Microbiologically confirmed tuberculosis in South Africa, 2004-2015

Ananta Nanoo[1], Linsay Blows[1], Farzana Ismail[1], Hendrik Koornhof[1], Judith Mwansa[1], Shaheed Vally Omar[1], Sue Candy[2], Nazir Ismail[1]

[1]Centre for Tuberculosis, NICD
[2]Surveillance Information Management Unit, NICD

Executive Summary

South Africa has the highest incidence of TB in the world. A total of 3 327 876 mPTB cases occurred in South Africa between 2004 and 2015. Four provinces (KwaZulu-Natal, Eastern Cape, Gauteng and Western Cape) accounted for 74.2% of the absolute mPTB burden in South Africa during 2015. mPTB incidence rates are on the decline with reductions of -4.1%, -6.0% and -4.8% year-on-year for 2013, 2014 and 2015 respectively, which is half of that required by the WHO End TB Strategy. Females between the ages of 25-44 have shown the sharpest decline in incidence rates (-33.6%) between 2008 and 2015, reflective of efforts in the HIV programme targeting this age group. Change in incidence rates among males has been minimal for the age group 25-44 years over the same period (-13.4%) and shows the highest incidence (2.5 times the national average), requiring initiatives aimed at this population. Among South Africa's provinces, KwaZulu-Natal has shown the sharpest decline in mPTB incidence rates and achieved a reduction of 37.1% over a four-year period (2011-2015). Antiretroviral therapy expansion, which has probably led to important early successes, has tapered off in several provinces (Gauteng, North West and Western Cape) and other aspects of TB control need to be targeted (pre-treatment loss to follow up, contact tracing etc.).

Introduction

Despite instituting interventions to control tuberculosis (TB) in South Africa over many years, it is still the leading cause of death due to an infectious bacterial agent[1]. The World Health Organization (WHO) estimated 454 000 new TB cases in South Africa in 2015[2] – the fifth highest globally. After adjustments for population size, South Africa has the highest incidence of TB among the 22 high-TB burdened countries in the world. It also has the largest number of HIV-associated TB cases. In 2015, 294 603 cases were registered on treatment[1] – presenting a very different picture from the estimated 450 000 cases by WHO. These variances could be due to poor health access or health seeking behaviour, incomplete records in registry data, loss to follow up of diagnosed cases or death prior to accessing treatment.[3-5]

A recent review[3] demonstrated the powerful utility of laboratory data in providing a robust surveillance system for tracking incidence, albeit only for microbiologically confirmed cases in South Africa. Most importantly, transformation of the laboratory data allowed for trend analysis at multiple levels of the healthcare system. These findings were made possible by South Africa's unique position, compared to many other developing and developed countries globally, in having a single integrated laboratory network that covers all public health sector facilities.

Since the publication of the review,[3] the algorithms used have been further refined to improve the accuracy of the system as attested by the updated incidence rates now reported for the preceding years. Three additional aspects were considered important for developing this report: 1. inclusion of more recent annual data, given that the Xpert MTB/Rif rollout only began in 2011 and the previous findings were reported up to and including 2012; 2. analysis performed at a much lower geographical unit to be meaningful in guiding future interventions; 3. presentation of data in a format that is easy to access, and easy to understand and interpret.

Methods

Data were sourced from the National Health Laboratory Service's (NHLS) Corporate Data Warehouse (CDW). The CDW collates information from the laboratory information management systems (LIMS) used by the NHLS. Specimens collected from people presenting at public health facilities with signs and symptoms of TB are sent to the NHLS' network of laboratories for testing and these results were the primary data included. Probabilistic matching of demographic data was performed to achieve patient-level analysis.

For each patient identified by the record linking process, TB-confirmed status was determined based on a positive TB result using an Xpert MTB/Rif test, culture, line probe assay or smear. A 12-month window period for each patient was calculated based on the date of the first confirmatory test with a positive result, and used to distinguish new episodes from existing episodes. This approach was based on the understanding that treatment for drug-susceptible TB spans six months, and that smear conversion for drug-susceptible TB is usually achieved within three months and allows for some delay between diagnosis and entry into treatment. If a case that was confirmed to have drug-susceptible TB was found to develop drug resistance later, the 12-month episode window was extended to 24 months to allow for the extension of treatment.

Geographic data in the form of shape files and boundaries with associated population data by gender and five-year age group were obtained from the Municipal Demarcation Board and Statistics SA respectively. Data from annual population estimates aggregated to sub-districts were linked to the laboratory-confirmed TB data at sub-district level. This enabled calculation of sub-district, district, provincial and national TB incidence rates as well as age/sex standardized incidence rates. Ninety-five percent confidence intervals were calculated for these incidence rates. Incidence trend graphs with fitted trend lines and confidence intervals were plotted for each administrative level. Population pyramids were used to show the age/sex distribution of TB cases nationally and provincially. All statistical analysis was undertaken using Stata v14.0 (Statacorp, College Station, TX, USA). All maps were developed using the Esri Maps for Microstrategy plugin (Esri, Redlands, CA).

Results

Over the 12-year period, a total of 3 327 876 incident microbiologically confirmed cases of pulmonary TB (mPTB) were diagnosed in South Africa (Table 1). This total excludes KwaZulu-Natal (KZN) Province for the period 2004-2010, for which data were unavailable as a laboratory information system covering the whole province was only introduced post-2010. Excluding KZN, incident mPTB peaked at 272 702 cases nationally in 2008, and was recorded at 214 543 cases during 2015. In 2015, KZN accounted for an additional 66 512 mPTB cases giving a total of 281 055 incident mPTB cases. The highest burden of mPTB incident cases in 2015 occurred in four provinces ranked by order: KwaZulu-Natal (66 512), Eastern Cape (59 205), Gauteng (44 822), and Western Cape (37 967) (Figure 1; Table 2). Together they account for 74.2% of the total burden in 2015. The overall trend in TB has been declining both in numbers of mPTB incident cases and in rates (Table 1) since 2008. Incidence peaked in 2008 at 689 (95% CI: 687-692) per 100 000 population, and declined to 520 (95% CI: 519-522) per 100 000 population in 2015. The annual change in incidence rates have been -4.1%, -6.0% and -4.8% respectively, for the last three years (2013, 2014, 2015).

Incidence trends by province have shown similar consistent declines in recent years, although variation in incidence rates did occur (Figure 2, Table 2). In 2015, Limpopo Province recorded the lowest incidence rate (251 per 100 000 population; 95% CI: 246-255) that is more than three-fold lower than that of the Eastern Cape (865 per 100 000 population; 95% CI:858-872), which recorded the highest incidence rate that year. However, all provincial incidence rates were still above 250 per 100 000 population in 2015, the threshold level above which WHO has previously declared to be a health emergency. Northern and Western Cape provinces recorded their highest incidence rates in 2004/5 and also showed sharp declines up to 2010; the former showing increases in the subsequent period coinciding with the implementation of the GXP, while for Western Cape Province the recent trend has stabilized. Although the KwaZulu-Natal data only date from 2011, modeled data previously published indicate that it too is one of the provinces with the highest incidence rates, and the downward trend only began in 2011. This province has shown the largest year-on-year declines since 2011 (988; 95% CI: 982-995) and in 2015 (621; 95%CI: 616-626) was down to the 4th highest in terms of incidence rates – a 37.1% reduction in mPTB incidence rate over the 4-year period.

The most affected age groups with mPTB were those in the economically active 25-44 year age group with an overall male dominance in 2015 (Figure 3). The absolute number of cases was however higher among females in the younger age groups and are reflective of the pattern seen with HIV-infected persons. The encouraging finding of a declining mPTB incidence rate is primarily driven by large declines in incidence rates in females (25-44 year age group) with a 33.6% decline in incidence rates between 2008 (1059 per 100 000 population; 95% CI: 1050-1067) and 2015 (703 per 100 000 population; 95% CI: 698-708) nationally.

In contrast, the changes in incidence rates among males in the most affected 25-44 year age groups remained relatively small for the same period (13.4%) starting at 1272 (95% CI:1262-1281) and declining to 1101 (95% CI:1094-1108) per 100 000 population respectively. These numbers are four times higher than the WHO threshold of 250 per 100 000 for a health emergency. The age/

gender specific incidence rates show a marked difference between the 25-44 year age group (703; 95% CI: 698-708) for males and the 45-64 year age group (439; 95% CI: 433-446) for females in the most recent year. Another interesting finding is the small but consistent upward trend in incidence over time in the >65y age group – especially among females.

Discussion

South Africa is on the World Health Organization (WHO) list of priority countries with regard to the categories of tuberculosis (TB), drug-resistant tuberculosis (DR-TB) and HIV-associated TB.[2] Important positive changes have occurred globally with signs of declining TB incidence, which has led to the launch of the END TB strategy by WHO. This strategy aims at reducing incidence and mortality with ambitious targets set for 2035. The current study builds on previously published data for South Africa, is updated to 2015, and confirms the trend in year-on-year reductions in mPTB incidence rates since 2012 (-4.1%, -6% and -4.8% nationally for the years 2013-2015). Although this is approximately half of what is required by the WHO END TB strategy (10%), it is higher than the global average of 2%.[6]

The national decline in mPTB incidence is the sum total of the efforts of South Africa's nine provinces. KwaZulu-Natal Province, which carries the highest absolute burden in the country, has shown the greatest success in the recent past with annual reductions of mPTB incidence rates in line with the END TB targets i.e. -13.4%, -9.7% and -8.5% for 2013-2015. Similar trends were also observed in Limpopo (much lower burden) and Free State (-2.5% in 2013, -4.8% in 2015 and approaching target in 2015 at -9.2%) provinces.

Gauteng, North West and Western Cape provinces showed excellent reductions in the early years but these trends have recently slowed. Western Cape Province showed an annual change of -0.8%, -1.3% and +1.8% for the period 2013-2015. The impact of the ART program on reducing mPTB incidence has been shown to be an important contributor in these provinces. However, this alone will not be enough even though these provinces initiated ART programs much earlier than the other provinces.
The newly revised national TB Plan updated for the period 2017-2021 has targeted five strategic interventions along the cascades of care; starting with finding undiagnosed cases and ending with the final objective of successful patient outcomes. In addition, two cross-cutting themes, namely quality improvement and data utilization, are envisioned. These sets of interventions will hopefully address the stagnation observed in some provinces. It is also encouraging to see that the National Department of Health's new TB plan will use a data-driven targeted approach and it is envisioned that this report will provide a solid foundation for monitoring progress of the END TB targets.

Northern Cape Province is an area where health systems and access are key elements impacting on success or failure. This province has demonstrated a concerning increase in mPTB incidence rates, and although it carries a relatively low mPTB burden nationally (3.4%), by incidence it is one of the highest, requiring further investigation.

A striking clue to the success and failure of the achieved reduction in incidence was observed by disaggregating data by gender. Most of the declines observed across the provinces and reflected nationally have been driven by successes achieved among females aged between 25-44 years. This group showed a 33.6% reduction between 2008 and 2015 nationally. This links closely with the large emphasis of the HIV program and greater health-seeking behaviour of this population. In stark contrast, the reduction among males in the same age category nationally was only 13.4% for the same period and, in addition, this is the age group with the highest mPTB incidence. Specific strategies aimed at this population are urgently required if the country is to reach the END TB targets, including targeted public messaging, increased access through men's health and wellness centres or days, and male role models.

South Africa's burden of mPTB is not homogenous and becomes more apparent at each successive tier in the health system. The highest burden is carried by just four provinces, yet upon closer inspection it is clear that selected areas, particularly the urban metropolitans, have the largest concentration. Efforts can thus be focused on specific geographic areas with achievable results.
Unlike HIV, TB is curable and the majority of infected individuals have achieved cure – a statistic often underappreciated.
This study cannot explain the reasons for the changes observed nor the relative burden of disease. These questions will need to be interrogated and research studies undertaken where appropriate. What this report has achieved is an important analysis of trend over a 10-year period. The reporting of mPTB data does however have its limitations – especially the lack of clinically diagnosed cases, which account for up to 30% of the case burden. This may well explain the difference in incidence observed in 2015 (510 per 100 000 population) compared with the substantially higher WHO estimate (834 per 100 000 population) for South Africa.

The current report provides valuable insights up to and including 2015 that should be closely integrated into TB control planning for the next five years. Annual updates will be provided to more closely monitor the situation of this priority disease in South Africa. Trend analysis of drug-resistant TB and extrapulmonary TB will be addressed in future reports.
Lastly, the National Institute for Communicable Diseases (NICD) proudly announces the release of an online dashboard upon

which this report is based and which will provide regular updates which cannot easily be achieved in a report format. The dashboard is accessible from the NICD website: www.nicd.ac.za.

Acknowledgements

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Table 1. Pulmonary tuberculosis (mPTB) incident case burden and rates by year, South Africa, 2004-2015.

Year	n	Incidence/100 000 population (95% CI)	Annual change in cases (n)	Annual change in incidence (%)
2004	214166	572 (569-574)	-	-
2005	260855	687 (685-690)	46689	20.1
2006	269197	700 (697-702)	8342	1.9
2007	260406	668 (665-670)	-8791	-4.6
2008	272702	689 (687-692)	12296	3.1
2009	252467	629 (627-632)	-20235	-8.7
2010	251951	619 (616-621)	-516	-1.6
2011*	343960	667 (665-669)	-$	-$
2012*	317439	606 (604-609)	-26521	-9.1
2013*	309088	581 (579-584)	-8351	-4.1
2014*	294590	546 (544-548)	-14498	-6.0
2015*	281055	520 (519-522)	-13535	-4.8

*includes data for Kwa-Zulu Natal Province

$ Annual change restarted with addition of Kwa-Zulu Natal Province data

Table 2. Pulmonary tuberculosis (mPTB) incident case burden and rates (per 100 000 population) by province, South Africa, 2004-2015.

Year	Eastern Cape		Free State		Gauteng		KwaZulu-Natal	
	n	Incidence	n	Incidence	n	Incidence	n	Incidence
		(95% CI)		(95% CI)		(95% CI)		(95% CI)
2004	42879	724(717-731)	16767	677(666-687)	49398	446(442-450)	-	-
2005	49511	825(818-832)	19160	763(752-774)	68352	609(604-614)	-	-
2006	51828	852(845-859)	18360	721(711-732)	69189	608(604-613)	-	-
2007	54455	883(876-890)	18594	721(710-731)	59155	513(509-517)	-	-
2008	64336	1029(1021-1037)	18870	721(711-731)	61327	524(520-528)	-	-
2009	62421	984(976-992)	17979	677(667-687)	58122	490(486-494)	-	-
2010	68440	1063(1055-1071)	16751	622(612-631)	57364	476(473-480)	-	-
2011	65236	998(991-1006)	16489	603(594-612)	54722	448(444-452)	101058	988(982-995)
2012	63018	950(942-957)	16552	596(587-605)	46490	375(371-378)	90075	868(862-873)
2013	65281	969(961-976)	16369	581(572-590)	47376	376(373-379)	79290	752(747-757)
2014	60518	884(877-891)	15833	553(544-562)	46467	363(360-366)	72743	679(674-684)
2015	59205	865(858-872)	14387	502(494-511)	44822	350(347-353)	66512	621(616-626)

Table 2. Pulmonary tuberculosis (mPTB) incident case burden and rates (per 100 000 population) by province, South Africa, 2004-2015 continues...

Limpopo		Mpumalanga		North West		Northern Cape		Western Cape	
n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence
	(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)
10184	209(205-213)	15906	436(429-443)	15854	500(493-508)	11669	1128(1108-1149)	51509	980(972-989)
13280	269(264-273)	18691	506(499-513)	24584	766(756-775)	12812	1223(1201-1244)	54465	1023(1014-1031)
15825	316(311-321)	20018	535(527-542)	27100	833(823-843)	11582	1090(1071-1110)	55295	1024(1016-1033)
18383	362(357-367)	22384	590(582-597)	23370	708(699-718)	10564	981(962-1000)	53501	978(969-986)
21034	408(403-414)	25558	664(656-672)	23355	698(689-707)	10615	972(953-991)	47607	858(850-866)
21698	415(410-421)	23485	601(594-609)	22191	654(645-663)	8487	766(750-782)	38084	676(670-683)
20775	392(386-397)	22294	562(555-570)	21675	629(621-638)	7129	634(619-649)	37523	657(650-664)
19765	367(362-372)	20447	508(501-515)	19205	549(542-557)	8796	771(755-787)	38242	660(653-666)
18706	342(337-347)	20192	494(488-501)	17014	479(472-487)	8502	734(718-750)	36890	627(620-633)
17071	308(303-312)	19413	468(461-475)	17545	487(480-494)	9550	812(796-828)	37193	622(616-628)
15921	282(278-287)	18439	438(431-444)	17790	486(479-493)	9607	804(788-820)	37272	614(607-620)
14124	251(246-255)	17271	410(404-416)	17085	467(460-474)	9682	810(794-826)	37967	625(619-631)

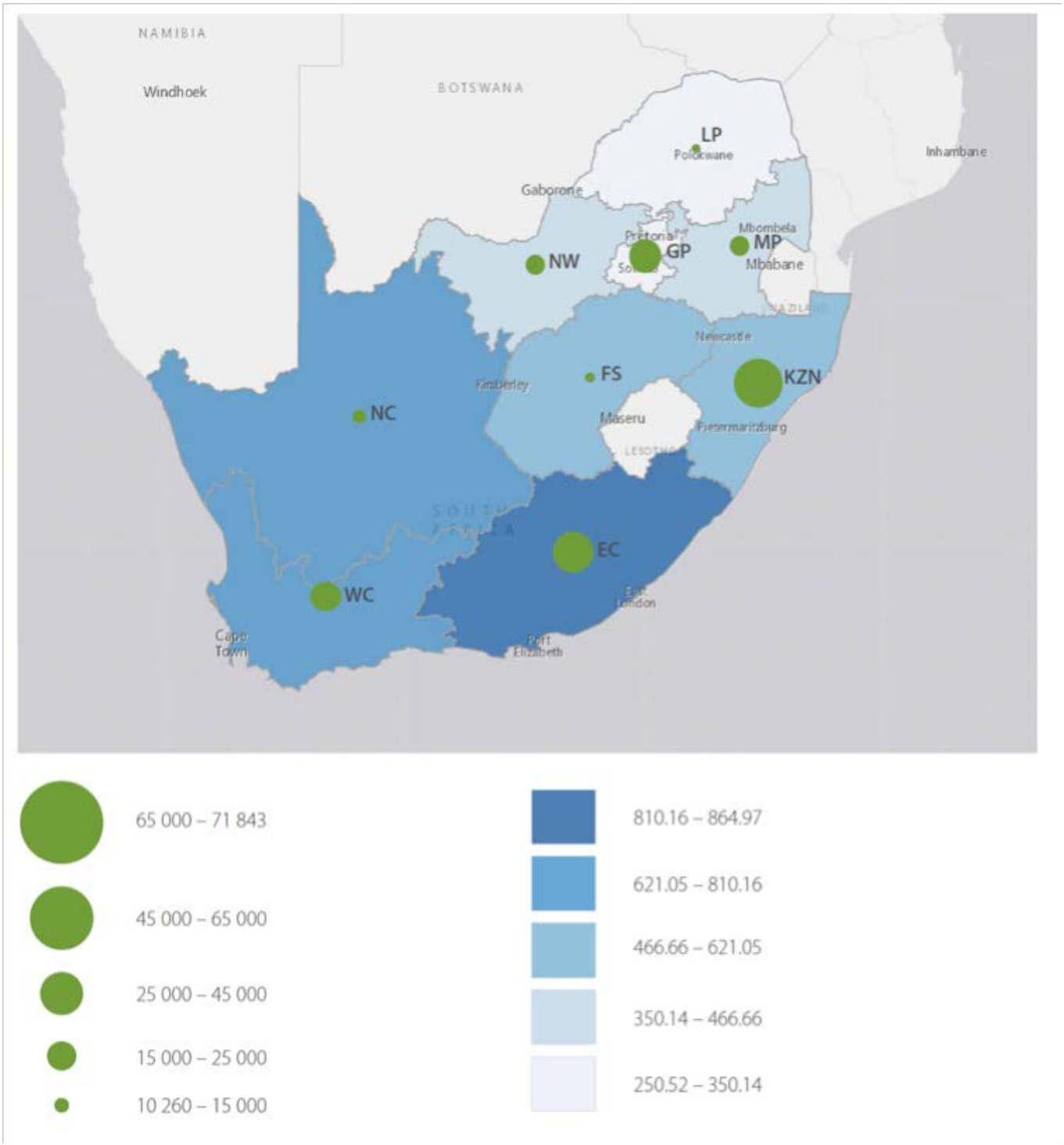

Figure 1. Spatial distribution of the pulmonary tuberculosis (mPTB) incident case burden (circles) and rates (shading), South Africa, 2015.

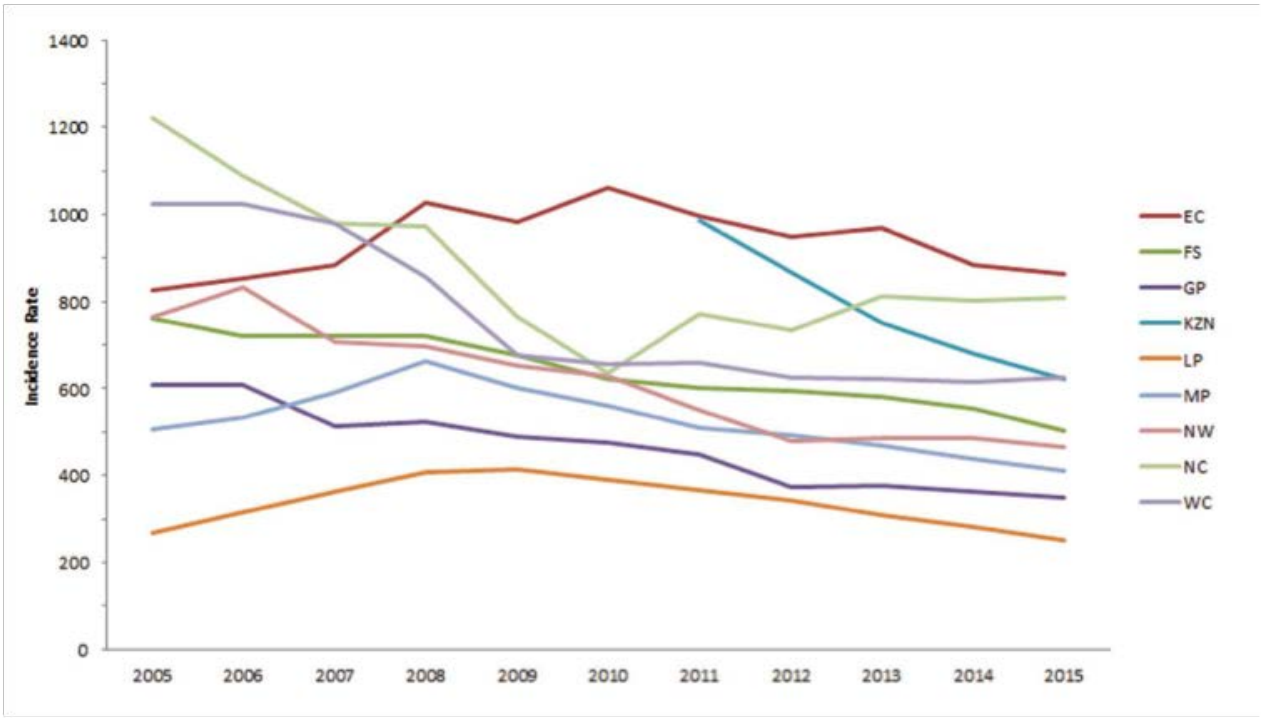

Figure 2. Trends in pulmonary tuberculosis (mPTB) incidence rates (per 100 000 population) by province, South Africa, 2004-2015.

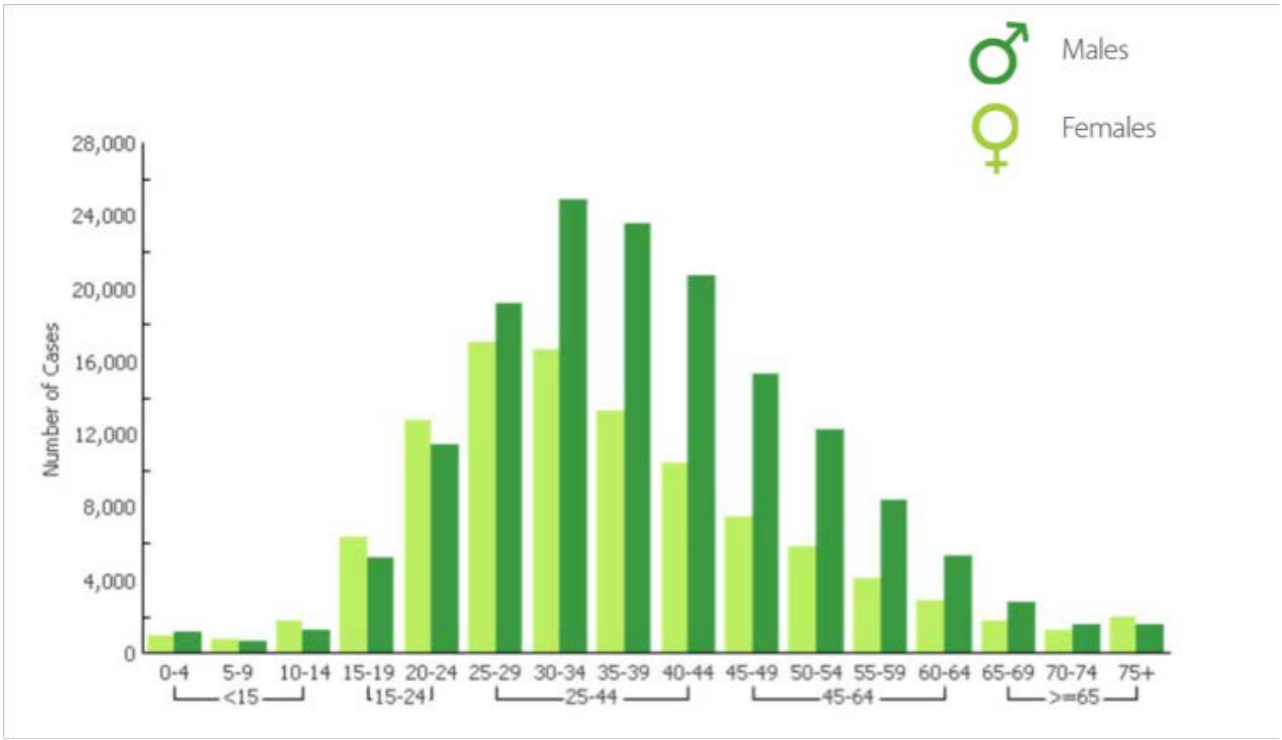

Figure 3. Age and gender population pyramid of pulmonary tuberculosis (mPTB) incident cases, South Africa, 2015.