

Table S1

Study isolates undergoing sequencing using Illumina and Oxford Nanopore Technology (ONT) platforms

(N=59)

Sample	Illumina Accession no.	ONT accession no.	Lineage*	Drug Resistance**	Drug resistance Mutations**
S1	ERR12328206	ERR12328582	1.2.1.2.1	Sensitive	
S2	ERR12328205	ERR12328581	1.2.1.2.1	Sensitive	
S4	ERR12328204	ERR12328580	1.1.1	Sensitive	
S5	ERR12328203	ERR12328579	2.2.1	Other	Streptomycin <i>gid</i> 351delG
S8	ERR12328202	ERR12328578	2.1	Sensitive	
S11	ERR12328201	ERR12328577	1.1.1	Sensitive	
S12	ERR12328200	ERR12328576	2.2.1	Sensitive	
S13	ERR12328199	ERR12328575	1.1.3.1	Sensitive	
S14	ERR12328198	ERR12328574	4.8	Sensitive	
S15	ERR12328197	ERR12328573	2.2.1	Sensitive	
S17	ERR12328196	ERR12328572	1.1.1	Sensitive	
S19	ERR12328195	ERR12328571	1.1.1.1	Other	Streptomycin <i>gid</i> Glu92
S20	ERR12328194	ERR12328570	1.2.1.2	Sensitive	
S21	ERR12328193	ERR12328569	2.2.1.1	Sensitive	
S22	ERR12328192	ERR12328568	1.1.1	Sensitive	
S23	ERR12328191	ERR12328567	1.1.1	Sensitive	
S24	ERR12328190	ERR12328566	2.2.1	Other	FQs <i>gyrB</i> Asp494Ala ***
S25	ERR12328189	ERR12328565	2.2.1	Sensitive	
S26	ERR12328188	ERR12328564	2.2.1	RR-TB	<i>rpoB</i> Ser450Trp
S27	ERR12328187	ERR12328563	2.2.1.1	Pre-XDR-TB	Rifampicin <i>rpoB</i> Ser450Trp; Isoniazid <i>katG</i> Ser315Thr; Ethambutol <i>embA</i> -16C>T; PAS <i>thyX</i> -16C>T; Streptomycin <i>rpsL</i> Lys43Arg; FQs <i>gyrA</i> Asp94Gly
S28	ERR12328186	ERR12328562	1.2.1.2.1	Other	Pyrazinamide <i>pncA</i> Ser104Arg; Ethionamide <i>ethA</i> Thr232Ala
S29	ERR12328185	ERR12328561	1.2.1.2.1	Other	Pyrazinamide <i>pncA</i> Ser104Arg; Ethionamide <i>ethA</i> Thr232Ala
S30	ERR12328184	ERR12328560	1.1.1	Other	Pyrazinamide <i>pncA</i> Thr142Lys;
S31	ERR12328183	ERR12328559	1.2.1.2.1	HR-TB	Isoniazid <i>fabG1</i> -15C>T; Streptomycin <i>rpsL</i> Lys88Arg; Ethionamide <i>fabG1</i> - 15C>T; Streptomycin <i>gid</i> c.351dupG
S32	ERR12328182	ERR12328558	1.2.1.2.1	RR-TB	Pyrazinamide <i>pncA</i> Ser104Arg; Ethionamide <i>ethA</i> Thr232Ala; Rifampicin <i>rpoB</i> Ser450Leu
S33	ERR12328181	ERR12328557	1.1.1	MDR-TB	Isoniazid <i>fabG1</i> -15C>T; Ethionamide <i>fabG1</i> -15C>T; Rifampicin <i>rpoB</i> Ser450Leu
S34	ERR12328180	ERR12328556	2.2.1	HR-TB	Isoniazid <i>katG</i> Ser315Thr;
S35	ERR12328179	ERR12328555	2.2.1	Other	Streptomycin <i>rrs</i> 514A>C
S36	ERR12328178	ERR12328554	1.1.1	Sensitive	
S37	ERR12328177	ERR12328553	2.2.1	HR-TB	Isoniazid <i>katG</i> Ser315Thr;

<b>S38</b>	ERR12328176	ERR12328552	1.2.1.2.1, 1.1.1	Sensitive	
<b>S39</b>	ERR12328175	ERR12328551	1.1.1	MDR-TB	Isoniazid <i>fabG1</i> -15C>T; Ethionamide <i>fabG1</i> -15C>T; Rifampicin <i>rpoB</i> His445Tyr
<b>S40</b>	ERR12328174	ERR12328550	1.2.1.2.1	Other	Pyrazinamide <i>pncA</i> Ser104Arg; Ethionamide <i>ethA</i> Thr232Ala
<b>S41</b>	ERR12328173	ERR12328549	1.1.1	Sensitive	
<b>S42</b>	ERR12328172	ERR12328548	2.2.1,1.1. 3.3	HR-TB	Isoniazid <i>katG</i> Ser315Thr
<b>S43</b>	ERR12328171	ERR12328547	1.1.1	Sensitive	
<b>S44</b>	ERR12328170	ERR12328546	1.1.1	HR-TB	Isoniazid <i>fabG1</i> -15C>T; Ethionamide <i>fabG1</i> -15C>T
<b>S46</b>	ERR12328168	ERR12328544	1.1.1	HR-TB	Isoniazid <i>katG</i> Ser315Thr
<b>S47</b>	ERR12328167	ERR12328543	1.2.1.2.1	Sensitive	
<b>S48</b>	ERR12328166	ERR12328542	1.1.1	Sensitive	
<b>S49</b>	ERR12328165	ERR12328541	2.2.1	MDR-TB	Streptomycin <i>rpsL</i> Lys43Arg; Ethambutol <i>embB</i> Met306Leu; Rifampicin <i>rpoB</i> Ser450Leu; Isoniazid <i>katG</i> Ser315Thr
<b>S50</b>	ERR12328164	ERR12328540	2.2.1	HR-TB	Streptomycin <i>rpsL</i> Lys88Arg; Isoniazid <i>katG</i> Ser315Thr
<b>S52</b>	ERR12328163	ERR12328539	1.1.1	Other	Ethambutol <i>embB</i> Arg507Lys
<b>S53</b>	ERR12328162	ERR12328538	4.5	Sensitive	
<b>S54</b>	ERR12328161	ERR12328537	2.2.1.2	Sensitive	
<b>S55</b>	ERR12328160	ERR12328536	2.2.1.1	Sensitive	
<b>S56</b>	ERR12328159	ERR12328535	1.1.1	Sensitive	
<b>S58</b>	ERR12328158	ERR12328534	2.2.1	MDR-TB	Rifampicin <i>rpoB</i> His445Asp; <i>katG</i> Ser315.Thr
<b>S60</b>	ERR12328157	ERR12328533	2.2.1	Sensitive	
<b>S62</b>	ERR12328156	ERR12328532	2.2.1	HR-TB	Isoniazid <i>katG</i> Ser315Thr
<b>S63</b>	ERR12328155	ERR12328531	2.2.1	Other	Streptomycin <i>rrs</i> 514A>C
<b>S64</b>	ERR12328154	ERR12328530	4.2,2.2	Other	Streptomycin <i>rrs</i> 517C>T
<b>S66</b>	ERR12328153	ERR12328529	1.1.1	Sensitive	
<b>S67</b>	ERR12328152	ERR12328528	3	Sensitive	
<b>S68</b>	ERR12328151	ERR12328527	2.2.1	MDR-TB	Rifampicin <i>rpoB</i> His445Tyr; Isoniazid <i>katG</i> Ser315Thr
<b>S69</b>	ERR12328150	ERR12328526	2.2.1	HR-TB	Isoniazid <i>katG</i> 1002_1003dupGA; Streptomycin <i>rpsL</i> Lys43Arg
<b>S70</b>	ERR12328149	ERR12328525	2.2.1	HR-TB	Isoniazid <i>fabG1</i> -15C>T; Ethionamide <i>fabG1</i> -15C>T
<b>S71</b>	ERR12328148	ERR12328524	1.2.1.2.1	Other	Pyrazinamide <i>pncA</i> Ser104Arg; Ethionamide <i>ethA</i> Thr232Ala
<b>S72</b>	ERR12328147	ERR12328523	2.2.1	Sensitive	

\* based on TB-Profiler, and matched identically between ONT and Illumina; \*\* based on TB-Profiler, and drug resistance type and mutations matched identically between platforms; HR-TB Isoniazid drug resistant; MDR-TB multidrug resistant TB; RR-TB rifampicin resistant TB, Fluoroquinolones (FQs): Moxifloxacin, Ofloxacin, Levofloxacin, Ciprofloxacin

**Table S2****Paired isolates (n=59) sequenced using Illumina and Oxford Nanopore Technology (ONT) platforms**

<b>Sample</b>	<b>Platform</b>	<b>Ave. Depth</b>	<b>No. SNPS*</b>	<b>% Mapped</b>	<b>Total Reads</b>
<b>S1</b>	ONT	5.4	1168	99.6%	6572
	Illumina	103.2	1954	98.8%	2963742
<b>S2</b>	ONT	13.5	1934	99.4%	19654
	Illumina	41.4	1944	98.8%	1176138
<b>S4</b>	ONT	9.9	1923	99.6%	17861
	Illumina	109.1	1985	98.8%	3137078
<b>S5</b>	ONT	6.1	985	99.8%	10075
	Illumina	78.3	1345	99.0%	2217701
<b>S8</b>	ONT	22.9	1322	100%	43766
	Illumina	73.2	1273	99.4%	2300179
<b>S11</b>	ONT	38.1	2095	99.2%	65534
	Illumina	100.1	1963	98.7%	2873142
<b>S12</b>	ONT	5.9	921	99.7%	15899
	Illumina	76.1	1376	99.0%	2163404
<b>S13</b>	ONT	9.2	1888	99.6%	17150
	Illumina	98.9	2012	98.8%	2837108
<b>S14</b>	ONT	31.7	548	99.8%	21618
	Illumina	135.5	561	99.6%	3912222
<b>S15</b>	ONT	23.9	1353	96.2%	28957
	Illumina	89.6	1313	98.9%	2561666
<b>S17</b>	ONT	11.7	1990	99.8%	18354
	Illumina	112.9	1952	98.9%	3260628
<b>S19</b>	ONT	15.2	1953	99.8%	22559
	Illumina	74.8	1971	98.8%	2121102
<b>S20</b>	ONT	10.2	1856	99.7%	24968
	Illumina	76.1	1925	98.8%	2164348
<b>S21</b>	ONT	18.1	1304	99.6%	32668
	Illumina	92.2	1316	99.0%	2634471
<b>S22</b>	ONT	10.7	1963	99.7%	9765
	Illumina	121.3	1967	98.8%	3506999
<b>S23</b>	ONT	27.1	2008	99.7%	38927
	Illumina	112.1	1959	98.7%	3227903
<b>S24</b>	ONT	30.4	1356	99.4%	70506
	Illumina	28.0	1296	99.0%	791827
<b>S25</b>	ONT	19.4	1263	92.7%	70402
	Illumina	80.7	1249	94.8%	2430535
<b>S26</b>	ONT	21.1	1321	99.8%	67333
	Illumina	54.1	1318	99.1%	1524118
<b>S27</b>	ONT	17.7	1508	88.9%	50492
	Illumina	53.4	1316	99.1%	1524609
<b>S28</b>	ONT	27.7	1955	99.6%	63762
	Illumina	79.9	1952	98.7%	2267204
<b>S29</b>	ONT	15.8	1947	99.6%	42272

	Illumina	74.5	1943	98.5%	2107027
	ONT	15.1	1927	99.5%	16899
<b>S30</b>	Illumina	105.8	1931	98.6%	3018371
	ONT	14.9	1947	99.6%	19093
<b>S31</b>	Illumina	109.9	1932	98.8%	3153821
	ONT	24.7	1952	99.5%	59494
<b>S32</b>	Illumina	52.6	1955	98.7%	1487658
	ONT	13.9	1991	99.6%	16399
<b>S33</b>	Illumina	110.7	1958	98.8%	3187457
	ONT	16.0	1332	99.8%	28349
<b>S34</b>	Illumina	108.4	1330	98.9%	3076148
	ONT	21.4	1330	99.6%	99886
<b>S35</b>	Illumina	49.6	1313	98.9%	1394378
	ONT	8.0	1713	92.4%	9976
<b>S36</b>	Illumina	139.3	1956	98.6%	4019976
	ONT	19.7	1311	99.7%	89722
<b>S37</b>	Illumina	70.3	1319	99.1%	2002450
	ONT	22.5	1926	99.5%	67398
<b>S38</b>	Illumina	74.4	1919	98.8%	2141460
	ONT	22.9	1958	99.2%	78058
<b>S39</b>	Illumina	84.1	1950	98.6%	2396636
	ONT	17.2	1975	99.5%	24331
<b>S40</b>	Illumina	110.0	1952	98.6%	3138449
	ONT	15.6	2000	99.6%	27693
<b>S41</b>	Illumina	137.5	1976	98.7%	3971276
	ONT	16.8	1328	99.5%	53347
<b>S42</b>	Illumina	25.1	1298	98.9%	707135
	ONT	28.9	1997	99.6%	34487
<b>S43</b>	Illumina	143.5	1972	98.8%	4174158
	ONT	19.4	1922	99.5%	34342
<b>S44</b>	Illumina	91.5	1919	98.7%	2617699
	ONT	21.5	1971	99.6%	31625
<b>S46</b>	Illumina	115.6	1959	98.7%	3309928
	ONT	22.3	1948	99.4%	31052
<b>S47</b>	Illumina	134.6	1958	98.8%	3911533
	ONT	22.1	1947	99.3%	36838
<b>S48</b>	Illumina	111.0	1963	98.7%	3190331
	ONT	13.9	1323	99.7%	52942
<b>S49</b>	Illumina	74.2	1327	99.0%	2108101
	ONT	21.0	1326	99.7%	80478
<b>S50</b>	Illumina	48.7	1338	99.0%	1373152
	ONT	7.3	1625	99.5%	8682
<b>S52</b>	Illumina	131.0	1972	98.6%	3779393
	ONT	6.0	556	99.6%	9726
<b>S53</b>	Illumina	130.5	839	99.0%	3780609
	ONT	13.9	1336	99.6%	27161
<b>S54</b>	Illumina	114.0	1335	98.9%	3268429
<b>S55</b>	ONT	15.6	1287	99.7%	36221

	Illumina	110.9	1309	99.0%	3176478
	ONT	19.1	1961	99.4%	49455
<b>S56</b>	Illumina	128.7	1964	98.9%	3731460
	ONT	7.0	1042	98.4%	24233
<b>S58</b>	Illumina	106.1	1345	98.5%	3029658
	ONT	16.3	1260	99.6%	53081
<b>S60</b>	Illumina	83.3	1269	98.9%	2366676
	ONT	28.0	1294	99.2%	111928
<b>S62</b>	Illumina	60.8	1313	99.0%	1726068
	ONT	14.4	1251	99.6%	20474
<b>S63</b>	Illumina	116.8	1258	98.9%	3344554
	ONT	9.0	1154	99.5%	22348
<b>S64</b>	Illumina	89.3	1328	98.7%	2534586
	ONT	6.6	1513	98.9%	17966
<b>S66</b>	Illumina	33.2	1934	97.9%	1513368
	ONT	21.8	1363	99.7%	46238
<b>S67</b>	Illumina	120.8	1327	99.1%	3475969
	ONT	23.9	1340	99.4%	121132
<b>S68</b>	Illumina	68.6	1367	99.0%	1949008
	ONT	20.3	1302	99.6%	116354
<b>S69</b>	Illumina	39.2	1315	98.9%	1099998
	ONT	12.7	1270	99.7%	34644
<b>S70</b>	Illumina	75.8	1278	98.9%	2140778
	ONT	17.4	1929	99.6%	41764
<b>S71</b>	Illumina	105.5	1945	98.7%	3017563
	ONT	22.0	1295	93.4%	120256
<b>S72</b>	Illumina	47.7	1254	98.8%	1344865

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\* High quality SNPs obtained at an alternate frequency of 0.7

\*\* including low depth SNPs due to entire sample being lower than the cut-off (of 5)

**Table S3**

**Regions of difference (RD) deletions detected using the Oxford Nanopore Technology (ONT) platform**

<b>Sample</b>	<b>Lineage</b>	<b>RD*</b>
S1	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, RD210
S2	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, RD210, <u>RD131e</u>
S4	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, RD131e, DS70
S5	2.2.1	RD105, RD3, RD152, RD715, RD206, MiD1
S8	2.1	RD105, RD715, RD720, RD721, RD152, RD314, N-RD25_tbB, RD131e
S11	1.1.1	RD11 RD715, RD147c, Rdbovis_wbbl2, RD3, RD236, RD239, <u>RD131e</u> , DS70
S12	2.2.1	RD105, RD181, RD311, RD3, RD181, RD311, RD3, RD207, RD715
S13	1.1.3.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD131e, RD5sur
S14	4.8	RD247b, RD715, MID4, RD219
S15	2.2.1	RD105, RD3, RD181, RD715, RD313, RD207, <u>RD131e</u> , RD152
S17	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, RD239
S19	1.1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, RD239
S20	1.2.1.2	RD147c, Rdbovis_wbbl2, RD715, RD239, RD121, <u>RD131e</u>
S21	2.2.1.1	RD105, RD715, RD3, RD150, RD152, RD181, RD311
S22	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD131e, RD3, RD313, RD236a
S23	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD236a, <u>RD131e</u>
S24	2.2.1	RD105, RD715, RD3, RD152, RD181, MiD1
S25	2.2.1	RD105, RD715, RD131e, RD3, RD152, RD181, <u>RD131e</u> , RD207
S26	2.2.1	RD105, RD715, RD3, RD152, RD181, RD311
S27	2.2.1.1	RD105, RD715, RD3, RD150, RD152, RD181, RD311
S28	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, RD210
S29	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, <u>RD131e</u> , RD210
S30	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, <u>RD131e</u>
S31	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, <u>RD131e</u> , RD210
S32	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, <u>RD131e</u> , RD210
S33	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, <u>RD131e</u> , DS70
S34	2.2.1	RD105, RD715, RD152, RD3, RD311, RD181, MiD1
S35	2.2.1	RD105, RD715, RD152, RD3, RD311, RD181, MiD1
S36	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD236a, <u>RD131e</u>
S37	2.2.1	RD105, RD715, RD152, RD3, RD311, RD181, MiD1
S38	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, <u>RD131e</u>
S39	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD313, RD236a, RD131e
S40	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, RD210
S41	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, RD131e, DS70
S42	2.2.1	RD105, RD715, <u>RD3</u> , <u>RD152</u>
S43	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, RD131e
S44	1.1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, <u>RD131e</u>
S46	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, RD236a, DS70, <u>MiD4</u>
S47	1.2.1.2.1	RD147c, Rdbovis_wbbl2, RD715, RD239, RD210
S48	1.1.1	RD715, RD147c, Rdbovis_wbbl2, RD239, RD11, RD3, <u>RD131e</u> , <u>DS70</u>

S49	2.2.1	RD105, RD715, RD3, RD152, RD181, RD311
S50	2.2.1	RD105, RD715, RD3, RD152, RD181, RD311
S52	1.1.1	RD715, RD147c, RDbovis_wbbl2, RD239, RD11, RD3, RD236a
S53	4.5	RD715, RD122, RD147c, RDbovis_wbbl2, RD239
S54	2.2.1.2	RD105, RD715, RD301, RD142, RD3, RD152, RD181, RD311
S55	2.2.1.1	RD105, RD715, RD3, RD150, RD152, RD181, RD311
S56	1.1.1	RD715, RD147c, RDbovis_wbbl2, RD239, RD11, RD3, RD236a, DS70
S58	2.2.1	RD105, RD715, RD3, RD152, RD181, RD311
S60	2.2.1	RD105, RD715, RD181
S62	2.2.1	RD105, RD715, RD3, RD152, RD181, RD311
S63	2.2.1	RD105, RD715, RD3, RD152, RD181, RD131e
S64	2.2.1	RD105, RD715, <u>RD152, RD181</u>
S65	1.1.1	RD715, RD147c, RDbovis_wbbl2, RD239, RD11, RD236a
S66	1.1.1	RD715, RD147c, RDbovis_wbbl2, RD239, RD11, RD236a, DS70
S67	3	RD715, RD152, RD750, RD316, N-RD25_tbA
S68	2.2.1	RD105, RD715, RD181, RD311
S69	2.2.1	RD105, RD715, RD3, RD152, RD181, RD311
S70	2.2.1	RD105, RD715, RD3, RD152, RS311
S71	1.2.1.2.1	RD147c, RDbovis_wbbl2, RD715, RD239, <u>RD131e</u>
S72	2.2.1	RD105, RD715, RD3, RD152, RD181, <u>RD131e</u>

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\* according to RDScan; \*\* underlined if not confirmed by Illumina

**Table S4**  
**Deletion analysis of Structural Variants in *pe/ppe* genes**

<b>Gene (locus)</b>	<b>SV identified</b>	<b>Lineage (n)</b>	<b>Known*</b>
<i>pe_pgrs1</i> (Rv0109)	Truncated	1.1.1 (1/17)	
<i>pe_pgrs2</i> (Rv0124)	Truncated	1.2.1.2.1 (10/10) 1.2.1.2 (1/1)	Deleted in L6 (RD701), truncated in L4.3.3
<i>pe_pgrs3</i> (Rv0278c)	Gene fusion	2 (25/25)	Gene fusion with <i>pe_pgrS4</i> in L2
<i>pe_pgrs4</i> (Rv0279c)	Gene fusion	2 (25/25)	Gene fusion with <i>pe_pgrS3</i> in L2
<i>ppe5</i> (Rv0304c)	Deletions	1.1.1 (2/17), 2.2.1 (1/20)	Truncated in L5/6/ <i>bovis</i> and in sporadic samples
<i>ppe6</i> (Rv0305c)	Small deletion	2.2.1 (2/20)	Deletions in several sub-lineages
<i>ppe8</i> (Rv0355c)	Truncated and Deletion	1 (29/30), 2 (24/25), 4.2 (1/1)	Truncated in some L2, and deletion in some ancient lineages
<i>pe_pgrs6</i> (Rv0532)	Truncated	1.2.1.2.1 (10/10)	Truncated in ancient lineages
<i>pe_pgrs7</i> (Rv0578c)	Deletions	Large (1.1.1 (6/17)) Small (1.2.1.2.1 10/10, 1.2.1.2 1/1)	
<i>pe_pgrs8</i> (Rv0742)	Truncated	1 (30/30)	
<i>pe_pgrs9</i> (Rv0746)	Truncated	End(1 30/30) Beginning(2 25/25)	Truncated in sporadic samples
<i>pe_pgrs10</i> (Rv0747)	Truncated	1.2.1.2.1 (2/10), 2.2.1 (16/20), 2.2.1.1 (3/3), 3 (1/1)	Truncated in L5 and sporadic samples
<i>pe_pgrs13</i> (Rv0833)	Truncated	1.1.1 (2/17), 1.2.1.2.1 (2/10), 2 (17/25), 4.2 (1/1)	Gene fusion with <i>pe_pgrs12</i> in ancient lineages, truncated in some L2 and sporadic samples
<i>pe_pgrs16</i> (Rv0977)	Truncated	1.1.1 (6/17), 1.2.1.2.1 (1/10)	Truncated in L4.1
<i>pe_pgrs19</i> (Rv1067c)	Gene fusion (L1)	1 (30/30)	Gene fusion with <i>pe_pgrs20</i> in L1
<i>pe_pgrs20</i> (Rv1068c)	Gene fusion (L1)	1 (30/30)	Gene fusion with <i>pe_pgrs19</i> in L1
<i>pe_pgrs21</i> (Rv1087)	Missing (L3) Truncated (L2) Large Deletion	1.1.1 (2/17), 1.2.1.2.1 (2/10), 2 (18/25), 3 (1/1), 4 (2/3)	Differences in sequence in L3
<i>pe_pgrs22</i> (Rv1091)	Truncated	1 (30/30)	Truncated in L1.1.3 and L5
<i>pe_pgrs23</i> (Rv1243c)	Large deletion and truncated	Large ( 1.2.1.2.1 10/10 1.2.1.2 1/1) Truncations (2 25/25)	Truncated in L3
<i>pe_pgrs24</i> (Rv1325c)	Large deletion and Truncated	1.1.1 (1/17) 1.1.3.1 (1/1)	
<i>pe_pgrs26</i> (Rv1441c)	Truncated	1.1.1 (7/17), 2.2.1 (2/20), 4 (2/3)	
<i>pe_pgrs27</i> (Rv1450c)	Large deletion and truncated	1.1.1 (1/17), 1.1.3.1 (1/1), 2.2.1 (3/20), 4.5 (1/1)	Truncated in some samples, different sequences



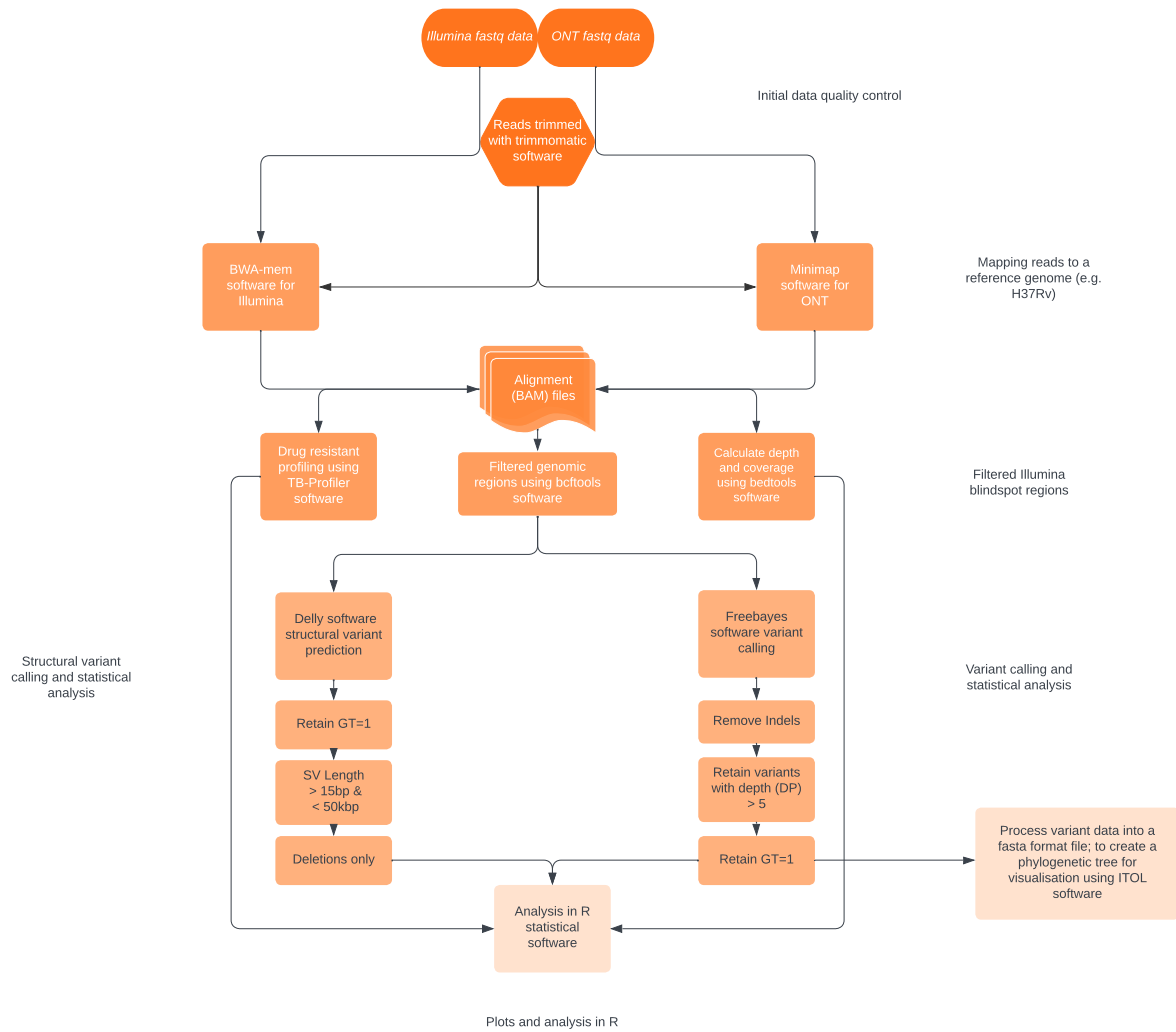
<i>ppe24</i> (Rv1753c)	Truncated	1.1.1 (2/17), 1.1.3.1 (1/1), 2.2.1 (1/20), 3 (1/1), 4.5 (1/1)	
<i>wag22</i> (Rv1759c)	Deletion	2 (25/25), 3 (1/1), 4 (3/3)	Deleted in some samples (RD152)
<i>ppe25</i> (Rv1787)	Truncated	1.2.1.2.1 (1/10)	Deleted in some samples
<i>pe_pgrs33</i> (Rv1818c)	Truncated	1.2.1.2.1 (10/10), 1.2.1.2 (1/1), 3 (1/1), 4 (2/3)	Truncated in L1
<i>ppe34</i> (Rv1917c)	Truncated	1 (25/30), 2.2.1 (2/20), 2.2.1.1 (1/3), 2.2.1.2 (1/1), 3 (1/1), 4 (2/3)	Truncated in most lineages due to IS6110
<i>pe_pgrs35</i> (Rv1983)	Missing	1.1.1.1 (1/1)	Missing in sporadic samples
<i>ppe38</i> (Rv2352c)	Deletion	1.1.3.1 (1/1), 2.2.1 (1/20)	Deletion in L2 (RD185)
<i>ppe39</i> (Rv2353c)	Deletion	1.1.3.1 (1/1), 2.2.1 (1/1)	Deletion of beginning of the gene in most isolates
<i>ppe40</i> (Rv2356c)	Truncated	1.1.3.1 (1/1), 2.1 (1/1), 2.2.1 (1/20)	Truncated in sporadic samples (IS6110)
<i>pe_pgrs45</i> (Rv2615c)	Deletions	Large (2.2.1 (3/20)) Small (2 24/25)	
<i>pe27</i> (Rv2769c)	Deleted	2.2.1.1 (1/3)	
<i>ppe44</i> (Rv2770c)	Deleted	2.2.1.1 (1/3)	
<i>ppe46</i> (Rv3018c)	Deleted	1.1.1 (1/17), 1.1.3.1 (1/1), 1.2.1.2 (1/1), 4.8 (1/1)	Truncated in 4.1.1.3 (IS6110) and in other sporadic samples
<i>pe27a</i> (Rv3018A)	Deleted	1.1.1 (1/17), 1.1.3.1 (1/1), 1.2.1.2 (1/1), 4.8 (1/1)	Deleted in some samples
<i>esxS/pe28</i> (Rv3020c)	Deleted	1.1.1 (1/17), 1.1.3.1 (1/1), 1.2.1.2 (1/1), 2.2.1 (1/20), 4 (2/3)	Deleted in some samples
<i>ppe47</i> (Rv3021c)	Deleted	1.1.1 (1/17), 1.2.1.2 (1/1)	Pseudogene
<i>ppe48</i> (Rv3022c)	Deleted	1.1.1 (1/17), 1.2.1.2 (1/1)	Pseudogene
<i>pe29</i> (Rv3022A)	Deleted	2.2.1 (2/20)	
<i>ppe50</i> (Rv3135)	Deleted	1 30/30	Deletion in L1
<i>ppe52</i> (Rv3144c)	Truncated	1.1.3.1 (1/1)	Truncated in some L3
<i>ppe53</i> (Rv3159c)	Truncated	1.1.1 (17/17), 1.1.1.1 (1/1)	Truncated across most lineages
<i>ppe54</i> (Rv3343c)	Truncated	1.1.1 (1/17), 1.2.1.2.1 (1/10), 2.2.1 (2/20), 3 (1/1)	Truncated in sporadic samples (IS6110/big insertions)
<i>pe_pgrs49</i> (Rv3344c)	Truncated	1.1.1 (4/17), 1.2.1.2.1 (10/10), 2 (23/25), 3 (1/1)	Gene fusion with <i>pe_pgrs50</i> across several lineages
<i>pe_pgrs50</i> (Rv3345c)	Deletion	1 (30/30), 2.1 (1/1), 2.2.1 (6/20)	Truncated in L1 and some L2;

<i>ppe55</i> (Rv3347c)	Large deletion	2.2.1 (1/1)	Truncated in sporadic samples
<i>ppe56</i> (Rv3350c)	Truncated	1.1.1 (5/17)	Truncated in L2 and L6
<i>pe_pgrs52</i> (Rv3388)	Truncated	1.2.1.2 (1/1), 1.2.1.2.1 (8/10), 2.2.1 (1/30)	Truncated in sporadic samples
<i>pe_pgrs53</i> (Rv3507)	Truncated	1 (19/30), 2 (17/25), 4.2 (1/1)	Truncated in L5 and some L2
<i>pe_pgrs54</i> (Rv3508)	Truncated	1 (26/30), 2 (16/25), 4 (2/3)	Truncated in L6, some L3, and sporadic samples
<i>pe_pgrs55</i> (Rv3511)	Gene fusion	1.1.1 (1/17), 1.2.1.2.1 (1/10)	Truncated in L5; gene fusion with <i>pe_pgrs56</i> in some other samples
<i>pe_pgrs56</i> (Rv3512)	Gene fusion	1.1.1 (1/17), 1.2.1.2.1 (1/10)	Gene fusion with <i>pe_pgrs55</i> in some samples
<i>pe_pgrs57</i> (Rv3514)	Truncated	1.1.1 (11/17), 1.2.1.2 (1/1), 1.2.1.2.1 (5/10), 2.2.1 (1/1), 4.5 (1/1)	Truncated in L6, most of L2, and in sporadic samples
<i>ppe66</i> (Rv3738c)	Deletion	2.1 (1/1) 3 (1/1)	Deleted in L3
<i>ppe67</i> (Rv3739c)	Truncated	3 (1/1)	Truncated in L3

\* found in Gómez-González et al. [12]

Figure S1

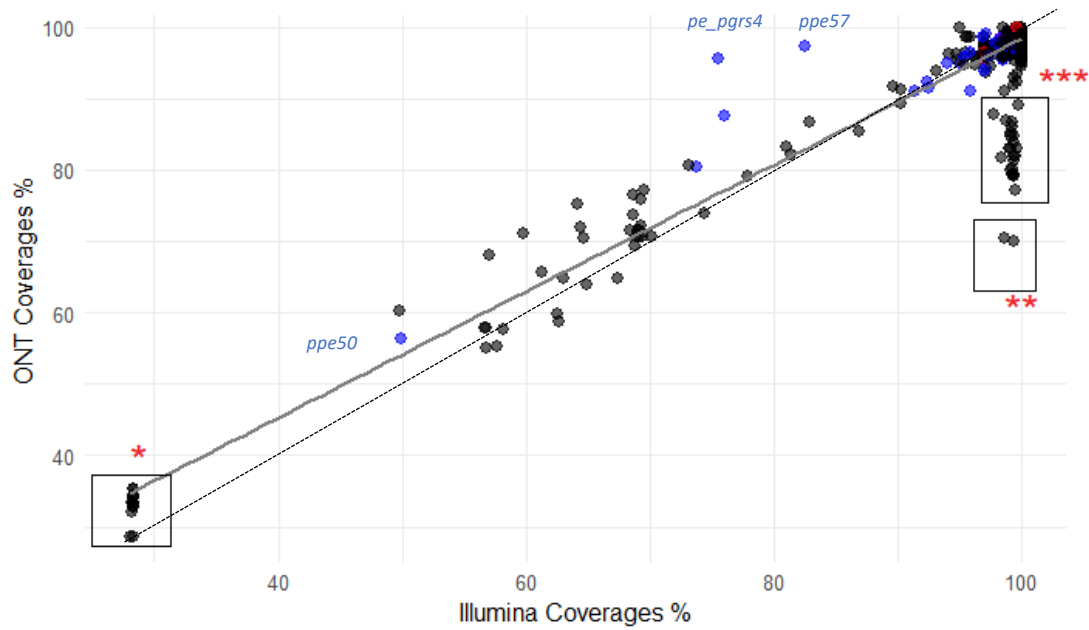
Whole genome analysis pipeline



ONT = Oxford Nanopore Technology; DP = read depth parameter; GT = genotype parameter; indels = insertions and deletions; SV = structural variant

Figure S2

Comparison of average percentage coverage of genes between Illumina and Oxford Nanopore Technology (ONT) platforms, coloured by drug resistance (red), *pe/ppe* (blue) or other (black) gene category.



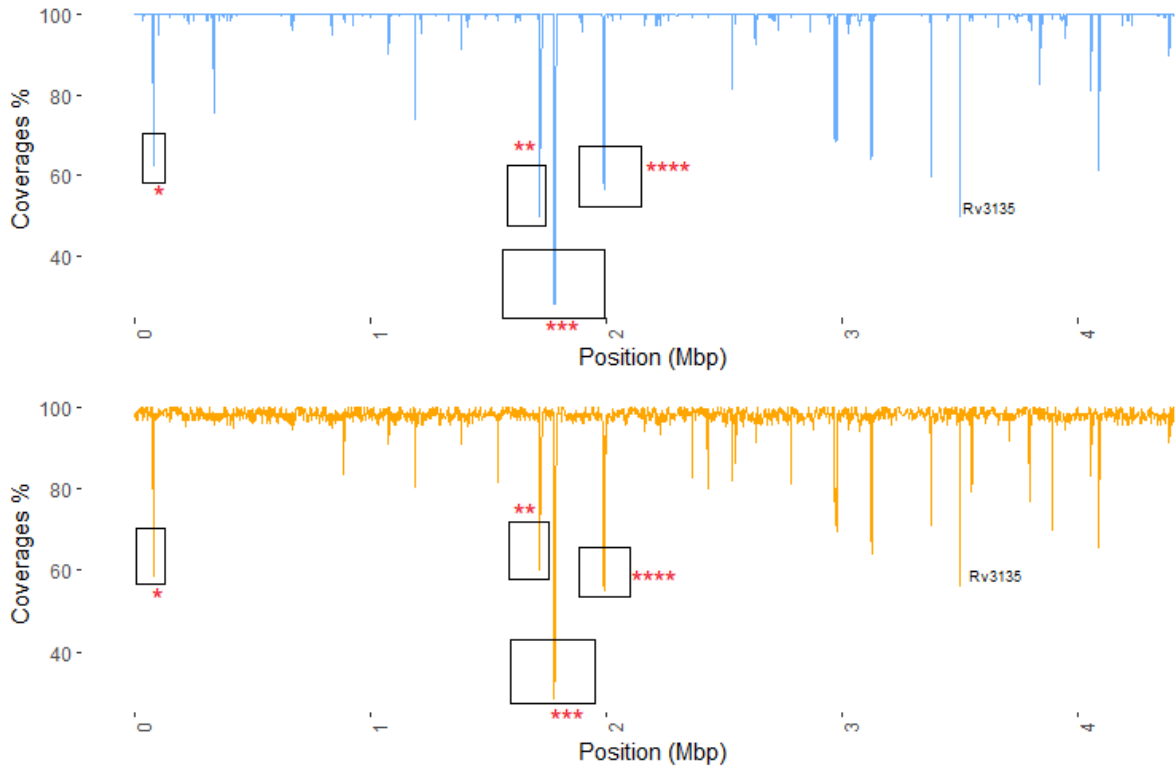
\* Genes within the region *Rv1573* to *Rv1586* (includes deletion RD3 linked to lineage 2)

\*\* Genes *Rv3474* and *Rv3475*

\*\*\* Genes *Rv0795*, *Rv0796*, *Rv1369c*, *Rv1370c*, *Rv1765*, *Rv2105*, *Rv2167*, *Rv2168c*, *Rv2479c*, *Rv2648*, *Rv2649*, *Rv3184*, *Rv3185*, *Rv3187*, *Rv3380*, and *Rv3381*

**Figure S3**

**Average coverage in genes across all 59 *M. tuberculosis* isolates for Illumina (top) and Oxford Nanopore Technology (bottom) platforms. Low coverage areas coincide with lineage-specific regions of difference (large deletions)**



\* Rv0072 and Rv0073, \*\* Rv1524 and Rv1525, \*\*\* Rv1573-Rv1586, \*\*\*\* Rv1758-Rv1762c