Review

Tuberculosis in Papua New Guinea: from yesterday until today

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Abstract

Little is known about the situation of tuberculosis in Papua New Guinea despite its high TB burden, emerging drug resistance and rising HIV co-infection. This review gives an overview on the current situation of TB in PNG and identifies knowledge gaps that should urgently be addressed in the future.
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1. Introduction

In 1999 WHO declared a TB crisis in the Western Pacific Region (WPR) where the incidence accounts for 19% of the global burden. In 2012, 2.4 million TB cases were reported for the Region, with the highest incidence rate of 411/100,000 occurring in Cambodia. Although the incidence of MDR-TB cases is increasing in the WPR, the estimated overall TB incidence rate seems to have fallen over the last 20 years [1].

Papua New Guinea (PNG) has one of the highest tuberculosis (TB) incident rates in the WPR (348/100,000 population). The goal of 85% treatment success has been achieved in all high burden countries in the Region but PNG, where treatment success was only reported for 69% of cases in 2011 [1]. With a population of almost 7 million it was estimated that there were 25,000 new TB cases in PNG in 2012 and that the national prevalence was 39,000 cases [1]. In 2006 PNG was held to be one of 7 countries with a high TB burden in the WPR and in 2011 PNG was reported to have a more than 10 times higher incidence rate compared to other Pacific island countries [2]. Recently, from a study in Kikori, Gulf Province, the TB incidence was reported to be 1290/100,000 per year [3], which would make it one of the highest estimated TB incidence rates of the world [1]. Furthermore, only in 2012 a country wide drug-resistance (DR) survey in a few provinces started, the same year in which the first XDR TB case from PNG was reported [4].

The land area of PNG is 462,840 km^2 and approximately 80% of the 7 million people live in rural areas [4]. Tuberculosis is the 3rd highest cause of morbidity and mortality and the burden is rising. Major factors are an inadequate treatment programme, an increase of DR, especially in Western Province [5], and an increase of people infected with HIV [6].

Unfortunately, the prevalence estimates of TB for PNG which were developed by WHO and are quoted above are mostly based on models and data sources for these are of uncertain validity as TB case estimates are derived exclusively from health facility records which are often of poor quality. The lack of national prevalence data on DR highlights the urgent need for information about the actual TB situation.

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This review aims to summarize information on TB in PNG. In order to understand the current situation, it is necessary to understand the history of TB introduction into PNG, its epidemiology, and to discuss current control strategies and the effectiveness of treatment. By using published research information and grey literature, probable knowledge gaps that need to be addressed could be identified.

2. History

When and how was TB introduced into PNG? Until recently, human infection with *Mycobacterium tuberculosis* (*Mtb*) was thought to date back to the Neolithic period, when humans first came into close contact with domesticated animals. Recent genetic evidence has now shown that TB in humans dates back as far as 70,000 years ago [7] suggesting that TB would have spread out of Africa with the first migrations of modern humans and thus would have come most probably to PNG with the early migration waves. The relevance for modern PNG is of likely host-pathogen co-evolution between humans and *Mtb* in which host and bacterial genotypes influence disease phenotype [8,9].

It is commonly accepted that the first migrations into New Guinea occurred 40,000 to 60,000 years ago when Australia and PNG formed one continent called Sahul. This explains a close genetic relationship between Australian Aborigines and PNG Highlanders [10]. Human Leucocyte Antigen (HLA) typing and skeletal findings indicate that inhabitants from the Eastern Highlands district Goroka represent descendants of the oldest migration waves [10,11]. A second migration wave into PNG occurred around 3,500 years ago from Taiwan and through the Philippines. These Austronesians (a language family which is found throughout islands of Southeast Asia and the Pacific) settled along the coast and on the islands and later populated islands throughout the Pacific. It has been suggested that Austronesian-speaking groups of PNG are more heterogenic than the non-Austronesian-speaking groups (e.g. highlands populations) [10].

3. Epidemiology

3.1. Disease distribution: prevalence and incidence

Dr. Wigley, the Specialist Medical Officer for TB in PNG during the late 1950ties to early 1960ties described in details how TB spread in PNG and how a first national TB control program was established [12,13]. It is unknown whether TB was present in PNG when the Europeans started to arrive in any number in the late 19th century, when missionaries and traders came to settle. Wigley, however, stressed the point that with the arrival of Europeans circumstances changed and conditions developed that favoured the spread of previously unknown diseases and of diseases that had been contained in small populations because of their comparative isolation.

At the time of colonization in 1884 the Northern part of PNG was occupied by the German Trading Company, forming German New Guinea (GNG), and the Southern part has been ruled as British New Guinea (BNG) which in 1906 was transferred to Australia. In 1975 PNG became independent (the administrative history of PNG is summarised in Table 1) [12,13]. The Germans and the Australians recruited national workers to the sugar cane fields in Samoa and Queensland, respectively, from 1869 until 1910. Living and working conditions were poor and reports suggested that workers brought back to their villages many diseases, and in Wigley's opinion TB then began to spread through the country because of the associated movement of the population [12].

From 1914 onwards population studies using the tuberculin skin test (TST) were conducted, showing an increasing number of TB cases in Papua New Guineans which were more often serious or fatal than in expatriates [14—16]. Infections appeared first in young men and spread later to children and women, especially in those villages where people had been recruited to work on the sugar fields in Rabaul or outside of PNG. For example, Kersten [14] reported that between 1912 and 1913 none of 44 men from the upper Waria river (Morobe province), with no experience of plantation work, reacted to the von Pirquet test whilst 23% of 135 male adults from the lower Waria river, where many had worked on plantations, reacted positively to tuberculin. The results of such studies [14—16] led to the building of an isolation hospital on an island near Port Moresby [17].

Wigley summarized data from various reports for the German Colonial Office during the first 40 years of the 20th century which showed that the von Pirquet test, applied to all new labour recruits in Rabaul, had an alarming increase of positive reactions over a period of only 5 years. A positivity rate of 5% in new recruits in 1920 increased to 42.8% in 1921 and to 51.5% in 1925. By 1922, 20.7% of all deaths in Rabaul were attributed to TB and infection rates seemed to be strongly correlated with contact to expatriates through labour trade or missionaries [12]. Tuberculin skin test surveys for the National TB Control Program were conducted from 1950 to 1966 and by 1963, evidence of infection in all provinces of PNG was found [13]. TB infection rates summarized in an undated monograph of Wigley [12] provide basic data for TB in PNG from 1950 through to independence in 1975, although methods of data collection and information on Bacille

Table 1
Administrative history of Papua New Guinea.

	Southeast New Guinea	Northeast New Guinea
1884	British New Guinea	German New Guinea
1906	Australian territory of Papua	
1914		Australian military administration
1921		League of nations mandated territory administered by Australia
1942	Military administration. Theatre of war	
1945	Provisional administration by Australia	
1949	Permanent civil administration by Australia of the territory of Papua and the United Nations Trust Territory of New Guinea	
1975	Independent state of Papua New Guinea	
1978	Organic law establishing Provincial Government	
1995	Organic law devolving health services to Provincial and Local government	

Calmette–Guerin (BCG) vaccination is lacking. There were major differences in TB infection rates between coastal and highlands provinces. Infection rates ranged from 86.7% in Kavieng Town (New Ireland Province) and 81% on Sisiame Island (Western Province) to 0.2% in Kopiam village and 0.9% Laiagam villages (both Western Highlands Province), reflecting the impact of the long isolation of the highlands from the outside world. Between 1950 and 1975 more studies reported TB infection rates obtained through various methods including Mantoux test, sputum smear examination and clinical examinations such as chest X-ray (CXR) [18,19]. Although direct comparisons are difficult there appears to be little doubt that infection with TB increased in most provinces in PNG throughout this period. It is noteworthy that infections in relatively isolated regions were still found mostly in adult males. For example, between 1959 and 1966 in the Highlands Region infection rates in females were 0–2%, whereas in males they reached up to 12.5% [12]. In less isolated regions higher infection rates were found in adults over 15 years regardless of gender and in settlements of Port Moresby active tuberculosis was almost equally present in children and adults [18]. Overall, the coastal population of PNG showed much higher TB infection rates than the highlands population, which seemed to have been free of TB until the 1950s, which supports again the hypothesis that occurrence of TB infections in the PNG population was dependent on the intensity of early contact with Europeans and the degree of urbanization.

Wigley showed that 80% of the coastal population had a positive reaction to TST before BCG vaccination which increased to 85% after vaccination [12]. In contrast, only 1% of the highlands population reacted to TST before vaccination and only 10% subsequently after vaccination. The duration of skin test reactivity also varied and waned quickly in the highlands population whilst it stayed for several years in the coastal population [20,21]. Bagshawe et al. [21] found almost no natural reaction to TST before vaccination in Karimui (Eastern Highlands Province) in the 1960s, but reactivity increased to 87.4% 3 months after vaccination only to drop to 60.4% within 9 months. It has been speculated that short-lived reactivity to tuberculin was due to the lack of superinfecting non-tuberculosis mycobacteria (NTM). Several studies suggested that almost no such infection occurred in the highlands, which could explain the low natural reaction rate [21]. This was further supported by a TST sensitivity study conducted by Brown et al. [22] in which also no reactivity to atypical mycobacterial antigens could be found. Still, it is yet unclear why these differences in reaction to tuberculin in different populations occur but genetic factors have been implicated in determining a TST reaction [23] and also influencing immune responses and memory to BCG [24]. In PNG with its human genetic diversity this could well play a role.

After independence in 1975, it was confirmed again that TB prevalence was higher in coastal sites than in the highlands. There was not only a difference in TB prevalence but TB presented itself with a different phenotype in the highlands [25]. Kaupa et al. reported that from 1980 to 81 only 23.2% (13/56) of all TB patients from the highlands presenting at

Goroka General Hospital (GGH) had pulmonary TB, all others suffered from extra-pulmonary TB. In comparison, 75% (2896/3809) of coastal patients suffered from pulmonary TB in 1979 [25]. There are limitations in the data since most extra-pulmonary TB is diagnosed on clinical signs and not confirmed bacteriologically, but it is evident that less pulmonary and less post-primary cavitating TB was found in the highlands.

The situation seems to be similar today and although case notifications reported in the National Strategic Plan are derived from only 9 of 20 provinces [4], it remains that most TB cases in 2010 came from coastal areas and a high prevalence of extra-pulmonary TB was reported from the highlands. Whether this pattern remains and reflects the epidemic situation in the highlands, where people rarely have encountered the bacilli in childhood and hence develop at older age primary tuberculosis either in the lungs or disseminated needs to be further investigated.

3.2. HIV/TB co-infection and risk factors

In 2011 HIV prevalence in the adult population aged 15–49 years was estimated to be 0.9% in PNG [6]; 9.8% of TB patients with known HIV status were HIV positive [1]. Seaton et al. [26] reported in 1996 that 56% of 67 enrolled HIV patients were diagnosed with TB at Port Moresby General Hospital (PMGH). This might have been overestimated since it was solely based on CXR for the diagnosis of pulmonary TB but nevertheless reflects the high level of co-infection.

Other known risk factors for TB include malnutrition, smoking and diabetes [27,28]. Diabetes is known to increase the risk of TB 2–3 fold, and its prevalence is increasing in PNG. In 5 of 160 diabetes patients attending PMGH, pulmonary TB was diagnosed which gives an 11 fold higher annual incidence rate for TB in this group than had been estimated for the general population [29]. Chewing of betel nut is very common in PNG (areca nut, nut of the areca catechu palm, "buai") and it has been shown to cause oral cancer and other oral diseases in humans [30]. There has been growing concern that spitting of betel nut saliva could contribute to TB transmission but no study has yet investigated this nor has the impact on TB of alcohol consumption or smoking been studied in PNG. Similarly, no studies have investigated any consequences of co-infections with helminths on the burden of TB in PNG, although there is a high prevalence of helminth infections and known effects of such co-infections on the immune response against TB [31].

3.3. Drug resistance

Only in 2012 did country-wide surveillance for DR commence in PNG and little information is available. There is no biosafety level three laboratory in PNG, thus sputa of suspected DR cases are sent to Australia for drug susceptibility testing (DST) [4] leading to a significant delay in diagnosing patients and in initiation of appropriate second-line treatment.

This increases the period in which transmission of resistant strains might occur. In 2012 the first XDR TB cases were reported [32]. Most information on DR in PNG is obtained from Australia where migrants are screened either in the Torres Strait Islands cross-border region [5,33], or migrants from PNG entering Australia by air [34]. Simpson et al. [34] showed that all MDR-TB cases detected in Far North Queensland between 1998 until 2002 were from PNG, and Lumb and colleagues from the Mycobacterium reference laboratory network [35] reported that a substantial proportion of MDR-TB cases in Australia in 2008–9 originated in Western Province, PNG (6/21 in 2008; 11/31 in 2009). Importantly, the majority of these MDR-TB cases seemed to be primary DR strains giving evidence for on-going transmission of MDR-TB in PNG [5].

Western Province has been estimated to be the province with the highest TB burden in PNG, with an estimated incidence 2–3 times higher than the national level [32]. From there the first PNG XDR TB case originated. Already in 2008 Gilpin et al. reported pre-XDR TB cases (MDR-TB also resistant to quinolones) from Western Province thus foreseeing the emergence of XDR TB [5]. A study in 2012 conducted in Madang Province in the north of PNG showed that 15.7% of 172 TB cases were resistant to at least one drug, and that 5.2% were MDR cases [36]. Although these numbers cannot be extrapolated to the whole country they are alarming and add force to the fact that PNG urgently needs to address the MDR-TB problem. This is reinforced by data from the Central Public Health Laboratory (CPHL) of PNG from 2011 where it was shown that 77% of 87 suspected drug resistant re-treatment cases (having received TB treatment for at least 1 month during a previous episode) were indeed resistant and of these 61% were MDR [4]. Consequentially, there is an urgent need for drug resistance testing in PNG either bacteriologically or by molecular means but also for monitoring drug quality, availability, and compliance to treatment. Improving the directly observed treatment strategy (DOTS) in PNG is not sufficient if drug resistance cannot be monitored simultaneously.

Overall, the few available studies provide baseline information on DR for some provinces but no inferences can be drawn for PNG as a whole. Large differentials are to be expected because of regional variation in incidence, the general diversity of the population and because of variable quality in the implementation of the National Tuberculosis Control Program (NTP) which is a provincial responsibility.

3.4. Mycobacterium tuberculosis genotypes

Compared to other bacteria the *M. tuberculosis* complex (MTBC) shows low genomic variability and very little horizontal gene transfer [37]. Outcome of TB infections and transmission are determined by a range of factors which include host genotypes [9], socio-economic conditions, and bacterial genotypes [38,39]. With the advent of genotyping methods in the early 1990s various studies found associations between certain MTBC genotypes and disease pattern,

differences in virulence of distinct strains, and an association of drug resistance with the so called Beijing family of strains [40].

In addition, genotyping is used to identify outbreaks, to investigate transmission dynamics, and to determine the origin of the *Mtb* strains circulating in a population. Genotyping is the only means of determining whether a strain has been introduced into a country or population; robust phylogenetic markers for MTBC exist [41]. *Mtb* can be separated into seven main lineages based on long sequence polymorphisms and these lineages have been found associated with specific geographic regions and human populations with differing incidence and risk for TB [40,42]. For example, Yen et al. showed that the indigenous population of New Zealand had a 6 to 18 times higher rate of TB than descendants of Europeans in New Zealand and that the lineage distribution differed significantly between those two groups [42]. Since *Mtb* is at least 70,000 years old and seems to have co-evolved and migrated with humans [7] one could speculate that TB was probably present in PNG before European contact. This leaves two options, either the disease had died out prior to the arrival of the Europeans due to small and isolated populations unable to sustain transmission, or, the "ancient TB" was sustained at a low frequency in some populations (e.g. in the highlands) but had been replaced by modern and more successful lineages in most populations with the arrival of Europeans. There is good evidence that "modern" strains show increased success and strain specific differences in virulence and progression to active disease [39] when compared to the "ancient" strains. It was reported for example, that the prevalence of *Mycobacterium africanum* (ancient) which used to be the predominant strain in Cameroon has drastically decreased and seemed to be replaced slowly by a recently emerged strain family of Lineage 4 (modern) between the 1970s and 2009 [43,44]. There is also little information available on *Mtb* lineage distribution in Melanesia or PNG. Aleksic et al. [45] found in Kiribati an almost equal distribution of Lineage 2 (East-Asian lineage) and Lineage 4 (Euro-American lineage). Since no MDR had been detected, an association with a specific lineage could not be investigated.

In PNG three studies involving *Mtb* genotyping were conducted. Gilpin et al. [5] found that between 2000 and 2006 15 of 60 isolates from severely ill patients from Western Province living in the Torres Straits were multi-drug resistant and belonged to the Beijing-type of Lineage 2. Ballif et al. [46] investigated TB cases from Madang and found a similar proportion of Beijing strains and showed that 77% of the collected samples belonged to Lineage 4. In contrast, in the small sample set from a study in Kikori, Gulf Province, Lineage 4 was much less represented (1 of 9 genotyped samples) than samples belonging to the Beijing family of Lineage 2 (8 of 9 samples) [3]. These results reflect that it is not possible to infer a genotype distribution in PNG as whole from such small samples representative of only three populations. Hence, it remains to be determined whether ancient strains are present in other parts of PNG, in particular in the more remote and isolated areas. Because disease phenotypes

appear to be determined by bacterial genotypes and because of the differences in disease presentation between highlands and coast [9,25,47], we are currently addressing this question by conducting studies in the coastal area of Alotau (Milne Bay Province) and in the Goroka district (Eastern Highlands Province).

4. TB control

The first attempt at TB control in PNG was probably the establishment of an isolation hospital on Gemo Island in 1937 [17] but the first official National TB Control Program (NTP) based on modern chemotherapy was implemented in 1950 [13,19,48]. A Tuberculosis Control Unit (TBU) of the Department of Health was formed which conducted mass examinations and determined TB prevalence in communities through mass miniature CXRs and TSTs. Subsequently, BCG vaccination was introduced and a mass vaccination campaign was conducted in the highlands [12,19]. The control program also included school medical services, the establishment of a thoracic surgery program [13,17] and facilitated cultivation of mycobacteria [17,49]. It emphasized mobile patrols for surveillance rather than depending on passive diagnosis from within health facilities, and was coordinated in a highly centralized way. This changed drastically with the establishment of the Organic Law on Provincial Governments and Local Level Governments in 1977 and the New Organic Law in 1995 in which 'the management and service delivery of rural health services' were handed over from the National Department of Health (NDoH) to the provincial and local governments [50]. This organisation remains in place until today and strongly affects the health service sector. Since the quality of a control program is dependent on the developmental state of a province it is difficult to extrapolate data from one province to the whole country. In this section we provide a short overview of various parts of the TB control program, namely prevention of TB, case detection and diagnosis, and treatment and management of TB patients.

4.1. Prevention

Because little TB was detected in the highlands in the late 1950s, it was thought that this population was at high risk of primary TB infection [12]. Throughout the 1960s BCG vaccine was therefore administered to all age groups in the highlands including adults [19,25]. The country wide expanded program on immunization recommended a 3-dose regimen for BCG in children because of waning tuberculin reactivity [48,51] although WHO recommendation was only one dose at birth. This 3-dose strategy was kept for decades and only changed in the late 1990s. BCG vaccination remains part of the PNG NTP until today.

Globally, the effectiveness of BCG varies in different populations and geographical regions [52] and with its large human genetic diversity and its environmental differences, PNG could be expected to differ not only when compared to other countries but also between provinces. This becomes

obvious since PNG neonates elicited a different immune reaction against atopic diseases compared to Western Australian neonates when primed with BCG [24]. For example, IFN-γ production in response to BCG was significantly enhanced in both study groups but to a much lower extend in PNG newborns compared to Western Australian neonates. Other studies have examined BCG coverage and TST reactivity before and after vaccination in specific study sites [22,53]. There has however never been a study of the efficacy of BCG in PNG.

4.2. Detection/diagnosis

For several decades in the early twentieth century, TB was diagnosed by TSTs such as the Mantoux test [14,19,54]. From the mid 1930ties CXR also became available in PNG and physicians began to biopsy lesions to diagnose TB [55,56]. Sputum smear microscopy became available in hospitals in the post-war period and sputum culture became available in a few. Sputum smear microscopy was widely introduced in 1975 [48], and became the main diagnostic tool to control the spread of TB in the community [57,58]. Although CXR has a higher false positive rate than sputum smear microscopy [59] it was - and is still today - widely used to diagnose pulmonary TB, particularly in sputum smear negative patients.

Historically, it is not clear whether a case-finding approach and treatment at home was integrated into the PNG control program with limited success as described by Levy et al. [48], or, whether there was no definite and planned case-finding strategy at all until 1990 [60]. In any case, in 1997 the internationally recommended DOTS strategy for the control of TB was being implemented in PNG [48]. DOTS requires the health system to provide access to standardized treatment, to ensure drug intake for all TB cases, and to provide quality-assured sputum microscopy. However, more than 10 years after the introduction of DOTS to PNG, the coverage rate was only 51% in 2010 [4]. The case detection rate was the lowest in 7 high TB burden countries of the Western Pacific Region in 2007 [61] and the cure rate was only 53% in 2011 [1]. It has been shown repeatedly that the most effective control strategy to decrease TB transmission would be to increase DOTS coverage [62] and indeed, treatment success rates were 80% in 2010 in those provinces that had implemented DOTS, whereas the lowest rates were observed in provinces which had not yet introduced DOTS [4]. The increase of DOTS coverage was a priority of the National Strategic Plan 2006 to 2010 [4] in which it was aimed to cover all 20 provinces and 80% of the population by the end of 2012. During that period the quality of DOTS coverage and case detection was questioned [63] since apparently all provinces had introduced DOTS but only 69% of the population was being reached. Nevertheless, cure rates had drastically been improved with 80% of smear positive cases being successfully treated but there was still a poor performance in terms of drug supply and only 40% of facilities sent quarterly reports on TB as required by national guidelines [64].

In 1961 Becker reported culturing of *M. tuberculosis* in PNG [49] but this has changed because of obvious safety

reasons and at the present time *Mtb* culture cannot be performed within the country. All samples requiring culture and DST have still to be sent to the Queensland Mycobacterium Reference Lab (QMRL) in Brisbane, Australia. This way, only samples of suspected MDR-TB cases are sent and no systematic monitoring of resistance is being conducted. Improvement of diagnosis but also of rapid detection of MDR-TB cases is possible through the use of the Xpert® MTB/RIF (Cepheid) which has been introduced in few centralized places in PNG [4], but needs urgently to be introduced generally. However, Isoniazid mono drug-resistance and DR combinations other than INH/RMP cannot be identified by this approach.

To significantly kerb TB in PNG, case detection rates have to increase and the DOTS program must ensure compliance and access to accurate treatment. An active case detection study conducted in rural communities in Madang province between November 2005 and March 2006 identified a substantial number of TB positive patients (Phuanukoonnon et al. *unpublished*). Reducing the number of non-identified infections would substantially reduce transmission but again requires diagnosis through quality smear microscopy and probably a changed health seeking behaviour. Xpert® MTB/RIF (Cepheid) could play an essential role here but its true value might only be assessed in a few years.

4.3. Treatment

The era of chemotherapy against TB started with Streptomycin (SM) in 1946 followed by Isoniazid (INH) in 1952 and Para-Amino-Salicylic Acid (PAS). The early treatment regimens in PNG consisted of an intensive phase with INH PAS and SM for three months and a maintenance phase of INH and PAS for 21 months. All Highlands patients were treated in coastal hospitals for the full two years to reduce chances of transmission in the highlands. In the 1970s Thiacetazone was added and the total duration of treatment shortened [65]. Compliance rates were then poor, but improved drastically with the introduction of the short course chemotherapy (SCC) in 1984 for children [66] and 1989 for adults [48] with a regimen including RMP and PZA reducing treatment duration drastically from 18 to 6 months. Jamieson et al. described in detail how the different presentations of TB were managed and treated in the 1950s before SCC [65] when surgery was conducted if chemotherapy was not an option. Ten years later surgery was still conducted if chemoprophylaxis failed but only in cases of spinal tuberculosis [65]. Since 2007 TB treatment in PNG follows WHO recommendations consisting of a fixed dose combination (FDC) of 4 different drugs [48]. Several studies showed an alarmingly high number of defaulters in PNG [48,63,67]. This is influenced by health seeking behaviour, belief in sorcery, lack of knowledge of the disease [68,69] but long distance to the closest health facility [65] social and financial pressure, the attitude and performance of health workers towards patients, and also limited drug supply are additional reasons [68]. To overcome this problem various approaches have been taken, such as out-patient

treatment with regular and close supervision of the patients in the 60s and 70s [68,70]. Garner et al. [67] described methods that were tried in Aitape, Sandaun province which included patient participation (former patients talking about their experience), showing patients their microscopy slides or CXR films, reduction of out-patient treatment duration, and even threatening patients to withhold treatment after defaulting. These strategies seemed to have improved compliance but not all of them are feasible today. Instead, reliable drug supply, intensifying follow-ups, and thorough contact tracing would not only decrease the defaulter rate but also increase TB case detection.

5. Conclusion

Although more data have been compiled on TB in PNG over the last few years there is still no comprehensive description of the disease for the whole country. Importantly, all available data suggest a threat of increasing transmission, the advent of MDR and even of XDR TB. Therefore comprehensive, accurate and timely data about the epidemiology of TB and prevalence of DR in PNG are an absolute priority. Although TB appeared to have been brought under control in the early 1970s [13] this was either overly optimistic or the situation has changed dramatically due to the emergence of DR and the epidemic of HIV/AIDS. Overall, reported cure rates are well below development goals for WPR and accuracy of diagnosis and DOTS coverage are well below international standards.

PNG has been isolated for a long time from the outside world and some parts remained without contact even until the 1980s. The human population with its vast genetic diversity and the limited outside interferences through human migration provide an ideal platform for TB research and its evolution. The emerging evidence that "modern" strains transmit more successfully than "ancient" lineages [8] could well be tested by genotyping samples from various sites in PNG, including remote sites, and thus might give insight into the evolution of *M. tuberculosis* in PNG. At the same time it would allow to explore differences in *M. tuberculosis* strains circulating in high or low incidence settings and in urban or rural settings. With this research addressing important evolutionary questions essential information of incidence, prevalence and degree of drug resistance for PNG could be obtained and thus would strengthen the TB control strategies in PNG for the benefit of the population of this country [5,33].

Conflict of interest

The authors declare no conflicting interest.

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