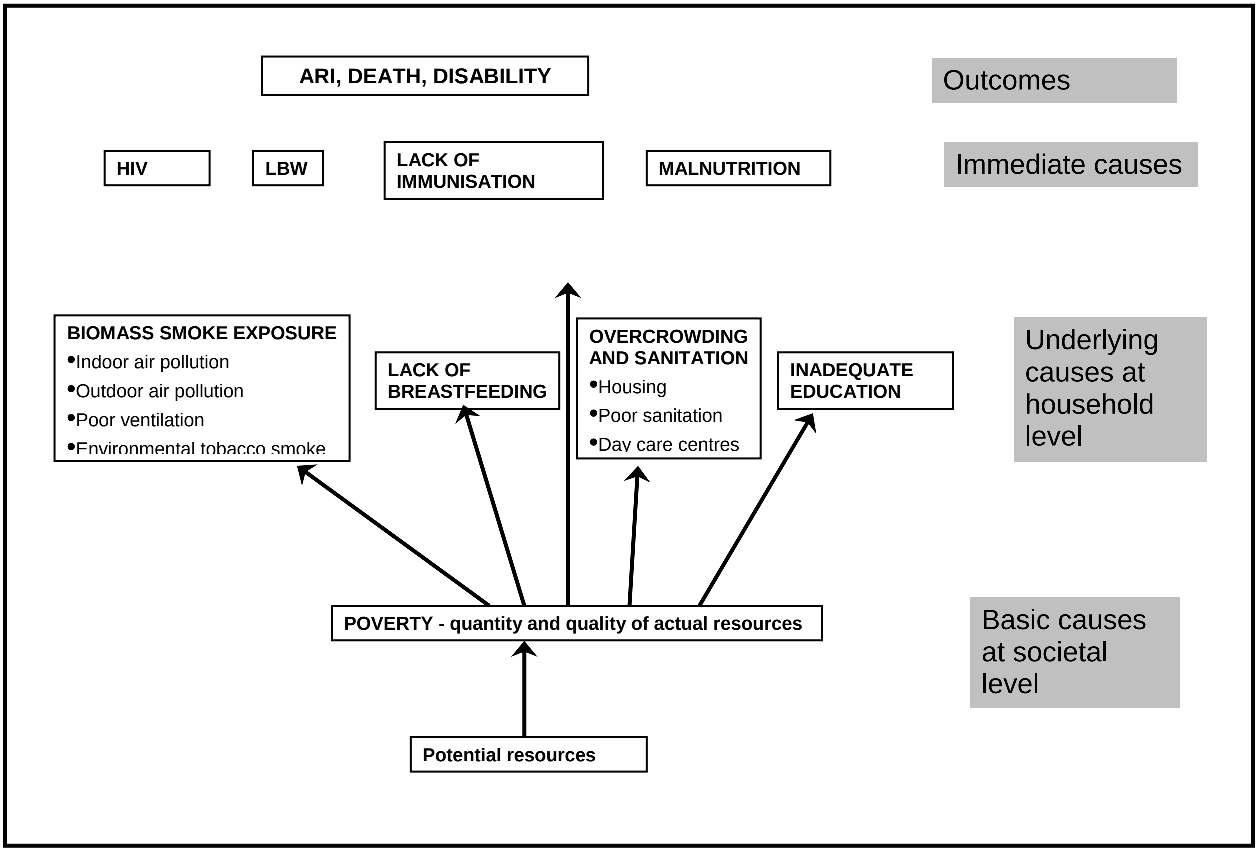
The HIV pandemic has resulted in a large increase in the incidence, severity and outcome of childhood pneumonia in developing countries. Respiratory disease especially ARI has been reported to be the dominant cause of hospitalization and death in HIV-infected African children (Zwi et al, 1999; Ikeogu et al, 1997; Lucas et al, 1996; Vetter et al., 1996). Pneumonia-specific mortality rates are higher in HIV-infected children with case fatality rates consistently reported as 3 to 6 times those of HIV-negative patients (Madhi et al., 2000a; Madhi et al., 2000b; Zar et al., 2001). In South Africa there are approximately 300 000 HIV-infected children of whom 10-12 000 live in the Western Cape (Zar, 2003). The mosr recent antenatal surveys indicate that approximately 16% of pregnant women in the Western Cape are HIV-infected. Although the Western Cape has instituted a provincial program to prevent mother to child transmission, substantial numbers of HIV-infected infants are still being born. Thus ARI remains one of the most important causes of illness and death in such children.

Besides the impact on the epidemiology and outcome from childhood pneumonia, HIV has changed the spectrum of pathogens responsible for childhood pneumonia with increased emergence of opportunistic infections such as *P jiroveci* pneumonia (PCP) and a large increase in TB incidence Zar, 2004; Zar et al., 2000; Graham et al., 2000; Ruffini et al., 2002; Chintu et al., 2002; Madhi et al., 2000a; Zar et al., 2001; Jeena et al., 2002).

The efficacy of usual management strategies such as choice of empiric antibiotic therapy or duration of therapy differs for HIV-infected children. The efficacy of preventative measures such as immunization is reduced in HIV-infected children particularly if they are not receiving anti-retroviral therapy (Zar, 2003). Therefore, the HIV-epidemic has increased the burden of childhood pneumonia with a concomitant need for health care resources.

RISK FACTORS FOR ARI

FRAMEWORK OF RISK FACTORS FOR ARI



Malnutrition

A study on the nutritional status of South African children (SAVACG 1995) found 7% of children in the Western Cape to be underweight and 11.6 % to be stunted. Although these figures may appear moderate, levels are likely to be higher in certain areas in which children are exposed to additional risk factors for ARI, as both underweight and stunting were more severe in children living in informal housing and whose mothers lacked education (SAVACG 1995).

Numerous studies in developing countries, particularly in South America and Asia, Have shown consistent, significant and dose-response relationships between malnutrition and both incidence of, and mortality due to, ARI in children (Victora et al, 1999; Fonseca et al., 1996, Broor et al., 2001). In Fortaleza, Brazil, for example, children moderate and severely underweight children were 4.6 times more likely to develop radiologically confirmed pneumonia compared to adequately nourished counterparts, while mortality studies have shown malnourished children to have between 2 and 25 times the risk of death from pneumonia (Victora et al, 1999). The dose-response relationship found in almost all studies is notable in showing that even relatively mild degrees of malnutrition increase risk for ARI.

The increased risk and severity of ARI associated with malnutrition is biologically plausible, as malnourished children are known to have impaired immunological (particularly cell-mediated) responses and more severe infections (Victora et al, 1999).

Malnutrition is itself both a cause of under-5 mortality as well as a risk factor for incidence of and mortality due to other major causes of under-5 mortality such as diarrhoeal disease and HIV-infection.

Lack of breastfeeding

Victora et al (1999) reviewed studies associated with ALRI from developing countries and/or low-income populations in developed countries and found consistently increased risk of ALRI among children who were not breastfed or partially breastfed compared to exclusively breastfed children, again with a dose-response relationship. The risk of ARI is increased by approximately 60% in children who are never breastfed, while non-breastfed children are between 2-3 times more likely to die from ALRI compared to those who are breastfed. (Broor et al, 2001; Fonseca et al, 1996; Victora et al, 1999)

The relative importance of this risk factor is obviously dependent on local breast feeding practices. SAVACG (1994) found that 24% of children in the Western Cape are never breastfed with a further 19% being breastfed for less than 6 months.

The protective effect of breastfeeding is primarily due to its unique anti-infective properties, providing passive protection against pathogens, stimulating the infant's immune system and inhibiting gastro-intestinal colonization by Gram-negative species (Victora et al, 1999.). In low-income settings, exclusively breastfed babies may have better nutritional status during the first few months of life and are less likely to be exposed to contaminated foods and thus contract gastro-enteritis, which would also impair nutritional status (Victora et al., 1999; Graham 1990). Interestingly, the protection afforded by breast-feeding against ALRIs persists well beyond the breastfeeding period (Victora et al, 1999).

Low birth weight (LBW)

While LBW is itself an important cause of childhood mortality, it is also associated with ALRI morbidity and mortality (Victora et al, 1999; Graham 1990).

Victora et al (1999) reviewed 4 studies of ALRI mortality and LBW and found a pooled estimate of 2.9 times increased risk of death for children with birth weight <2500g. There is also consistently increased incidence of ALRI in LBW infants in almost all studies with relative risks between 1.4 and 3 times, depending on the severity of LBW (Fonseca et al, 1996; Victora et al, 2004; Graham 1990).

LBW may be associated with increased risk of ARI due to its association with other measures of socio-economic deprivation as well as because it may lead to shorter duration of breastfeeding and poorer nutritional status, both of which are independent risk factors for ARI. Nevertheless, the associations between LBW and ARI morbidity and mortality are robust to adjustment for confounding, and there are other mechanisms by which LBW itself may predispose to ARI, namely reduced immune competence and impaired lung function (Victora et al, 1999).

Lack of immunization

Global immunization programs through the Expanded Program of Immunization (EPI) have produced a decline in measles pneumonia and childhood pertussis. In the Western Cape a recent survey (Corrigall, 2005) found that overall vaccine coverage was 80%, 77% and 48% for vaccines due by 14 weeks, 9 months and 18 months respectively. A significant number of children are therefore not even receiving their early vaccines, while a large proportion of children are not receiving full courses of Diphtheria, Pertussis, Teatanus (DPT) and measles vaccines. Children in the Boland region were significantly less likely to have received vaccines due by both 14 weeks and 9 months compared to those in the Cape Town Metro region.

South Africa has also included the *H influenzae* type b (Hib) vaccine into national guidelines, with potential to reduce Hib invasive disease by 46% to 93% in vaccine recipients (Mulholland et al., 1997; Swingler et al., 2003; Madhi et al., 2002). However, the efficacy of this vaccine for protection against invasive disease is reduced in HIV-infected children not receiving anti-retroviral therapy, (44% in HIV-infected compared with 96% in uninfected children) (Madhi et al., 2002).

Cost is however a major challenge to the adoption of the new generation of childhood conjugate bacterial vaccines, such as the pneumococcal conjugate vaccine, into the EPI schedules in developing countries. The potential effectiveness of these vaccines is outlined in the interventions section below. Furthermore investment is required to ensure that the most vulnerable children have access to vaccines by development of the infrastructure and resources required for a successful vaccine programme.

Environmental tobacco smoke (ETS) and maternal prenatal smoking

More than 150 studies have been published linking ETS to respiratory illness in children, with meta-analyses finding strong evidence for associations between both prenatal maternal smoking and postnatal ETS exposure and risk of ARI in children. (DiFranza et al, 2004.)

In a review of 38 studies, Strachan et al (1997) found all but one to be consistent with an increased risk of ARI for children exposed to parental smoking, with pooled ORs of 1.57 (95% CI 1.42 to 1.74) for smoking by either parent and 1.72 (95% CI 1.55 to 1.91) for maternal smoking. Risk of chest illness was also increase if household members other than the child's parents smoked. (OR: 1.29, 95% CI 1.16 to 1.44). When limited to children under 5, the effect is even more marked with an OR of 2.5 (95%CI: 1.86-3.36) (Brims and Chauhan, 2005) These associations with parental smoking are maintained after adjustment for confounding factors, and there is evidence of a dose-response relationship. (Brims and Chauhan, 2005)

Several reviews have concluded that the relationship between ETS exposure and ARI in children is likely to be causal and as a result of a direct adverse effect on the child's pulmonary function , and not simply due to the parents themselves being more likely to acquire and thus transmit ARIs in the home. (DiFranza et al, 2004; Brims and Chauhan, 2005)

In addition to the increased risk of ARI morbidity among children exposed to ETS, there is also an increased risk of hospitalization and mortality. (DiFranza et al, 2004; Brims and Chauhan, 2005)

Maternal smoking during pregnancy appears to further increase the risk of ARI associated with ETS exposure, with term infants dying from respiratory disease being 3.4 times more likely to have had mothers who smoked during pregnancy. This effect was not simply attributable to differences in birth weight between infants of smokers and non-smokers. (Malloy et al, 1988; DiFranza et al, 2004)

Indoor air pollution

Use of biomass fuels for cooking and heating with resultant indoor air pollution is common in many areas in South Africa, with the rapid growth of informal housing without proper infrastructure being an important cause. (Sanyal and Maduna, 2000). Although only a small proportion of all Western Cape households use solid fuels for cooking and heating (3.5% and 7.5%) respectively, extent of SFU would be notably higher among those in certain areas likely to have other risk factors for ARI, such as poverty (Statistics South Africa 2001). Studies in two townships in Gauteng indicated that the levels of particulate matter far exceeded standards laid down by the WHO. (Terblanche et al, 1992)

Biomass fuels produce small amounts of energy but large amounts of indoor pollutants, often emitting 50 times more pollutant concentrations than energy equivalent natural gas (Graham, 1990). Housing characteristics in developing countries with poor ventilation and dispersion may exacerbate pollutant concentrations. (Brims et al, 2005) A study in very low and low income communities in an Eastern Cape township, for example, found levels of NO2 and SO2 to be 7 times and 13 times higher respectively than the risk-free levels considered acceptable. (Sanyal and Maduna, 2000)

Air pollutants associated with SFU may adversely affect specific and non-specific host defenses of the respiratory tract against pathogens and, while, smoke from SFU is a complex and variable mixture containing a number of potentially toxic substances about which only broad generalizations can be made, there is sufficient understanding of the toxicological properties of these mixtures for them to plausibly increase risk of ARI. (Smith et al, 2004)

Children are particularly vulnerable to the hazardous respiratory effects of SFU because of the large amount of time spent with their mothers doing household cooking. (Smith et al, 2004)

There is strong international evidence from developing countries, especially Africa, linking SFU with increased incidence and severity of ARI in children under 5. (Smith et al, 2004; Desai et al, 2004; Brims et al, 2005, Broor et al, 2001) In a review of 13 studies from developing countries, (Smith et al, 2004) almost all studies found positive associations between SFU and ALRI in children. Although studies were too different to determine a combined measure of effect, barring 2 studies finding no significant association, SFU was associated with approximately twice the risk of ARI. In the single study examining mortality, the risk of death from ARI was increased 12 times in those exposed to SFU. In addition, Pandey et al (1989) have shown a dose response relationship between maternally reported time spent near the cooking stove and ARI.

In a local Eastern Cape study, increased incidence of ARI was ecologically linked with communities in which indoor air pollutants were highest. (Sanyal and Maduna, 2000) These communities were also the poorest. Although lack of adjustment for socio-economic status is a weakness of this study, this nevertheless highlights the interplay between poverty and other risk factors for ARI and other causes of childhood illness. The important role of affordability, rather than safety or efficiency in choice of fuel among many poor South Africans is clear. Notably although nearly 90% of dwellings there is still a significant minority using solid fuels for heating and cooking. (Statistics South Africa 2001) Targeted interventions in these groups likely to have other risk factors for ARI may have significant impacts on the burden of disease.

Outdoor air pollution (OAP)

Episodes of OAP in developed countries have been associated with significant increased mortality, and it has been suggested that children are particularly at risk from extreme pollution. (Romieu et al, 2002) Evidence from a number of studies supports concern that exposure to pollution, especially fine particles and ozone, icrease risk of ARI in children. Air pollutants adversely affect immune function and cause inflammatory reactions, which may increase susceptibility to bacterial infection. (Romieu et al, 2002)

Crowding and number of siblings

Many children are exposed to very crowded conditions at home, and this increases risk of transmission of illness. Most studies in developing countries have found that the average area of habitable space per person is well below the WHO recommendation of 12m2 (Cardoso et al 2004), and the situation in many areas of the Western Cape is no different. While nearly 20% of Blacks in the Western Cape live in households of 6 people or more, 70% of Black dwellings comprise 3 rooms or less (Statistics South Africa 2001; Watson 1994).

In a case-control study in Sao Paulo, Cardoso et al (2004), found crowding ($\geq$ 4 people sharing the child's bedroom) to be associated with 2.5 fold increased risk of ALRI, with cases tending to live in smaller houses than controls. Other studies from developing and developed countries have found similar effects both for crowding and number of siblings. (Fonseca et al, 1996a; Brims et al, 2005; Ozcirpici et al, 2004; Howden-Chapman, 2004; Graham 1990)

Crowding is a result both of larger family size and smaller, poor quality housing. These are both associated with poor socio-economic status, which itself exacerbates crowding with more than one family unit sharing a single dwelling.

Crowding may occur outside the home in day care centers. Numerous studies in both developed and developing countries have shown children attending day care to be at increased risk of both acquiring upper and lower ARI (Fonseca et al, 1996b; Lu et al, 2004; Bell et al, 1989; Fleming et al, 1987) as well as of needing hospitalization for ARI. (Anderson et al, 1988) Risk of acquiring ARI in day care centers is particularly increased for younger children (less than 18 months of age) and those with poorer access to health care services. (Lu et al, 2004) Specifically in a developing country context, incidence of ARI increases with the proportion of time since the child was born that the mother has been working (Fonseca et al, 1996b)

Sanitation

Cardoso et al. (2004) found children with respiratory illness to come from houses with poorer sanitation than controls, while in developed countries promotion of hand washing has been associated with reduced incidence of respiratory illness (Luby et al, 2005). Even in urban areas in South Africa, 20% of people use inadequate sanitation facilities, while in rural areas this is as high as 35%. (UNICEF 2007)

Housing quality

Poor quality housing is defined in various ways by different studies and thus it is difficult to determine effects of specific housing characteristics across a number of studies. Nevertheless, there is consistent evidence that damp and humid conditions are associated with ARI in children (Howden-Chapman 2004; Rylander and Megevand, 2000) while Ozcirpici et al. (2004) found a composite poor housing status score, was associated with increased incidence of ARI.

Socio-economic status (SES) (including poverty and lack of education)

SES is measured in different ways by different studies and includes, inter alia, components of status, income, education and housing. Poverty and low SES are associated with so many other independent risk factors for ARIs, such as overcrowding, poor sanitation, poorer access to medical care, poorer immunization coverage, malnutrition, poor housing, LBW and SFU, that it is difficult to tease out the effect of low SES *per se*. Interestingly, after adjusting for many of these known risk factors, many studies have found no residual effect of low SES, however this may in part be due to the lack of diversity in SES within these studies (Fonseca et al 1996; Broor et al, 2001).

Nevertheless, the underlying influence that low SES has on many of the known risk factors for ARI, makes it an important factor to consider, particularly when seeking interventions to reduce ARI incidence and mortality.

Some studies have found associations between SES and parental education and ARI incidence but these have not been consistent or robust to adjustment for confounding

(Graham et al, 1990). However, a review by Von Ginneken et al (1996) found strong relationships between ARI mortality and maternal education consistent across a number of studies. The authors estimate that approximately half of this effect is related to the economic advantages afforded to better educated mothers. These may be attained both through women increasing their own earnings and because educated women are more likely to marry educated and wealthier men. Apart form its economic impact, maternal education was found to have little effect on crowding and indoor air pollution, but to dramatically increase the health care use. There is thus a more appropriate response when pneumonia occurs, hence effects on mortality.

In the Western Cape, although current levels of school enrolment are not that poor, the legacy of apartheid means that existing educational status of reproductive age women is inadequate. Twenty percent of women have incomplete primary school education or less, and nearly 10% of African women have no schooling at all. (Statistics South Africa, 2001 census)

Interestingly, O'Dempsey et al (1996) in the Gambia found children of mothers with a personal source of income to be at lower risk of ALRI. This highlights the dilemma faced by mothers who while enhancing their children's health by increasing their income through working, may paradoxically place their children at risk by the required shortening duration of breastfeeding and placing children in daycare centers from a young age.

INTERVENTIONS

Existing and potential interventions that address the risk of ARI morbidity and mortality in young children can be grouped into targeted, specific interventions that address specific risk factors and broader interventions that address a number of risk factors and may have far reaching health impacts beyond ARI and even childhood illness in general. Ehiri and Prowse (1999) propose that for real effects on childhood mortality, interventions cannot be limited to the health sector, but need to address environmental and societal factors underlying childhood diseases. This review therefore focuses on these factors, with only limited inclusion of specific medical interventions that could impact on ARIs.

Specific risk factor interventions

1. Malnutrition, Low birth weight and Breastfeeding

Interventions addressing these risk factors will primarily be covered by other subgroups of the childhood diseases working group. Nevertheless, it is important to highlight that malnutrition is a major cause of morbidity and mortality in childhood ARI with approximately 50% of death due to ARI associated with comorbid malnutrition in children under 5 years (Black et al., 2003).

Victora et al (1999) have calculated the potential benefits of improvements in each of these risk factors according to the prevalence of that risk factor and the proportion that can be prevented by a particular programme or set of programmes. Assuming 40% improvement in each risk factor, the predicted reduction in ALRI deaths would be 10% for both reductions of malnutrition and low birthweight, and 3% for increasing proportion of children breastfed. Although these percentages appear relatively modest, given the large number of childhood deaths due to ARI, the potential mortality prevented is significant.

With regard to malnutrition and breastfeeding, the Integrated Nutrition Programme (INP) is the major existing health sector intervention in the Western Cape. Aspects of the INP include breast-feeding promotion, growth monitoring, the Protein-Energy Malnutrition Scheme (PEM), provision of food supplements to undernourished children and adults and referral of caregivers to poverty alleviation services where necessary.

A review of the PEM scheme in a peri-urban area (Malek and Hussey., 1997) found that while it had the potential to improve nutritional status in more than 60% of children who completed 2 – 6 months of follow-up, with nearly a quarter achieving >0.5 SD increase in WFA, there are major weakness, with nearly 40% of children not returning for follow-up and deterioration in anthropometric indices of a quarter of children. Schoeman *et al*. (2004) report similar suboptimal effectiveness of the INP as a whole with poor follow-up, delivery of supplements and consequent inadequate nutritional improvement in malnourished children, as well as erratic growth-monitoring and thus detection of malnourished children, particularly after they have reached 1 year of age.

2. Immunisation

Interventions to address the suboptimal vaccine coverage in the Western Cape need to be sought.

Furthermore, consideration should be given to adding the pneumoccocal conjugate vaccine that has recently been licensed in SA, to the routine vaccine schedule. Because of cost-constraints, this vaccine has not as yet been included in the EPI program and hence remains inaccessible to the majority of South African children. However, it has great potential to reduce the burden of ARI in children as pneumococcus remains the major cause of bacterial pneumonia and death in children under 5 years (Lucero et al., 2004).

A recent South African trial found that the use of a 9 valent pneumococcal conjugate vaccine reduced invasive pneumococcal disease caused by vaccine serotypes by 65% and 83% in HIV-infected and uninfected children respectively, while the incidence of radiologically confirmed pneumonia was reduced 13% and 20% in these two groups respectively (Klugman et al., 2003). Although the efficacy of the conjugate pneumococcal vaccine was lower in HIV-infected compared to uninfected children, the overall burden of pneumonia prevented in HIV infected children was 9.7 fold greater mainly because of the higher underlying burden of pneumococcal pneumonia in HIV infected children (Madhi et al., 2005).

Similar results have been reported by a Gambian study, where in addition to reducing the incidence of radiologically confirmed pneumonia by 37%, the vaccine was also found to reduce all-cause childhood mortality by 17% (Cutts et al., 2005).

Although the focus of this document is on intersectoral, rather than health sector-specific interventions, it would clearly be amiss not to acknowledge the enormous difference in ARI incidence and mortality that introduction of pneumococcal conjugate vaccine into the vaccine schedule for all children in the Western Cape could make. While the current South African cost of this vaccine in the private sector is approximately R500 per dose, introduction of a two-tiered pricing system for developing countries, as is applied to other vaccine prices in international public markets, could significantly reduce its cost. A cost-effectiveness analysis by Sinha *et al*. (2007) has shown that pneumococcal vaccine at a price of up to $5 per dose would be highly cost effective in almost all of 72 developing countries included in the study. Advocacy for reduction in the price of the vaccine and inclusion in the EPI schedule should therefore be a priority.

3. Zinc supplementation

Daily prophylactic elemental zinc, 10 mg to infants and 20 mg to older children may substantially reduce the incidence of pneumonia, particularly in malnourished children. 78 A pooled analysis of randomized controlled trials of zinc supplementation in children in developing countries, found that zinc-supplemented children had a significant reduction in pneumonia-incidence compared to those receiving placebo[OR of 0.59 (95% CI 0.41 to 0.83)] (Bhandari et al., 2002; Bhutta et al., 1999).

4. ETS exposure

Environmental tobacco smoke exposure remains a major risk factor for childhood ARI especially as the incidence of smoking in certain population groups in the western Cape is amongst the highest in the world. Measures to reduce ETS exposure in public places (e.g regulation of tobacco industry and advertising, legislation forbidding smoking in public places) are already in place and are beyond the scope of this review and will be address by the Cardiovascular Disease working group.

A Cochrane review of 18 studies of family and carer smoking control programmes (Roseby et al, 2006) found reductions in reported or actual ETS exposure in both intervention and control groups in 12 of 18 studies, but statistically significant better results for the intervention group in only 4 studies. Programmes with intensive counselling tended to work better, as did those that focused on participants' attitudes and behaviour rather than change in knowledge. The context of the intervention (well child, respiratory ill child, non-respiratory ill child, peripartum) did not affect success of the programme. Smoking cessation interventions perhaps targeted to certain groups eg antenatal attendees, school attendees may be of benefit.

5. Indoor and outdoor air pollution

An economic analysis by Leiman et al (2006) found that interventions at household level to reduce air pollution had the greatest impact on health and were thus the most cost effective at reducing health care costs. They argue that further industry controls are not justifiable at this point. The specific interventions recommended in order of cost effectiveness are:

- Education on "top down" ignition of fires
- Stove maintenance and replacement
- Housing insulation
- Electrification

Specifically, the Gauteng and Mpumalanga project "Basa njengo magogo" (light a fire like a grandmother) which educates about and encourages efficient fuel stacking and top down ignition of fires, resulting in a cleaner and less polluting start to the fire, was identified.

With regard to stove replacement, a Guatemalan study found that households with self-purchased or NGO-funded chimney stoves had significantly lower 24 hour kitchen CO level and lower child CO exposure, compared to those using open fires (Bruce et al, 2004). Levels were lowest for households with self-funded stoves, as these were more likely to be adequately maintained and repaired. This highlights the importance of affordability in any intervention aiming to reduce indoor air pollution, and the underlying role of poverty in choice of fuel use.

Housing improvements to improve energy efficiency have also been shown to result in reduced respiratory illness, however outcomes measured in these studies are not specific for ARI in children (Thomson et al, 2001).

6. Housing improvement and overcrowding

Rehousing is associated with improved self-reported physical health, but again, outcomes reported are not specific to children. (Thomson et al, 2001)

A number of projects to provide and improve housing are currently in place in the Western Cape. (PGWC: Housing subsidies and assistance, 2006) These include:

- Individual housing subsidies for low-income households wishing to buy a residential property for the first time.
- Rural subsidies for farm workers who do not have legal tenure but wish to build a house on the property where they reside
- Settlement schemes for farm workers
- Relocation assistance
- Housing subsidies for the disabled/health stricken
- Project-linked subsidies

- People's Housing process whereby people use their own labour to build their house, so that more of the housing subsidy can be used for building materials and a bigger house can be built. ($36m^2$ vs the standard council house of $30m^2$)

The effectiveness of these projects in reducing illness and ARI in children specifically was not obtainable.

7. Handwashing

A recent study in squatter settlements in Pakistan (Luby et al, 2005) points to a simple and potentially extremely effective measure to reduce ARI incidence. In a community randomized trial, in households receiving handwashing promotion and free plain soap children under 5 had a 50% lower incidence of pneumonia compared to those from control households. Incidence of diarrhoea was also halved. The reduction in pneumonia particularly affected the winter peak incidence, and, notably, the intervention was effective regardless of nutritional status. Effective hand washing implies that people have access to running water. Therefore access to running water should be a primary objective for all households.

Although results from a trial setting do not necessarily extrapolate to effectiveness in large-scale roll out, handwashing and provision of soap nevertheless may be a potential "magic bullet" in reducing ARI and diarrhoea incidence.

8. Maternal Education

Von Ginneken et al. (1996) showed that reduction in post-neonatal mortality (a large proportion of which is known to be due to ALRI) in 8 developing countries closely reflected improvements in maternal education (regular schooling received by woman) over a 15 year period. They thus predicted that worldwide improvements in maternal education over the next 15 years could result in reductions of pneumonia mortality of between 2 and 11% depending on the existing level of education in a given context.

Since levels of female education in the Western Cape are generally high (Statistics South Africa census 2001), the potential for further intervention in this area is probably limited in our setting, however it is important to maintain the existing situation. It is also important in measuring outcomes, to be aware that maternal education is of course a long-term investment, with the benefits in terms of child health and survival only being reaped by the next generation.

9 Poverty alleviation

Since poverty underlies so many risk factors for ARI and other childhood as well as adult causes of morbidity and mortality, measures to address it are critical to improving the health status of all people, but particularly children, in the Western Cape.

The major existing intervention for destitute parents in South Africa is the Child Support Grant (CSG) and, in the case of disabled children, the Care Dependency

Grant (CDG). Currently major obstacles to accessing the CSG include lack of awareness of the grant and lack of registration of caregivers and children with the Department of Home Affairs. In this regard, in 2004 the Department of Social Development embarked on a door-to-door campaign to increase registration in the poorest and most remote regions of the province and succeeded in registering 100 000 children within the 3 month period of the campaign (PGWC: 100 day deposits: a caring home for all, 2006). The department aimed to have all children under 11 years in the province registered by early 2005, however have not reported on whether this target has been achieved.

Evidence on the impact of these grants, as well as potentially more far-reaching redistributive poverty alleviation strategies, such as a Basic Income Grant, on health, and ARI incidence and mortality in particular, was unfortunately unobtainable. However, such information would be crucial in guiding appropriate poverty alleviation strategies.

Broader interventions

1. Integrated Management of Childhood Illness (IMCI)

Evidence suggests that this broad intervention that includes improvement of maternal health, immunization and nutritional rehabilitation is very effective. Use of case management guidelines for treatment of childhood pneumonia can significantly reduce overall and pneumonia-specific mortality in children under 5 years. A meta-analysis of community-based studies found a reduction in all-cause mortality by 27% (95% CI 18-35%), 20% (11-28%), and 24% (14-33%) among neonates, infants, and children 0-4 years of age, respectively. In addition, pneumonia-specific mortality was reduced by 42% (22-57%), 36% (20-48%), and 36% (20-49%) amongst these three groups (Sazawal et al., 2003).

2. Fauveau et al (1992) report on a community-based programme to reduce ALRI in rural Bangladesh in an area with low literacy rates and IMR approximately double that of South Africa. The programme consisted of 2 years of general interventions including promotion of oral rehydration therapy, family planning, promotion of childhood immunization, distribution of Vitamin A, referral of severely ill children to clinics and nutritional rehabilitation of malnourished children. These services were primarily provided within the health sector by Community Health Workers (CHWs) with referral to higher levels of health care where appropriate.

This initial programme was followed by an ALRI-specific intervention, namely systematic detection and case management by CHWs linked to a referral system for support.

Compared to a control area receiving only usual services, there was a 28% reduction in mortality in the intervention area during the initial non-ALRI specific services period. In the intervention area, ALRI mortality was reduced by a further 32% compared to the preceding period during the ALRI-specific intervention.

This study highlights the equal importance of non-ALRI specific interventions, such as immunization, family planning and nutritional improvement, together with specific case management in reducing ALRI mortality. Although a major reason for the reduction in ALRI mortality in this study was improved measles and DPT vaccine coverage which would not yield similar benefits in our setting where vaccine coverage is high, improvements in contraceptive use, crowding and duration of breastfeeding were also noted.

3. A Nepalese ARI control programme reports similar success with case management. (Pandey et al, 1989) However it was found that while a health sector specific programme including health education, immunization and case management resulted in substantial reductions in ARI-specific death rates, there was still unacceptably high mortality from malnutrition, chronic diarrhoea and other factors, many of which themselves impact on ARI incidence and severity. This study points to the need managing controlling many of the major disease killers of children.

4. A community-wide intervention to improve delivery of preventive services to children from low-income families in North Carolina was effective in reducing a number of risk factors for ARI, although neither ARI incidence itself nor childhood mortality was one of the outcome measures. (Margolis et al, 2001)

This was a multi-level intervention, which included formation of an intersectorally representative community board, involvement of state-health policy makers to enhance co-operation between different departments, and meetings between primary care practices to share new approaches in preventive care delivery. Primary care practices also received resource and training support to improve their preventive service delivery system. At the family level, participants received "intensive" home visiting (2 – 4 visits per month) throughout the first year of the infant's life. The focus of these visits was education, strengthening of informal support systems and linking with health and social services.

Women who received the family-level intervention were significantly more likely to use contraceptives, not smoke tobacco and have a safe home environment. Their children were also more likely to have had an adequate number of "well-child" visits and less likely to be injured. Although this study does not show an impact on ARI incidence, its impact on many ARI risk factors is notable.

5. Bhutta et al (2005) identified a number of studies in developing countries assessing the effectiveness of integrated neonatal care packages in reducing neonatal mortality, of which death due to ARI is an important cause. These packages focused on training of traditional birth attendants and or community health workers to ensure safer birthing practices, provide health education to new mothers, promote breastfeeding and immunization and appropriate management and referral of sick children. Some programmes included provision of nutritional support, family planning services and transport to health care facilities. All programmes were associated with significant reductions in neonatal mortality.

6. An existing broad intervention in the Western Cape is the Integrated Seviced Land Project (iSLP) (PGWC website: iSLP 2006). This aimed to address the socio-economic needs of 40,000 families living in informal settlements on the Cape Flats. The project served these communities in an integrated fashion by providing for their housing, education, health, economic and human development needs in a coordinated way.

Objectives of the project included building of houses, schools, clinics, community halls and recreational facilities as well as building capacity in early childhood development, economic development and environmental projects. The project was run as a partnership between the communities concerned, all 3 tiers of government, community-based organizations, utility companies, non-government organisations and consultants.

Since this project addresses many of the risk factors for ARI, its potential impact could be significant; however no outcomes have been reported.

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