Strategies for the early detection and management of chronic kidney disease–tertiary and primary health care working together

The burden of chronic kidney disease is increasing, along with other chronic diseases.

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Chronic kidney disease (CKD) and cardiovascular disease (CVD) share common risk factors such as smoking, hypertension, diabetes, obesity and hyperlipidaemia, and both have links to poverty and malnutrition. The burden of these chronic diseases is increasing.[1] CVD comprised 30% of all deaths in the world in 1998, most (78%) occurring in low- and middle-income countries.[2] The global burden of diabetes and CVD is set to rise by around 50% and 150% in the developed and the developing worlds, respectively. It is estimated that by 2020, in Africa alone, nearly 22.3 million people will have diabetes, resulting in concomitant increases in the prevalence of CKD and end-stage renal disease (ESRD).[3] This means that more patients will die of stroke, heart failure and kidney failure, with the greatest impact in developing world regions such as South Africa.

Chronic kidney disease (CKD) and cardiovascular disease (CVD) share common risk factors such as smoking, hypertension, diabetes, obesity and hyperlipidaemia, and both have links to poverty and malnutrition.

In resource-challenged health systems the focus has to move from expensive 'end-of-the-road' interventions such as dialysis and transplantation to early intervention and primary prevention strategies. We have to move towards involving and integrating care between specialists, primary care clinicians and the community to tackle this massive challenge.

As mentioned above, because both CVD and CKD share common risk factors, we can therefore employ common prevention strategies. These risk factors remain the leading causes of death worldwide

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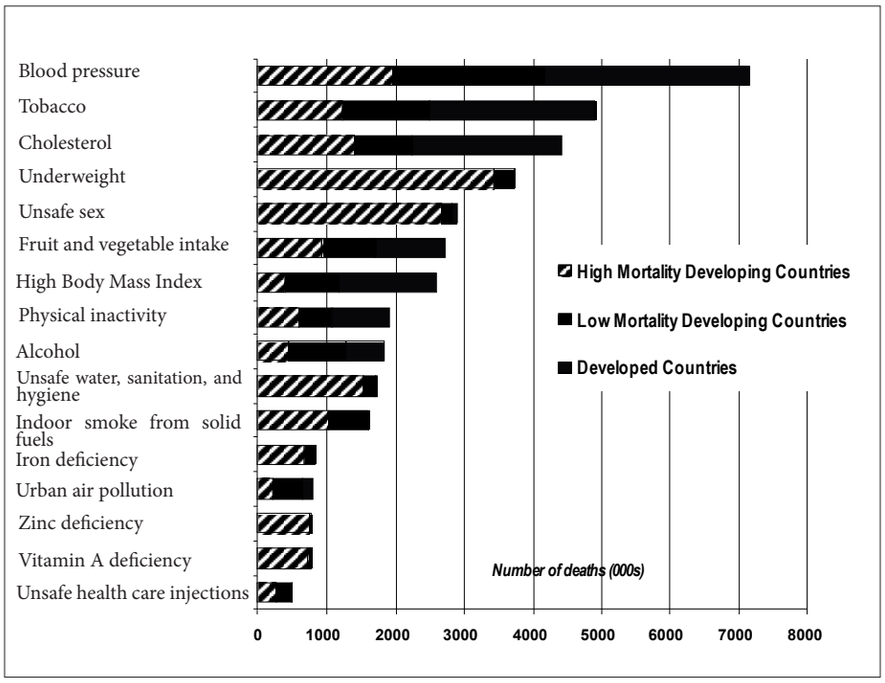
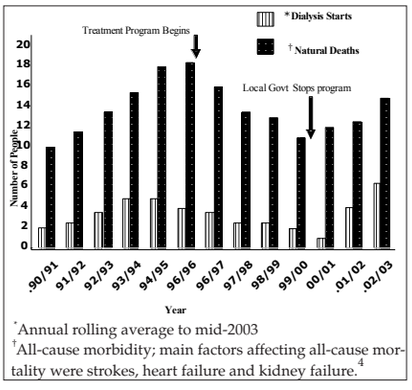


Fig. 1. World deaths in 2000 attributable to selected leading risk factors, World Health Report 2002.[2]

in developed and developing countries (Fig. 1).[2] The early diagnosis and treatment of chronic diseases produces striking reductions in morbidity and mortality, as can be seen from the evidence produced by Wendy Hoy in the Australian integrated Chronic Disease Outreach Program (Fig. 2).[4] Unfortunately there is little information to inform planning of systematic chronic disease management programmes in South Africa. In chronic illness treatment programmes it is noted that most affected people have more than one morbidity, justifying integrated, rather than disease-specific, programmes (Fig. 3).[5]



*Annual rolling average to mid-2003
†All-cause morbidity; main factors affecting all-cause mortality were strokes, heart failure and kidney failure.[4]

Fig. 2. Patients starting dialysis and natural deaths in adults (≥ 18 years) being managed on the Australian integrated Chronic Disease Outreach Program.

In addition to the large burden of non-communicable diseases (NCDs) in developing countries, there is the problem of infectious diseases having an impact on the increased prevalence of CKD.

Seriousness of the problem in South Africa

NCDs account for 37% of all deaths in South Africa, and HIV for a further 30%.[6] The HIV/AIDS epidemic continues to grow at a rapid rate. UNAIDS estimated that in 2000, 19.9% of adults were infected. Projections differ somewhat, but suggest that between 2000 and 2010 from 4 to 7 million people will die of AIDS.[7] The estimated burden of renal deaths in HIV is unknown. HIV, when treated with antiretroviral agents, can behave like a chronic disease. The combined effect of diseases such as diabetes, hypertension and HIV will have a large impact on CKD.

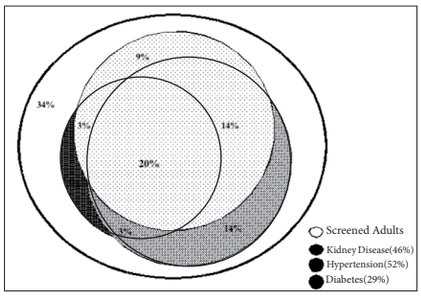


Fig. 3. Overlapping morbidities of chronic disease among screened adults in Australian Chronic Disease Outreach Program.[4]

The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines have significantly improved our focus for detecting, following and managing patients with CKD.[8] No reliable statistics for CKD exist for any African country, including South Africa. In a chronic disease outreach programme (CDOP) running in Soweto it was found that among 619 patients being managed at primary care clinics with high-risk diabetes (diabetes with hypertension or proteinuria) and uncontrolled hypertension, 12% had advanced kidney disease, i.e. a glomerular filtration rate (GFR) < 60 ml/min, and of these some (2%) required immediate dialysis (Fig. 4).[9] Considering that only a small number of the 40 000 patients being treated at these clinics were screened, the problem is larger than we would like to think.[10] We need to understand and grasp the burden of risk factors in South Africa so that we can recognise the need for a comprehensive early detection and prevention strategy.

Causes of kidney and cardiovascular disease–population-based risk factors

In South Africa the CVD and CKD burden, both sharing the same disease risk factors of hypertension and diabetes, were evaluated to some extent in the Demographic and Health Survey in 1998. This national cross-sectional survey is probably the most geographically representative survey to date.[6] In a random sample of 13 802

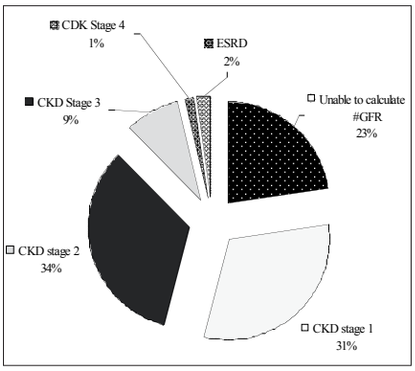


Fig. 4. Patients screened for chronic kidney disease in a chronic disease outreach programme in Soweto.(KDOQI CKD stage determined by calculating the GFR using the modified Modification of Diet in Renal Disease (MDRD) formula and required patient, gender, race and serum creatinine µmol/l).

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Table I. Blood pressure prevalence, awareness, treatment and control in South African population-based survey (adults ≥ 15 years of age)[6]

	Men(%)		Women(%)	
	BP ≥ 140/90 mmHg	BP≥ 160/95 mmHg	BP≥ 140/90 mmHg	BP≥ 160/95 mmHg
Prevalence	20.9	11	21.2	14
Aware	26	41	51	67
Treated	21	39	36	55
Controlled	10	26	18	38

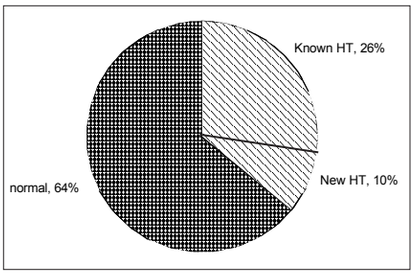

Fig. 5. Patients screened in Heart Awareness Day programmes in Soweto. (Normal = blood pressure found to be < 140/90 mmHg; known hypertension (HT) = person being treated or aware of HT diagnosis; new HT = person unware that he/she had high blood pressure).

people the prevalence and treatment status of hypertension in South Africans ≥ 15 years old were evaluated. The cut-off blood pressure levels used for analysis were ≥ 160/95 mmHg, but later analysis by Steyn *et al.* included the more appropriate cut-off of ≥ 140/90 mmHg.[6] The prevalence of hypertension in the SA survey was found to be 21% in both men and women, overall and the level of control was worse in men compared with women (11% and 18% respectively). This was worse than the level of control in the NHANES III survey, where there was only 27% hypertension control overall (Table I). Just over 50% were aware of their diagnosis and less than 50% were being treated. Thus, hypertension remains poorly diagnosed and managed in South Africa. In an unpublished review of chronic disease control in Soweto clinics, the control of hypertension and diabetes was dismal.[11] Only 8.4% of patients seen at the clinics had moderately acceptable control of blood pressure (< 140/90 mmHg), which was similar for diabetes control (< 7% having blood glucose < 8 mmol/l).

Diabetes is conservatively estimated to occur in 4 million South Africans.[6] In South Africa diabetic nephropathy remains a very important risk factor for CKD and CVD. Incipient nephropathy is reported in 32 - 57% of patients, with a mean known duration of diabetes of 5 - 10 years in a hospital-based study.[12] Overt proteinuria was reported in 5 - 28% and it increased with duration of diabetes.

The South African Demographic and Health Survey further indicated that 4 million South Africans are suspected of having hyperlipidaemia. It also showed that 29% and 9% of females and males, respectively, were obese (BMI > 30 kg/m^2), and 55% and 29%, respectively, were overweight (BMI > 24 kg /m^2). In the pilot Soweto CDOP the presence of major risk factors was extremely prominent and over 60% of patients were obese.[6] In the same population group 35% had evidence of proteinuria. In a recent survey of 551 people in the 'normal population'

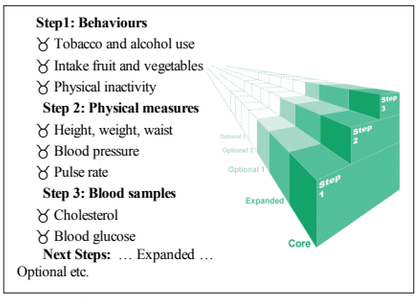

Fig. 6. The WHO STEPS Framework – integrating NCD surveillance into research on high blood pressure.

in Soweto, as part of the Heart Awareness Day programme, similar risk factor profiles were observed: 43% with a BMI of > 30 kg/m^2, 8% with diabetes, 5% with cholesterol levels > 5.5 mmol/l, 29% with 1+ or more microalbuminuria on single testing, 16% smokers and 26% with hypertension. It was also noted that as many as 8% of people screened were unaware of their hypertension status (Fig. 5).[13]

Various forms of kidney disorders occur in patients who are HIV positive. Han *et al.*,[14] at a single centre in KwaZulu-Natal, screened 615 asymptomatic outpatients who had no evidence or symptoms of CKD or renal risk factors other than HIV. Of these patients 7.8% were found to have persistent microalbuminuria: all had had renal biopsies and 85% had HIV-associated nephropathy (HIVAN), with most patients having a CD4 count < 250 x 10^6/l. Considering that 4 - 7 million South Africans have HIV, this is potentially an additional large CKD burden.

These studies highlight the existence of co-existing risk factors and co-morbidities in chronic disease and 'normal' populations. It also demonstrates the poor awareness and management of these risk factors and chronic diseases in patients diagnosed with a problem.

Early detection and prevention: tackling the problems

A clear, simple and integrated approach to risk factor and chronic disease management needs to be adopted. Lifestyle measures remain the key to the epidemic of NCDs and HIV in the developing world. Public education and commitment to a healthy lifestyle, e.g. no smoking, low-salt diets, prudent eating plans, exercise and reducing high-risk sexual behaviour, need to be emphasised. An integrated plan, also focusing on high-risk groups, with effective management at all levels of CVD and CKD remains essential.

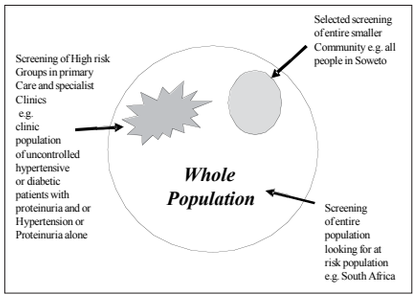

Fig. 7. Potential approaches for early screening for detection and prevention of CKD and CVD risk factors.

The WHO recognises the difficulty in achieving ideal circumstances and therefore advises those in the developing world to follow a more practical approach, which can still be further modified according to one's capacity. The WHO outlines methods for achieving this approach by advising the development of a hierarchical framework to unify surveillance and prevention programme activities, recognising that these should be flexible across a range of risks, conditions, ages and areas.[15] Standard methods and tools are adaptable to local settings. Starting with common core methods, tools and treatments optional extras are then developed if possible. If, for example, the only method available is lifestyle modification then this is where the programme focus should begin. The

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primary aim is to develop basic sentinel surveillance and treatment sites, and then to add on to existing systems when resources allow (Fig. 6).

Implementing programmes for chronic disease screening and management

It would be ideal to do large population-based screening studies before embarking on a prevention strategy, but this is not feasible or cost effective in a developing country such as South Africa. A more cost-effective approach must be established taking into account that the majority of people will need to be managed by the primary health care sector. The approach in South Africa and other countries has been to focus on high-risk population groups (Fig. 7).

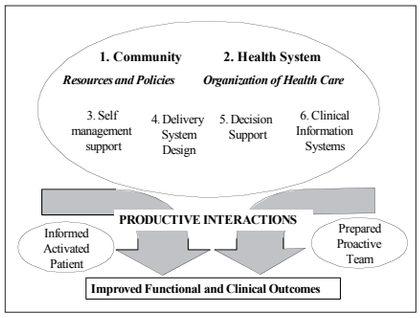

Fig. 8. Wagner Chronic Illness Care Model – recognises the complexity of chronic disease care and that changes in the health system, community resources and policies will improve chronic illness care.

Integrated model for managing chronic illnesses

The CDOP was initiated in 1999 in Soweto – a city of predominantly indigenous South African people. It is a melting pot of 'transitional' people, moving from a culturally healthy traditional lifestyle to a predominantly unhealthy westernised urban lifestyle. This community is also at high risk of chronic diseases, including HIV.[16] Against a known background of poor blood pressure and glucose control the programme was implemented in 20 primary care clinics in Soweto and nearby regional clinics. It is developed around the Wagner Chronic Illness Care Model that focuses on creating a prepared and proactive health team and an informed patient (Fig. 8).[17] The WHO has adopted this integrated model of managing chronic illnesses such as hypertension, diabetes

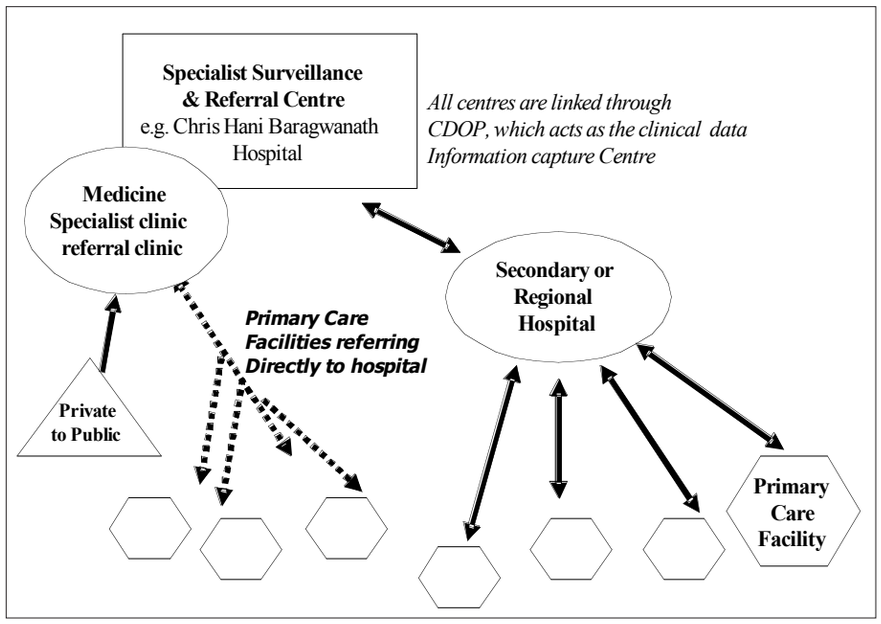

Fig. 9. A CDOP 'Functioning unit' indicating the structure of the CDOP Early Detection and Prevention Programme.

and HIV. The CDOP is an integrated chronic illness programme based on an understanding that adequate blood pressure control, diabetic control and risk factor control will confer a specific effect (advantage) in preventing, reversing or retarding diabetes, hypertension and proteinuria as well as established CKD and CVD.[16]

It does this by focusing on critical components of disease and treating people, as well as tracking and analysing clinical outcomes. These components include simplifying the targets for blood pressure, glucose and proteinuria control, providing ongoing patient education, management support for health workers, and regularly evaluating the achievement of clinical outcomes. It should have a qualitative component that serves to assess the health delivery system, health workers and patient compliance and satisfaction, ensuring that chronic illness care is dynamic, achieving its targets, and meeting the needs of the population at risk. The focus in developing countries is also on high-risk groups, recognising the resource capabilities of these health services. In Soweto the CDOP, an integrated care programme that has been running since 1999, has progressed from a pilot phase (1999 - 2001) to a paper-based system (2003 - 2005). Most recently CDOP has developed and started a web-based system of patient management, including up and down referral to improve efficiency and communication. The programme focuses on both kidney and cardiovascular risk factors and on achieving quantitative clinical targets, e.g. HbA_{1c} and random glucose control. The programme provided important baseline surveillance data of the community and proved very popular with primary health clinicians and managers, providing ongoing decision support and health information. Reduction in end points (kidney failure, heart attack, strokes) and qualitative evaluation of the programme remain targets in the ongoing phases, although control of clinical targets has been achieved. A decrease in blood pressure was observed in programme participants, which, if sustained, would offer both cardiovascular and renal benefits. The blood glucose levels at baseline were all high (95% > 12 mmol/l) and by 6 months nearly 75% had glucose levels ≤ 10 mmol/l. This was a significant movement relative to baseline but above desired targets of control, i.e. < 8 mmol/l. It reflected difficulties to achieve control even with active intervention. Changing health workers' health practices, and people's eating habits and lifestyle, is more difficult than just adding a drug, as is the case for hypertension. Similar trends for risk factor control have continued into the paper-based and web-based phases.[18]

Changing health workers' health practices, and people's eating habits and lifestyle, is more difficult than just adding a drug, as is the case for hypertension.

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It is definitely possible to establish a chronic disease outreach programme in the developing world.

Integrated health care model and structure

A tertiary hospital (Chris Hani Baragwanath) served as the focal point for decision support for primary care clinicians, data collection (surveillance), data analysis and overall management of the programme (Fig. 9). The CDOP 'Functioning unit' was established to fit into the cluster of primary, secondary and tertiary hospitals in a region. This model is the basis for public health primary and tertiary care communication as well as up and down referral of patients. It is also a model suitable for private health care. It recognises that a single academic or tertiary hospital takes referrals from a region of health services including primary health clinicians (family practitioners) and smaller hospitals, e.g. regional hospitals. The key component of this model is firstly recognising which patients can be managed by a primary care centre, which patients need advice only (decision support) and which patients need referral (specialist management). In developing this model it is critical to understand what primary care clinicians and existing resources can cope with, and when they should refer patients for specialised care. The 'red', 'orange' and 'green' traffic light approach was used to open doors or keep them closed for referral. The programme defined red to mean that the door for referral was open, e.g. GFR < 60 ml/min and multiple risk factors. Orange was used to indicate that the health worker should continue with caution and should observe the clinical problem until a further review in 6 -12 months, e.g. HbA_{1c} not at target < 7%. A specialist still provided regular decision support if required. When a green light was given then the primary care clinician was permitted to continue with management and would screen again at a later date.

This restructuring of the health system, as per the Wagner model, allowed patients to be referred directly to a specialist clinic without being referred via a casualty department. Patients would then arrive at the specialist centre with the appropriate investigations completed and a history of his/her disease and progress already known. This resulted in improved efficiency in the management of the patient at the time of consultation. Once patients were stabilised they could be referred back to their primary clinic for ongoing care, unless their disease was too advanced, e.g. GFR < 30 ml/min. Such a patient would remain at the tertiary centre's kidney disease remission and regression clinic and be prepared for dialysis or transplantation if necessary at a later stage. This process has been developed by nephrologists and takes into account factors causing both the initiation and progression of CKD and is a key in its management as a public health problem.[19]

Additional fundamental challenges when establishing chronic disease programmes

It is definitely possible to establish a chronic disease outreach programme in the developing world. There are some additional, important fundamental issues to consider and remember when developing and implementing programmes for preventing kidney disease. It is important to develop strong links with experts and try to receive assistance when needed from local or international organisations that have had experience in prevention and early detection programmes. One has to ensure that when managing chronic diseases in less developed countries, the establishment of an informed and proactive health team and strong patient and community partnerships is a priority. Establishing links and improved communication between primary, secondary and tertiary services involves ongoing joint planning and commitment. These components remain as important as adequate funding. One has to focus not only on the technical aspects but also on supporting or caring for staff. It is critical to recognise that good-quality chronic disease management is best care delivered by a well-functioning team, and does not rest only on the specialist or primary care clinician alone. Ultimately one has to have the long-term commitment and stamina to build a chronic disease programme.

Conclusions – integrated approach to CKD management

Novel methods of tackling the increased burden of CKD and CVD have to be established in the developing world if we are to tackle the daunting future burden facing our communities. We have to move from the 'find and fix it' model of treating diseases to a more proactive, integrated approach of tackling common risk factors, early detection of high-risk patients and then joint specialist and primary health care management. In treating the common diseases and risk factors such as diabetes, hypertension, obesity, hyperlipidaemia and HIV we will ultimately be reducing the burden of CKD and CVD in our communities. The examples and lessons learned in South Africa could serve as a template as well as a stepping stone for other developing world and African communities.

Acknowledgement

The research in the Dumisani Mzamane African Institute of Kidney Disease, University of the Witwatersrand, Soweto, is supported by the Bara Renal Fund – a research fund managed by the Wits Foundation of the University of the Witwatersrand. Support has been received from numerous donors.

Acknowledgments go to Professors Sarala Naicker and Helen Schneider. Grants to run the outreach programme have been received from Servier Laboratories South Africa and the Anglo American Fund.

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In a nutshell

- There is a close relationship between chronic kidney disease (CKD) and cardiovascular disease (CVD) and both are rising worldwide.
- In resource-challenged health systems we have to place a large emphasis on early detection and comprehensive high-quality management of chronic illnesses.
- Most affected people have more than one chronic illness, e.g. hypertension and obesity, justifying integrated rather than disease- specific programmes.
- Non-communicable diseases (NCDs) account for most deaths in South Africa and, together with HIV (a chronic illness), make chronic illnesses a major burden of illness and death in this country.
- Research and subsequent clinical guidelines have significantly improved our focus for detecting, following and managing patients with CKD and CVD.
- A clear, simple and integrated approach to risk factor and chronic disease management needs to be adopted, using chronic illness management models such as the Wagner Chronic Illness Care Model.
- Primary health care clinicians and specialists have to work together as a team to ensure that patients with a significant disease burden are detected and treated.
- An integrated model requires an understanding of existing resources capacity, when patients should be managed in primary care and when they should be referred for specialised care.

Single suture

Antibodies fight malaria

Antibodies taken from Gambian people who are immune to malaria could be used to protect others from infection. Researchers already know that certain people are resistant to malaria because of a potent antibody that they have to a protein on the parasite's surface called merozoite-surface protein (MSP-1). But attempts to make vaccines using these antibodies have failed because they are difficult to test on animals.

Now, Richard Pleass and others of the University of Nottingham, UK, have developed a system for testing the antibodies in mice and used it to extract and refine antibodies taken from 10 Gambian individuals who are immune to malaria. They did this by genetically modifying *Plasmodium berghei,* which infects mice, so that it makes MSP-1, which is recognised by the human immune system. Tests in culture had already shown that the antibodies killed the human malaria parasite but, by giving the genetically modified malaria parasite to mice, the team showed that the antibodies would protect the engineered animals as well. Mice without the human antibodies died.

New Scientist, 26 May 2007.

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