

# Service transformation plans in the Eastern Cape informed by a needs-based gap analysis

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**Objectives.** Part I of this research paper presented a needs and gap analysis for the management of schizophrenia, bipolar mood disorder and major depression for the Eastern Cape Province, South Africa. It identified deficits and inequitable distribution of human resources and beds in the province. In this article, Part II, the authors propose a plan for public sector mental health services to address the human resource needs in the poorer eastern regions of the province. The plan focuses on human resource training and development.

**Methods.** Evidence-based data on staff development in mental health from low-middle income countries were utilised to develop strategies to increase staff capacity to address unmet need. A financing model with a poverty index was developed to sustain a needs-based plan. Databases searched included Pubmed, Medline, Google and Google Scholar. The key words used included: mental health, mental health training, mental health resources, mental health in low-middle-income countries, mental health policy and plans, mental health needs-based planning, primary healthcare, primary mental healthcare, mental health financing. In addition the websites of the World Health Organization and the World Psychiatric Association were searched for similar resources.

**Conclusions.** It is feasible, with careful attention to planning and implementation of evidence-based tools, to improve public mental health service delivery in this province. Sustained political will and professional commitment will ensure successful delivery of mental health services in a resource-limited province.

*S Afr J Psychiatr* 2015;22(2):62-66. DOI:10.7196/SAJP.823



Part I of this research paper<sup>[1]</sup> identified deficits in specific human resource categories in provision of mental health services in the Eastern Cape (EC) Province, South Africa (SA). These included psychiatrists and nurses, two vital components in a mental health service delivery plan. The province required increased numbers of nurses trained in psychiatry. The study also demonstrated an inequitable distribution of resources in the province. Deficits were identified mainly in the eastern regions of the province. The development of a needs-based plan in this region will have several advantages. These include improved mental health information systems, and therefore improved financial planning and equitable distribution of all resources.

The eastern regions of the province include the districts of Alfred Nzo, Amathole, OR Thambo and Ukhahlamba. These districts include the entire former homeland of Transkei and large areas of the former Ciskei. It is evident from Part I<sup>[1]</sup> that there are no mental health services in the districts of Alfred Nzo and Ukhahlamba. Alfred Nzo district is dependent on OR Thambo, while Cacadu and the Nelson Mandela Metropolitan provide services to the district of Ukhahlamba. Amathole, which currently has two psychiatrists, requires an additional eight psychiatrists to provide a comprehensive mental health service. These shortfalls place increased demands for services on limited resources.

Merwin *et al.*<sup>[2]</sup> proposed two important strategies in addressing equitable distribution. These were the retention of current staff (i.e. preventing migration from rural to urban settings) and integrating the role of specialists and non-specialists. The application of this strategy in the EC will assist in addressing the scarcity of psychiatrists and improve capacity of nursing professionals in the eastern regions.

## Task shifting

*Task shifting* is defined as the use of specialist mental health staff in the training of, and in supervisory roles to, non-specialist health workers, as a mechanism for more efficient and effective care.<sup>[3]</sup> The training of nurses, who provide essential services at districts not serviced by psychiatrists, will prove to be the foundation in providing an accessible mental health service for the eastern regions of the EC. The National Department of Health (NDoH) has clearly outlined the areas of competence required by staff at both primary and district level. These include the recognition of mental illness, organisation of services and patient management at both levels of care. Competency levels are escalated at district levels, viz. the management of substance withdrawal, suicide risk assessment and delirium.<sup>[4]</sup>

In the EC the Nelson Mandela Metropolitan University, Port Elizabeth, provides a training course in Advanced Psychiatry for nurses.<sup>[5]</sup> This course equips nurses who have background training in psychiatry with advanced techniques in identifying and managing

patients with psychiatric illnesses, including the correct administration of psychotropic agents for common mental illnesses. There is sufficient evidence that training programmes can have a substantially positive impact on nurse prescribing behaviour. However, the course is expensive and requires nurses to be present onsite in Port Elizabeth, which will be difficult for nurses employed in the eastern parts of the province, where services are most lacking.

The authors suggest that nurses selected for training originate from the communities they work and live in. As an incentive the DoH (provincial) should cover their study costs. These costs would be reduced if training were to be provided at Walter Sisulu University, Mthatha, which is situated in the eastern region of the province and has a School of Nursing. A hurdle in providing this educative forum is that this school has a 100% vacancy rate for teaching posts in psychiatry.<sup>[6]</sup>

Training alone is insufficient. It is imperative to provide healthcare workers with incentives, such as career advancements, ability to work in communities where they live and access to facilities such as schools. Klaas<sup>[7]</sup> recommends that the key requirements for the retention of nurses, particularly in rural areas, are the provision of resources, autonomy and salary increments.

A further incentive to the nursing fraternity would be to provide 244 of the 494 enrolled nurses in the province with a 2-year bridging course, which will effectively promote them to the role of professional nurses. This will allow them to be trained in psychiatry and therefore meet the deficit for nurses trained in psychiatry. This process can be facilitated by the Lilitha Nursing College in the EC, which has campuses throughout the province.<sup>[8]</sup>

The other category of staff that needs to be addressed is medical personnel. They may fear deployment away from cities to rural areas. Their role should be limited to the treatment and management of complex cases and they should become increasingly more involved in the training and supervision of primary healthcare personnel. This implies improving both in- and outreach services, without the necessity of deployment.

Inreach services could include both training and supervision of primary and district health staff, as well as consultation of patients with complex disease. Outreach services would entail a similar approach but with patients having greater access to specialised services within the community they live in. A major hurdle is the lack of specialised services in the periphery, such as psychotropic medication and laboratory investigations. The development of a down-referral system from a centralised hospital would be optimal; however, this requires intensive staffing, a well-developed health information system and proper supply-chain monitoring.

All psychiatric institutions within the province provide outreach services to primary care centres and district hospitals. This service is important as it provides a platform for training of staff in the recognition and management of mental illness. It improves access to mental health services and decreases stigma. This service is however erratic throughout the province for the following pervasive reasons: lack of staff, transport and psychotropic medication.

The lack of staff could be addressed by the Clinical Associate Training Programme launched by the NDoH in 2008. Their scope of practice includes patient consultation, physical examination, diagnostic and therapeutic procedures, assisting with emergencies and inpatient care and counselling.<sup>[9]</sup>

Walter Sisulu University was the first university to train 23 students. At the end of 2012, 80 clinical associates had been trained and deployed at district hospitals. While this mid-level category of staff obtains 160 hours of training in mental health, there are currently no data to indicate their proficiency in diagnosis and management of mental illnesses. The lack of medical officers at district facilities will hamper supervision of clinical associates and therefore their ability in filling the human resource gap in mental health is questionable.<sup>[9]</sup>

Expenditure on nursing staff calculated in Part I<sup>[1]</sup> may appear exorbitant; however, it must be noted that the indirect cost of mental illness is far higher. The World Health Organization (WHO) has reported that four of the six leading causes of disability-adjusted life-years globally are mental illnesses. Mental illness is estimated as being responsible for 37% of healthy years lost from all non-communicable diseases.<sup>[10]</sup>

The strategies outlined above will assist the provincial DoH to address the high percentages of vacant posts in the public sector. As of 2008 the vacancy rate for nurses and doctors stood at 53.6% (highest in South Africa) and 40.1% (third highest in the country) for these categories of staff, respectively.<sup>[11]</sup>

The large number of staff requirements reflected in Part I<sup>[1]</sup> could be due to the variances in prevalence rates of mental disorders. Summerfield<sup>[12]</sup> commented that the use of tools validated in Western settings may give inflated prevalence rates in non-Western settings. WHO-reported prevalence rates for 12 months vary from 8.4% to 29.1% and lifetime prevalence rates from 12.2% to 48.6%. He further points out that it is not accurate translation between languages but accurate translation between worlds that adds validity to screening instruments.<sup>[12]</sup> This could be another reason for the wide variance in prevalence rates.

The WHO World Mental Health Survey Consortium discovered in their research that wide variance in prevalence rates meant that even wealthy countries would not be able to treat all persons with a mental illness.<sup>[13]</sup> The same Consortium reported that up to 50% of cases 'discovered' by the Composite International Diagnostic Interview were mild. This declaration demonstrates the lack of validity of survey instruments in determining prevalence across different nationalities. The authors concurred with Summerfield's conclusion that interpretation of concepts could be different from the Western world, therefore impacting on prevalence rates.

The South African Stress and Health Study (SASH)<sup>[14]</sup> does not provide comprehensive epidemiological data. This study depended heavily on household sampling and excluded other important sources of data, such as hospitalised patients, outpatients, prisons and the homeless population.

One unit in the EC consulted approximately 13 000 outpatients in the period January to December 2011. Of these, 15% were new patients. The average number of patients consulted per day equated to 52. These statistics will influence prevalence rate calculations and ultimately mental health planning in terms of ambulatory staff, psychotropic prescription and allied mental health services.

The lack of reliable epidemiological data hinders mental health policy development. There are no prevalence data for schizophrenia and bipolar mood disorder (low-prevalence disorders), while for high-prevalence disorders (major depression, dysthymia and anxiety disorders) there is only 50% population coverage in prevalence data.<sup>[15]</sup>

The problem then for mental health planners/commissioners is the interpretation and translation of these data in the development of a feasible plan for the provision of services, often in a resource-limited setting.

The EC DoH should engage with patients, carers, families and other advocates for mental health, in the development of a policy and plan. The DoH should also aim at providing a service that provides promotion, prevention and rehabilitative services at primary care level and within community settings.

### Mental health at primary healthcare level

The South African National Mental Health Plan<sup>[2]</sup> defines primary healthcare in accordance with the Alma Ata Declaration: 'essential health care made accessible at a cost a country can afford, with methods that are practical, scientifically sound and socially acceptable.'

The province could adopt the model implemented in Kenya, a low-middle-income country, for strengthening primary healthcare by the provision of training of staff in mental health.<sup>[16]</sup> In collaboration with international partners, including the WHO, a detailed curriculum was developed consisting of five modules. Trainers were trained over a period of 5 days. In 5 years over 1 500 primary healthcare workers were trained utilising this methodology. The mean change in knowledge score for the first 1 000 participants increased from 42% to 77%. Primary healthcare workers also initiated and maintained intersectoral collaboration with community members, chiefs, traditional healers and non-governmental organisations.

The advantages of this model are the low cost, the wide coverage it provides and the development of a reliable mental health information system. The implementation of this model will require involvement of key stakeholders, which will include both the public and private sectors. However, Armstrong *et al.*<sup>[17]</sup> argue that improving the mental health literacy alone of primary healthcare staff is insufficient. There should be continued supervision and training manuals should be culture-sensitive and adaptable to local contexts.<sup>[17]</sup>

Nigeria opted to include mental health in primary health in 1989. However, a 2013 research article indicated that this had not been implemented.<sup>[18]</sup> As early as 2001, Omigbodun<sup>[19]</sup> reported that despite the incorporation of training in mental health into the curriculum of primary healthcare workers, mental health was absent at primary healthcare level in Nigeria. One of the reasons put forward for this failure was that training of community health officers in mental health was insufficient. The 2-week, 80-hour programme was conducted at psychiatric hospitals and consisted of lectures and ward rounds. The main weaknesses identified were the short duration of the course, the lack of exposure of specialist staff to primary care settings, no training needs assessment was conducted by specialist staff, no contact with specialist staff post training and the lack of a monitoring and evaluation component.

The province can learn from the Nigerian experience. The translation of policy in practice will require training of primary care staff *at* primary care centres, after a training needs assessment has been conducted. A training needs assessment will allow for the evaluation of current levels of knowledge of primary healthcare staff and therefore influence teaching methods. This will provide training within the local context of primary healthcare centres, thus avoiding wastage of resources. There will have to be continuing supervision by

specialist staff and a monitoring and evaluation component factored into the training programme.

Supervision and support from specialist staff is also advised by the authors of the Mental Health Gap Action Programme (mhGAP) Intervention Guide.<sup>[20]</sup> This guide was developed in 2010 and provides general principles for the management of the eight priority conditions set by the WHO. The manual is set out in modules in an easy-to-understand and practical stepwise approach to management of these disorders in non-specialist settings.<sup>[20]</sup>

A vital factor in the success of any training programme in the province will be to decrease reliance on current primary healthcare staff to provide mental health services. Therefore the inclusion of nurses with training in advanced psychiatry in the training programme and the redeployment of general nurses translated to professional nurses at primary health centres as part of a community service programme will decrease reliance on the small number of psychiatrists and current primary healthcare staff. In addition nurses with advanced training in psychiatry could operate as mental health co-ordinators at primary care level, therefore ensuring continuing access to supervision and the assessment and evaluation of the successes and pitfalls of training programmes. A nurse-led model of primary care for mental health has proven successful for the Ehlanzeni District, Mpumalanga Province.<sup>[21]</sup>

The model described here is the provision of mental health services *at* primary healthcare centres and not integrated into primary healthcare. This service is provided by mental health professionals (nurses) and auxiliary staff. These professionals form an intermediary link between primary and secondary mental health services.<sup>[22]</sup>

Lazarus and Freeman<sup>[22]</sup> make several recommendations to ensure the success of providing mental healthcare at primary care level. These include: primary care tasks must be limited and doable; a mental health service co-ordinator is crucial; integration is a process not an event; financial and human resources are needed; and patients must have access to essential psychotropic medication.

SA possesses a well-developed standard treatment guidelines and essential drug list.<sup>[23]</sup> This document provides treatment guidelines (pharmacotherapy only) for eleven psychiatric syndromes, which include the three considered in Part I of this study. The essential drug list includes antidepressants, anxiolytics and antipsychotics, including second-generation antipsychotics. The province has two pharmaceutical depots that provide all levels of health facilities with medication. The provision of psychotropics, however, is poorly managed, as psychotropics are constantly unavailable at all levels of healthcare. These include antidepressants and first-generation antipsychotics.

Any needs-based plan must consider health expenditure and funding. Expenditure on medication is difficult to determine in the public sector as records are not readily available. In the private sector, antidepressants had the fourth largest contribution to total medicine expenditure. Selective serotonin reuptake inhibitors contributed 48.8% and tricyclic antidepressants contributed 6.6%.<sup>[24]</sup>

The WHO *International Drug Price Indicator Guide*<sup>[25]</sup> provides information on the costing of medication. This guide provides comparable drug prices to ensure easy procurement of medication at affordable prices worldwide, improving access to psychotropics and other classes of medications. According to this guide the cost per month

(in 2010) of treating major depression with amitriptyline at a defined daily dose of 75 mg is ZAR5.24, schizophrenia with haloperidol at a defined daily dose of 8 mg is ZAR15 and bipolar mood disorder with sodium valproate at 1 000 mg/day is ZAR98. According to this study the monthly cost for the management of these three severe mental illnesses equates to ZAR1 747 567. This figure represents costs if all patients in the target population were treated; however, in reality the majority of patients do not present for treatment.

### Financing model

A redistribution of financial resources to improve mental health services in the poorer eastern region is possible. A needs-based formula for financing, based on research findings in Part I, will prove advantageous. This will increase funding to the eastern regions, which may then be utilised in the recruitment and retention of human resources. The divergence of funding from payments made to Life Esidemeni for rehabilitative services (at an approximate monthly cost to the province of ZAR6 million) to nationally established non-governmental organisations will assist to develop and maintain community residential facilities here (personal communication, Directorate of Specialised Services, EC DoH). This will improve accountability and decrease the corrupt use of financial resources.

The authors propose the following needs-based formula with the addition of a poverty index:

$$EN_1 [P_r \times P_o] \times M_c \times D_{rx} + S_c + PI[G_{co} \times EN \times D_{rx}]$$

Where: EN = expected number at 100% coverage,  $P_r$  = prevalence rate,  $P_o$  = population,  $M_c$  = medicine cost,  $D_{rx}$  = duration of treatment,  $S_c$  = staff cost, PI = poverty index,  $G_{co}$  = Gini coefficient.

**Example:**  $0.045 \times 100\ 000 \times ZAR6 \times 365 + S_c + [0.65 \times 4500 \times 365]$   
 $9\ 855\ 000 + 1\ 026\ 336 + 1\ 067\ 625 = ZAR11\ 948\ 961$

The example calculated above is for the management of depression. The addition of a poverty index results in an additional allocation of R1 067 625, which may be utilised to provide additional locally required services, e.g. the employment of a specialist psychiatrist or the development of a telepsychiatry unit for the training and supervision of primary healthcare staff.

The advantages of this formula are:

- Dependable population statistics, including population growth, are available in South Africa, therefore eliminating the potential for the creation of perverse incentives.<sup>[26]</sup>
- Regional differences in poverty are considered within the province, allowing for increased allocation in areas of need.
- The formula is set at a regional and not district level. This eliminates the need for small area estimations.

The disadvantages of this formula include:

- Its reliance on prevalence data, which are often unavailable for specific mental illnesses. It may be rectified by the utilisation of an overall prevalence rate for any disorder. The formula does not consider hidden costs, such as transport.
- Medication costs fluctuate.
- Dependence on the Gini coefficient. A neural network method to determine the poverty index would be more reliable than the Gini

coefficient. This method allows for the measurement of multi-dimensional poverty. This tool demonstrated degrees of poverty, rated from maximum deprivation to no deprivation and was based on census data. Results for the EC showed that 29% of households experienced maximum deprivation, while 14% experienced no deprivation. It can be utilised to map poverty at magisterial levels.<sup>[27]</sup>

- It does not consider the migration of people to wealthier regions in the search for employment, thereby affecting population size.

The success of this method of financing will depend on the formation of a monitoring and evaluation system, which will ensure that funds are being utilised for the purpose allocated. The creation of a local mental health authority as suggested by Hadley *et al.*<sup>[28]</sup> at regional level within the province will assist in consolidating funding and monitor efficiency and quality of mental health services. Local mental health authorities could also be actively involved in the purchasing of services for their respective regions.

### Conclusions

The province has to focus on addressing needs in the poorer more rural eastern regions. The need for services is compounded by psychosocial factors such as high HIV prevalence rates, crime, unemployment, homelessness and poor access to health services in general.

Training programmes for non-specialist mental health professionals should aim at improving confidence in making diagnosis, management and referral to specialist care. These programmes must be sustained by continued supervision by specialist staff.

Umukoro<sup>[18]</sup> points out that sustained political will and goodwill, professional commitment, support and supervision of staff and monitoring and evaluation are essential components to ensure the success of a mental health plan. These components will allow for the translation of the strategy outlined above from paper to practice in the EC.

In his narrative, Gionfriddo,<sup>[29]</sup> a former state legislator in mental health in the USA, clearly indicates that the development of mental health policies and plans is not only about the statistics, but should mainly consider the lives of the people that they impact on and the support these policies and plans will provide throughout the course of their mental illness.

**Acknowledgement.** This study was sponsored by a Discovery Foundation Academic Fellowship Award.

**Contributors.** K Sukeri was the principal investigator, conducted the literature review, designed the study, collated the data, did the data analysis and wrote the draft manuscript. O Alonso-Betancourt and R Emsley supervised the study and contributed to the study design and the final drafting of the manuscript.

### References

1. Sukeri K, Alonso-Betancourt O, Emsley R. Needs-based gap analysis for service transformation in the Eastern Cape. *S Afr J Psychiatr* 2015;21(1):3-7. [http://dx.doi.org/10.7196/SAJP.609]
2. Merwin EI, Goldsmith HF, Manderscheid RW. Human resource issues in rural mental health services. *Community Mental Health Journal* 1995;31(6):525-536.
3. South African Department of Health. National Mental Health Policy Framework and Strategic Plan 2013-2020. Pretoria: Government Printer, 2012.
4. South African Department of Health. District Health Services.
5. Faculty of Health Sciences Prospectus, Nelson Mandela Metropolitan University, www.nmmu.ac.za (accessed March 2011).
6. Faculty of Health Sciences Prospectus, Walter Sisulu University, www.wsu.ac.za (accessed



- March 2011).
7. Klaas NP. Factors influencing the retention of nurses in rural health facilities of the Eastern Cape Province. A thesis submitted in partial fulfilment for the degree of Master of Arts (Health Studies), University of South Africa, 2007.
  8. Eastern Cape Department of Health. Lilitha Nursing College, [www.eccdo.gov.za](http://www.eccdo.gov.za) (accessed November 2011).
  9. Hugo JFM, Slabbert J, Louw JM, et al. The Clinical Associate Curriculum: The learning theory underpinning the BCMP programme at the University of Pretoria. *Afr J Health Professions Educ* 2012;4(2):128-131.
  10. World Health Organization. Dollars, DALY's and Decisions: Economic aspects of the mental health system; 2006. [www.who.int/mental\\_health/evidence/dollars\\_dalys\\_decisions](http://www.who.int/mental_health/evidence/dollars_dalys_decisions) (accessed November 2011).
  11. Eastern Cape Provincial Department of Health. [www.doh.ecprov.gov.za](http://www.doh.ecprov.gov.za) (accessed November 2011).
  12. Summerfield D. Afterword: Against 'global mental health'. *Transcultural Psychiatry* 2012;49(3):1-12.
  13. World Health Organization. World Mental Health Survey Consortium. Prevalence, severity and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *JAMA* 2004;291(21):2581-2590.
  14. Herman AA, Stein DJ, Seedat S, Heeringa SG, Moomal H, Williams DR. The South African Stress and Health Study. 12-month and lifetime prevalence of common mental disorders. *S Afr Med J* 2009;99(5):339-334.
  15. Baxter AJ, Patton G, Scott KM, Degenhardt L, Whiteford HA. Global epidemiology of mental disorders: What are we missing? *PLoS One* 2013;8(6):e65514. [<http://dx.doi.org/10.1371/journal.pone.0065514>]
  16. Jenkins R. Integration of mental health into primary health in Kenya. *World Psychiatry* 2010;9(2):118-120.
  17. Armstrong G, Kermod M, Raja S, Suja S, Chandra P, Jorm AF. A mental health training program for community health workers in India: Impact on knowledge and attitudes. *International Journal of Mental Health Systems* 2011;5(1):17. [<http://dx.doi.org/10.1186/1752-4458-5-17>]
  18. Umukoro OL. Development and roll-out of primary care mental health services in Ogun State, Nigeria. *Commonwealth Health Partnerships* 2013:97-99.
  19. Omigbodun OO. A cost-effective model for increasing access to mental health care at primary care level in Nigeria. *J Mental Health Policy Econ* 2001;4:133-139.
  20. World Health Organization. mhGAP: Mental Health Gap Action Programme: Scaling up care for mental, neurological and substance use disorders, 2008. [http://www.int/mental\\_health/evidence/](http://www.int/mental_health/evidence/) (accessed November 2011).
  21. World Health Organization. Integrating Mental Health into Primary Care: A Global Perspective, 2008. [http://www.who.int/mental\\_health/resources/mentalhealth\\_PHC\\_2008.pdf](http://www.who.int/mental_health/resources/mentalhealth_PHC_2008.pdf) (accessed November 2011).
  22. Lazarus R, Freeman M. Primary-Level Mental Health Care for Common Mental Disorders in Resource Poor Settings: Models & Practice – A Literature Review. Pretoria: Sexual Violence Research Initiative, Medical Research Council, South Africa, 2009.
  23. Department of Health. Standard Treatment Guidelines and Essential Medicines List. Pretoria: Department of Health, Republic of South Africa, 2012.
  24. Medicines Review 2011. [www.mediscore.net](http://www.mediscore.net) (accessed November 2011).
  25. Frye JE, ed. International Drug Price Indicator Guide, 2010. Geneva: WHO, 2010.
  26. Pearson M. Allocating public resources for health: Developing pro-poor approaches. London: Health Systems Resource Centre, 2002, for the British Government's Department for International Development.
  27. Naidoo AGV. A multi-dimensional measure of poverty in South Africa. A thesis submitted in partial fulfilment of the degree of Doctor in Commerce in the Faculty of Management and Economic Sciences, University of Pretoria, 2007.
  28. Hadley TR, Goldman HH. A partial solution: A local mental health authority for the UK. *J Mental Health Policy Econ* 1998;1:73-76.
  29. Gionfriddo P. How I helped create a flawed mental health system that's failed millions – and my son. *Health Affairs* 2012;31(9):2138-2142.