Institution: University of East Anglia		
Unit of Assessment: 2 - Public Health, Health Services and Primary Care		
Title of case study: Strengthening effective clinical practice and integrated disease management in primary care in low and middle income countries		
Period when the underpinning research was undertaken: 2000 to 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Max Bachmann	Professor	2003 to present
Garry Barton	Professor	2007 to present
Jamie Murdoch	Senior Fellow	2007 to present
Period when the claimed impact occurred: 2014 to December 2020		
Is this case study continued from a case study submitted in 2014? Yes		

1. Summary of the impact

Misdiagnosis and undertreatment of chronic diseases places huge burdens on developing countries. Five African and Brazilian randomised trials by UEA researchers demonstrated that clinical decision tools and health care worker training significantly improved patients' care and health, and established pioneering nurse-led antiretroviral treatment (ART) for HIV in South Africa. The Practical Approach to Care Kit (PACK), incorporating these interventions, was delivered to all 3500 government clinics in South Africa (population 59 million), throughout Ethiopia (population 112 million), and in three regions of Nigeria. Since 2014 >12,000 health workers received PACK training and >1.9 million South Africans started nurse-led ART, improving the health and saving the lives of millions.

2. Underpinning research

Chronic diseases like tuberculosis, HIV, asthma, diabetes and hypertension are common, but often undetected, misdiagnosed and undertreated, in low and middle income countries, largely because frontline health workers lack the requisite clinical skills. In most of those countries, policies, guidelines and training typically focus on single diseases, undermining comprehensive primary care. These defects in the quality of primary health care harm the health of hundreds of millions of people worldwide, and overload already struggling health systems with severe illness and costs.

2.1 Practical Approach to Lung Health in South Africa (PALSA)

Since 2000, UEA researchers (Bachmann, Barton and Murdoch) have collaborated with the University of Cape Town's Knowledge Translation Unit (KTU) to show that educational interventions, developed incrementally by KTU, continued to improve primary health care in low and middle income countries. This started with development of the **PALSA (Practical Approach to Lung Health in South Africa)** clinical guidelines and training on integrated care of tuberculosis and lung diseases, working with the World Health Organisation. PALSA guidelines used algorithmic flow charts guiding health workers to make accurate diagnoses and prescribe effective treatments, building on national policies and evidence of effectiveness. Training to use the guideline was delivered iteratively to health workers at their workplaces by KTU-trained health ministry trainers, enabling delivery at scale. Our randomised trial showed in 2005 that PALSA increased diagnosis of tuberculosis (by 72%), asthma treatment (by 90%) and emergency referrals (by 159%) [3.1], and was cost effective.

2.2. PALSA PLUS

PALSA PLUS expanded PALSA to cover HIV, AIDS and other sexually transmitted infections. Our randomised trial of PALSA PLUS showed in 2011 that it increased the diagnosis of tuberculosis by South African primary care nurses by 28%, and appropriate treatment of HIV by 17% [3.2].

2.3 Primary Care 101 and Practical Approach to Care Kit (PACK)
PALSA PLUS guidelines and training were expanded to cover diabetes, hypertension and depression. This intervention - **Primary Care 101** - was evaluated with a randomised trial which in 2016 demonstrated that it intensified treatments of diabetes by 68% in obese participants, hypertension by 44%, and cardiovascular disease by 176% [3.3].

PACK Global was the international version of Primary Care 101, delivered at scale in Brazil, Nigeria and Ethiopia. Our randomised trial of **PACK Adult Brazil** showed in 2019 that PACK improved testing and treatment for respiratory disease [3.4, PI Bachmann]. The PC101 and PACK Brazil trials thus supported large scale delivery of PACK in low and middle income countries beyond South Africa.

2.4 Nurse-led initiation and monitoring of antiretroviral treatment (ART)
STRETCH (Streamlining Tasks and Roles to Expand Treatment and Care for HIV), was a package of guidelines, training and primary care reorganisation, enabling nurses to take over ART prescribing from doctors in South Africa. Our randomised trial of 15,500 patients with HIV showed in 2012 that nurse-led ART, supported by STRETCH, improved patients' health and was safe [3.5, co-PI Bachmann]. Our parallel economic evaluation showed that STRETCH was cost-effective, and affordable by other middle income countries. Our cohort study of ART rollout in South Africa showed in 2015 that ART halved tuberculosis incidence [3.6].

3. References to the research

[3.1] Effect of educational outreach to nurses on tuberculosis case detection and primary care of respiratory illness: pragmatic cluster randomised controlled trial
Fairall, L.R., Zwarenstein, M., Bateman, D., **Bachmann, M.O.**, Lombard, C., Majara, B., Joubert, G., English, R., Bheekie, A., Mayers, P., Peters, A., Chapman, R.
British Medical Journal, **2005,** 331:750-754. DOI: 10.1136/bmj.331.7519.750

[3.2] Outreach education for integration of HIV/AIDS care, antiretroviral treatment, and tuberculosis care in primary care clinics in South Africa: PALSA PLUS pragmatic cluster randomised trial.
Zwarenstein, M., Fairall, L.R, Lombard, C., Mayers, P., Bheekie, A., English, R.G., Lewin, S., **Bachmann, M.O.**, Bateman, E.
British Medical Journal, **2011**, 342:d2022. DOI: 10.1136/bmj.d2022

[3.3] Educational outreach in an integrated clinical management tool for nurse-led non-communicable chronic disease management in primary care in South Africa: pragmatic cluster randomised controlled trial.
Fairall, L.R., Folb, N., Timmerman, V., Lombard, C., Steyn, K., **Bachmann, M.O.**, Bateman, E.D., Lund, C., Faris, G., Gaziano, T., Georgeu-Pepper, D., Zwarenstein, M., Levitt, N.S.
PLoS Medicine, **2016**. 13(11), p.e1002178. DOI: 10.1371/journal.pmed.1002178

[3.4] Effects of PACK guide training on the management of asthma and chronic obstructive pulmonary disease by primary care clinicians: a pragmatic cluster randomised controlled trial in Florianópolis, Brazil.
Bachmann, M.O., Bateman, E.D., Stelmach, R., Cruz, A., Pacheco de Andrade, M., Zonta, R., Zepeda, J., Natal, S., Cornick, R., Wattrus, C., Andersen, L., Geogreu-Pepper, D., Lombard, C., Fairall, L.R.
BMJ Global Health, **2019**, 4(6) 4:e001921. DOI: 10.1136/bmjgh-2019-001921

[3.5] Effectiveness of task-shifting antiretroviral treatment from doctors to primary care nurses in South Africa (STRETCH): pragmatic cluster randomised trial.
Fairall, L., **Bachmann, M.O.**, Lombard, C., Timmerman, V., Uebel, K., Zwarenstein, M., Boulle, A., Georgeu, D., Colvin, C.J., Lewin, S., Faris, G., Cornick, R., Draper, B., Tshabalala, M., Kotze, E., van Vuuren, C., Steyn, D., Chapman, R., Bateman, E.
The Lancet, **2012**; 380: 889–898. DOI: 10.1016/S0140-6736(12)60730-2.

[3.6] Effect of antiretroviral treatment on risk of tuberculosis during South Africa's programme expansion: cohort study.
Bachmann, M.O., Timmerman, V., Fairall, L.R.
AIDS, **2015**, 29(17), 2261–2268. DOI: 10.1097/QAD.0000000000000806

Grants
Project: Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH)
PI: **Bachmann, M.O**.
Funder: Medical Research Council. Value: GBP 820,004. Dates: 2008 - 2010

Project: PACK Child. Strengthening the quality of paediatric primary care in South Africa: Preliminary work for a pragmatic randomised trial.
Co-Is: **Bachmann, M.O.** & **Murdoch, J.**
Funder: UK Department For International Development, Economic and Social Research Council, UK Medical Research Council, and Wellcome Trust. Value: GBP188,748 (UEA GBP46,064).
Dates: 2017 – 2019

4. Details of the impact

Our REF2014 impact case study described how, in South Africa until 2013, our research led to delivery of PALSA, PALSA PLUS and Primary Care 101 [2.1-2.3], and enabled nationwide expansion of antiretroviral treatment for HIV based on STRETCH [2.4]. Since 2014, impact has evolved and expanded. The previous four interventions were incorporated into PACK, which was further developed and delivered throughout South Africa and internationally [5.1-5.7], while ART expansion continued in South Africa [5.8].

4.1 From Primary Care 101 to PACK in South Africa

Building on our evidence that Primary Care 101 guidelines and training, and their predecessors, led to improved management of TB, HIV, respiratory disease, diabetes, hypertension and cardiovascular disease, KTU developed Primary Care 101 into a comprehensive clinical decision support tool called PACK Adult (also called Adult Primary Care (APC)) [5.1,5.2]. PACK Adult and APC now cover the commonest and most important adult conditions, including 40 symptoms, and 20 communicable and non-communicable diseases. In 2015 the South African National Department of Health launched its Ideal Clinic programme, based on PACK and APC, aiming to integrate and strengthen chronic disease management in all 3500 primary care clinics in the country. These clinics are the main source of health care for 50 million South Africans without health insurance. Evidence that a clinic uses PACK or APC is an Ideal Clinic audit standard [5.2]. Four South African nursing schools and three medical schools added PACK to their undergraduate curricula since 2014 [5.1].

4.2 PACK extended to Brazil, Nigeria and Ethiopia

KTU adapted PACK for international dissemination. PACK Global Adult is the prototype, which is then adapted for each country. KTU updates the guides annually, using the latest evidence about accurate diagnosis and effective treatment (supported by the BMJ Evidence Centre). By 2020, over 185,000 guides had been distributed and 30,000 health workers trained in 6 countries, (including >12,000 trained and 3 new countries involved since 2014) [5.1].

Since 2015, PACK Global Adult has been marketed internationally to government and private providers, in partnership with BMJ Publishing Group. PACK Global Adult is delivered to each country through a comprehensive localisation package which includes: i) PACK Adult Guide (mentoring local partners to adapt content to match local policies and priorities, with annual updating), ii) training (mentoring to adapt training methods), iii) health system strengthening, and iv) monitoring and evaluation [5.4-5.6]. PACK Adult was implemented, through training and dissemination of materials, in 52 clinics in 3 Nigerian states from 2016 to 2018, with World Bank funding [5.4]. In 2018 PACK Adult was adapted for Ethiopia, and 100 master trainers from the Ethiopian Ministry of Health were trained; they are currently training frontline primary care workers in every primary care facility in all 9 regions of the country [5.5]. PACK Adult was first rolled out as a randomised controlled trial in the Brazilian city of Florianopolis in 2016, and in 2018 was

extended to cover the whole city of 480,000 residents [5.6, 5.7]. Expansion of PACK Adult Brazil to all of Brazil is currently being negotiated, although disrupted by COVID-19.

Using PACK Adult principles, PACK Child guidelines and materials were written, training was piloted and optimised in South Africa from 2017-2019, and planning for province- and nationwide implementation are under way. PACK Adolescent guidelines have been written, and piloting of training begins in 2021. Using this experience, Bachmann is also working with UK and East African researchers, and health ministries, on a randomised trial and upscaling of integrated primary care for HIV, diabetes and hypertension in Uganda and Tanzania, which began in 2020. Impact from this research is expected after 2020.

4.3 Further expansion of antiretroviral treatment in South Africa

Continuing the impact of the 2010 STRETCH trial of nurse initiation and monitoring of antiretroviral treatment (ART) [2.3], ART continues to expand in South African, reaching 5.2 million people by 2019, with over 1.9 million having started ART since 2014 [5.8].

4.4 Health impact

The health impact of these programmes on African and Brazilian populations is likely to be huge. Independent research has shown that implementation of Primary Care 101 guidelines in South Africa would reduce the burden of cardiovascular disease and diabetes by 7.5 disability adjusted life years (DALYs) per 1000 population per year and would save USD24,902 per DALY gained [5.3].

Almost everyone currently receiving ART in South Africa would eventually die of AIDS without it. Our cohort study (Fairall LR, Bachmann MO, Louwagie G, et al, 2007), completed before and justifying the STRETCH trial, used data from a province-wide government HIV programme and rigorous causal modelling, to estimate that ART reduced the risk of death by 86%. This means that >4.4 million lives would be saved (85% of 5.2 million), including >1.6 million who started ART since 2014 (85% of 1.9 million). Tuberculosis incidence in South Africa decreased by about 177,000 cases per year from 2014 to 2019 [5.9], primarily due to ART expansion.

5. Sources to corroborate the impact

[5.1] Knowledge Translation Unit, accessed on 05.03.2021.
This website describes in detail the PACK programme, its supporting research, and its impacts in each country. The Research page reports numbers of health workers trained and guides distributed, and other indicators, and lists 31 peer reviewed publications co-authored with Bachmann, Barton and Murdoch.

[5.2] Ideal Clinic Monitoring System, accessed on 05.03.2021.
This website describes South Africa's national primary care quality improvement system based on PACK (also known as Adult Primary Care). The Guidelines page confirms that Adult Primary Care is a core part of the Ideal Clinic and Integrated Clinic Management Systems. The Ideal Clinic Framework document (page 36) confirms that evidence of PACK or Adult Primary Care guides being in a clinic is an audit quality criterion.

[5.3] Basu S, Wagner RG, Sewpaul R, Reddy P, Davies J. Implications of scaling up cardiovascular disease treatment in South Africa: a microsimulation and cost-effectiveness analysis. Lancet Global Health 2019;2: e270-e280. DOI: 10.1016/S2214-109X(18)30450-9. Accessed on 04.03.2021
This independent modelling study demonstrates the impact of implementing Primary Care 101 on reducing population health burden and costs for cardiovascular disease and diabetes.

[5.4] Awotiwon A, Sword C, Eastman T, et al. Using a mentorship model to localise the Practical Approach to Care Kit (PACK): from South Africa to Nigeria. BMJ Glob Health 2018;3: e001079. DOI :10.1136/ bmjgh-2018-001079. Accessed on 09.12.2020. Describes impact of Primary Care 101 and PACK on primary care delivery in Nigeria.

[5.5] Feyissa YM, Hanlon C, Emyu S, et al. Using a mentorship model to localise the Practical Approach to Care Kit (PACK): from South Africa to Ethiopia. BMJ Glob Health 2019;3:e001108. DOI:10.1136/ bmjgh-2018-001108. Accessed on 09.12.2020.
Describes impact of Primary Care 101 and PACK on primary care delivery in Ethiopia.

[5.6] Wattrus C, Zepeda J, Cornick RV, et al. Using a mentorship model to localise the Practical. Approach to Care Kit (PACK): from South Africa to Brazil. BMJ Glob Health 2018;3:e001016. DOI:10.1136/ bmjgh-2018-001016. Accessed on 09.12.2020.
Describes impact of Primary Care 101 and PACK on primary care delivery in Brazil.

[5.7] Website of the municipality of Florianopolis, Brazil, describing implementation of PACK. Accessed on 09.12.2020.

[5.8] UNAIDS Factsheet on HIV/AIDS in South Africa 2019. Accessed on 04.03.2021.
Provides evidence of continued ART expansion in South Africa: “People living with HIV who are on ART: 5 200 000.” Graphs show ART coverage among people with HIV increasing from 48% of 8.8 million in 2104 to 70% of 7.4 million in 2019, that is, an increase of 1.9 million.

[5.9] World Health Organisation, 2021. Tuberculosis profile: South Africa. Accessed on 05.03.2021
This web page shows graphically that incidence of HIV-positive tuberculosis decreased from about 700 to 400 per 100,000 population per year, from 2014 to 2019. With 59 million population, that decrease is equivalent to 177,000 cases per year.