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"It's more than them just using the box" The feasibility of using medication monitors and a differentiated care approach to improve TB treatment adherence in South Africa

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2
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4 2 monitors and a differentiated care approach to improve TB treatment adherence in South
5 3 Africa
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2
3 37 **ABSTRACT**
4

5 38 **Objectives**
6

7 39 The TB MATE study evaluated whether a differentiated care approach (DCA) based on
8 40 tablet-taking data from Wisepill evriMED digital adherence technology could improve
9 41 tuberculosis treatment adherence. The DCA entailed a stepwise increase in adherence
10 42 support starting from short message service (SMS) to phone calls, followed by home visits
11 43 and motivational counselling. We explored feasibility of this approach with providers in
12 44 implementing clinics.
13

14 45 **Design**
15

16 46 Between June 2020 to February 2021, In-depth interviews were conducted in the provider's
17 47 preferred language, audio recorded, transcribed verbatim and translated. The interview
18 48 guide included three categories: feasibility, system-level challenges and sustainability of the
19 49 intervention. We assessed saturation and used thematic analysis.
20

21 50 **Setting**
22

23 51 Primary healthcare clinics in three provinces of South Africa.
24

25 52 **Participants**
26

27 53 We conducted 25 interviews with 18 staff and seven stakeholders.
28

29 54 **Results**
30

31 55 Three major themes emerged: Firstly, providers were supportive of the intervention being
32 56 integrated into the TB programme and were eager to be trained on the device as it helped to
33 57 monitor treatment adherence. Secondly, there were challenges in the adoption system such
34 58 as shortage of human resources which could serve as a barrier to information provision once
35 59 the intervention is scaled-up. Health care workers reported that some patients received
36 60 incorrect SMS's due to delays in the system that contributed to distrust. Thirdly, DCA was
37 61 considered as a key aspect of the intervention by some staff and stakeholders since it
38 62 allowed for support based on individual needs.
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63 **Conclusions**

64 It was feasible to monitor tuberculosis treatment adherence using the evriMED device and
65 DCA. To ensure successful scale-up of the adherence support system, emphasis will need
66 to be placed on ensuring that the device and the network operate optimally and continued
67 support on adhering to treatment which will enable people with TB to take ownership of their
68 treatment journey and help overcome TB related stigma.

70 **Strengths and limitations of this study**

- 71 • We conducted the study in three provinces with different health service characteristics,
72 TB epidemiology and population characteristics which allowed us to understand
73 feasibility of implementation from a broader perspective.
- 74 • Another strength was that the study was done in a routine setting with limited resources
75 and without the use of incentives to providers to increase uptake.
- 76 • One limitation is that some of the interviews were conducted by a member of the study
77 management team, although this was limited to senior stakeholders who were unlikely to
78 feel reluctant to freely express their views and to withhold some of their opinions.

80 **Key messages**

81 **What is already known on this topic**

82 Both globally and in South Africa, there is limited information on the value of Digital
83 Adherence Technologies (DATs) in TB treatment.

84 **What this study adds**

85 Knowledge on the feasibility of using DAT to monitor TB treatment adherence while using a
86 differentiated care approach (DCA) as adherence support for people with TB (PWTB) in
87 South Africa.

88 **How this study might affect research, practice or policy**

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2
3 89 This research shows that technology on its own will not solve treatment adherence issues
4
5 90 especially those related to stigma and lack of support. Sound communication between
6
7 91 PWTB and providers serves as a key tool to improving treatment outcomes.
8
9
10 92

93 **INTRODUCTION**

94 Globally the treatment success rate for new and relapse drug-sensitive TB (DS-TB), is 86%
95 while in South Africa (SA) this is much lower at 79%, 78% for those who are HIV positive
96 with TB and 67% for those previously treated with TB(1). Treatment failure is often a result of
97 non-adherence to treatment, loss to follow-up or unevaluated outcomes(2). Typical reasons
98 that people with TB (PWTB) might not adhere to treatment include false perceptions of being
99 cured once they feel better; stigma; forgetfulness; lack of social network support; and poor
100 user experience of accessing care at clinics(3). Traditional methods such as Directly
101 Observed Treatment Short course (DOTs), pill counts and self-report have limitations and
102 have not been shown to improve treatment adherence in PWTB(4),(5). Digital adherence
103 technology (DAT) including medication monitors may overcome challenges to monitoring
104 tuberculosis treatment adherence through remotely documenting dosing patterns of PWTB.
105 DATs have been recommended by the World Health Organization (WHO) based on
106 evidence from a study in China where drug-sensitive TB patients received an electronic
107 medication monitor to support self-administered treatment for TB(6).

108
109 Despite this recommendation, both globally and in South Africa, there is limited information
110 on the value of DATs in TB treatment. A study done in KwaZulu-Natal SA amongst drug
111 resistant TB-HIV co-infected inpatients using an older version of the Wisepill device, the
112 RT2000 3G, showed that feasibility challenges for digital pillboxes may include battery
113 failure, device malfunction and problems related to cellular networks(7). Previous studies
114 have found that other DAT such as SMS reminders for TB treatment were insufficient to
115 improve treatment adherence alone. Barriers included frequent changing of phone numbers

1
2
3 116 and uncertainty whether patients were taking their tablets immediately after they received
4
5 117 the SMS or not(8). Another study done in Uganda for HIV treatment showed that challenges
6
7 118 for cellphone-based strategies included: use of shared cell phones, technical failures
8
9 119 preventing receipt of SMS texts, electricity outages and changing phone numbers(9, 10).
10
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12 120

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14 121 Most DATs have focused on monitoring adherence and few studies have used DATs to
15
16 122 differentiate between those patients who are struggling and need individual support, and
17
18 123 those who are doing well. Given this gap in knowledge, we evaluated the feasibility of using
19
20 124 the Wisepill evriMED DAT to monitor TB treatment adherence while using a differentiated
21
22 125 care approach (DCA) with a stepwise increase in adherence support for PWTB in South
23
24 126 Africa.

127 **METHODS**

128 **Study design and study setting**

129 This qualitative study was embedded within a cluster-randomized trial (CRT) that took place
130
131 in six clinics in each of three provinces of South Africa: Gauteng (Ekurhuleni district);
132
133 Western Cape (Klipfontein and Mitchell's Plain districts); and Kwa-Zulu Natal (eThekweni
134
135 district), the details of which have been published elsewhere(11). In the intervention arm of
136
137 the CRT, PWTB received medication monitors with reminders triggering differentiated care
138
139 approach (DCA) in response to adherence data uploads, carried out from a central
140
141 database(11). The DCA was implemented in a progressive manner depending on the
142
143 number of doses a participant missed(11). If one dose was missed, then a short message
144
145 service (SMS) reminder was sent to the participant(11). If a second or third dose was
146
147 missed, then study staff would make a telephone call to the participant and once the fourth
148
149 dose was missed then a home visit was conducted during which motivational counselling
150
151 took place(11). We describe the *feasibility* of implementing Wisepill evriMED device and
152
153 differentiated care from a stakeholder perspective.
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156
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160

143 **Site selection**

144 There were a total of nine intervention clinics, three in each province. Clinics were selected
145 based location, HIV prevalence and numbers of patients starting TB treatment per
146 month(11).

148 **Study population**

149 The study population consisted of seven purposively selected stakeholders from the
150 Department of Health (DOH): one national, one provincial and five district-level
151 representatives, who worked closely with the facilities using the electronic device (Wisepill
152 evriMED DAT). From each intervention facility, we interviewed one facility staff (government
153 employee) and one study staff member. All study staff worked on the project for at least
154 three months. Facility staff-initiated patients on TB treatment and monitored patients for their
155 scheduled monthly follow-up visits while study staff offered PWTB the device, followed-up on
156 those who had missed doses and provided motivational and adherence counselling.

158 **Patient and public involvement**

159 Patients or the public were not involved in the design, or conduct, or reporting, or
160 dissemination plans of our research.

162 **Conceptual framework and themes explored**

163 Using the feasibility framework suggested by Bowen et al(12), we developed an in depth
164 interview guide that covered the following topics; (i) the relative ease of implementation and
165 operation of the technology within existing health systems, technology infrastructure and
166 supply chain; (ii) system level challenges of delivering, sustaining and integrating the
167 intervention into the existing TB programme. We used the framework on the 'Integration and
168 sustainability of interventions into health systems'(13) to organize the data.

170 **Data collection**

171 We conducted a total of 25 in-depth interviews. The sample was representative of providers
172 involved in the intervention while also considering saturation where themes usually start to
173 converge after 15 interviews. The IDI guide was piloted with one stakeholder, two facility and
174 one study staff between January to February 2020. The probing questions were adapted
175 after the pilot. These interviews were conducted face-to-face, and the data was included in
176 the analysis. Data collection continued between June 2020 to January 2021 with each
177 interview lasting between 45 – 90 minutes. The interviews were all conducted in the
178 providers preferred language by a female PhD student (RM) and a female study coordinator
179 who was a PhD student with qualitative experience (VM). Both researchers established a
180 prior relationship with the providers enabling them to understand the reasons for the study.
181 The interviews were digitally recorded with the providers consent and transcribed verbatim
182 by trained research assistants (Masters students). The transcripts were not returned to the
183 providers for comment or correction. Due to the impact of COVID-19 and the national
184 lockdown that took place, these interviews were conducted virtually over Microsoft Teams.
185 No one else was present in the interviews besides the providers and the researchers and
186 field notes were made during the interviews. Saturation was assessed during data collection
187 through asking the same question in different ways and reviewing a sample of the recordings
188 until no new information was obtainable. No repeat interviews were carried out.

189

190 **Data analysis**

191 Thematic analysis was used with deductive and inductive approaches(14, 15). At least 10%
192 of the transcripts were coded inductively by two independent researchers so as to reduce
193 bias and improve reliability(14). A codebook of emerging themes was developed, guided by
194 the framework on the 'Integration and sustainability of interventions into health systems'
195 (13),with discrepancies being resolved through discussion. Where there was no inter-rater
196 agreement, the theme was dropped(14). The final codebook was used to code the remaining
197 transcripts and any new codes that emerged were also included in this codebook. MAXQDA

1
2
3 198 qualitative software was used for the coding process. We highlight the major themes and
4
5 199 soft themes that emerged and use supportive direct quotations from providers. Providers did
6
7 200 not provide feedback on the findings.
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9

10 201 **RESULTS**

11
12 202 We conducted 25 interviews in total with 18 staff (9 facility staff and 9 study staff) and 7
13
14 203 stakeholders (1 national, 1 provincial and 5 at district-level) across 3 provinces. Majority of
15
16 204 the providers (23 out of 25) were female. None of the approached providers declined to
17
18 205 participate. Major themes included (1) Providers were supportive of the intervention, (2)
19
20 206 Intervention challenges within the adoption system and broad context, and (3) Ensuring
21
22 207 intervention sustainability through constant training of staff and education of PWTB
23
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27 209 **Main Theme 1: Providers were supportive of the intervention**

28
29 210 There was buy-in from staff who felt involved and were supportive of the intervention.
30
31 211 Stakeholders were also very supportive of the intervention despite their limited involvement.
32
33

34 212

35
36 213 *“... to me it was a very good idea and it was working very well ... it improved our cure*
37
38 214 *rate because we had a lot of patients who were defaulting and who and to be*
39
40 215 *referred to the hospital because they developed multi, MDR. So since we had ...this*
41
42 216 *intervention, at least we had less patients who developed multi-drug resistance.”*
43

44 217 *- Female, facility staff*
45
46

47 218

48 219 *“...I think...it's magnificent. I think it's... a tool box, it's really a way for us to see*
49
50 220 *what's really happening at the point of ... TB treatment, where the patient take... the*
51
52 221 *medication when they open the box. So I think it's really innovation that can be used.*
53
54 222 *... I think it also is a reminder for the patient. You know? That ... “I need to take my*
55
56 223 *medication”. And it's a way to ...to ensure the quality of the programme, that patients*
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3 224 *are adhering to the ... medication...I think it is a critical intervention.” – Female, DOH*
4
5 225 *stakeholder (District level)*
6

7 226

9 227 Both facility and study staff found the device easy to learn and facility staff who had received
10
11 228 a briefing on the study were eager to receive the complete training to support the study staff.
12

13 229

15 230 *“Because sometimes she (referring to study staff) [might not be here and it happens*
16
17 231 *that she’s not here, either she is sick or she’s gone on holiday for December. She*
18
19 232 *says: “...we can show you and then you do this things when we are not here”. I said:*
20
21 233 *“... it will be easy... As long as you show us, we can do that device”.*
22
23

24 234 *- Female, facility staff*
25

26 235

28 236 The staff described the activities of the intervention such as issuing devices, phone calls and
29
30 237 making home visits as being well integrated into the TB programme. Providers had strong
31
32 238 support for the device for two main reasons that we classified as sub-themes in our analysis:
33

34 239

37 240 **Sub-theme 1: Device as a useful reminder and early notification tool**

39 241 Most providers found the alarm that was fitted on the device to be a useful reminder to
40
41 242 patients to take their treatment on time and to attend their clinic visits. The device also
42
43 243 alerted providers to PWTB who were not using the device and not taking treatment.
44

45 244

47 245 *“I feel like it assists with the real time monitoring because now if you check on the*
48
49 246 *system, you would be able to check instead of waiting like someone waiting for their*
50
51 247 *appointment that is months after, you can actually check now on the system that this*
52
53 248 *person there’s no activity, let me call and you would actually find that the person has*
54
55 249 *died or maybe the person has- is in hospital is admitted..”- Female, study staff*
56

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3 251 *“So, it will help us because ...sometimes we notice the other patient...didn’t take their*
4
5 252 *medication and start to recall all of them and then the other just default ... With the*
6
7 253 *box, someone is getting ... a notification that this person is not taking her*
8
9 254 *treatment...” – Female, facility staff*
10

11 255

12
13
14 256 However, some staff distrusted that opening of the device meant that PWTB took their pills.

15 257

16
17
18 258 *“...some patients do that when they open the pill box and ... show an adherence of*
19
20 259 *100%, but still they... have not been taking their medications. So we would try to*
21
22 260 *motivate them, counsel them, explain the disadvantages of not of them not taking the*
23
24 261 *medication.” – Female, study staff*
25

26 262

27
28 263 *“I think because you know patients always find a way to find loopholes within the*
29
30 264 *health system, so at some point they will understand that you’re recording the*
31
32 265 *opening and the closing of the box not necessarily them actively taking the*
33
34 266 *medications. So they can easily open and close the box without really taking the*
35
36 267 *medication.” – Female, DOH stakeholder (District level)*
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39 268

40 41 269 **Sub-theme 2: Differentiated Care Approach allows for patient-centred care**

42
43 270 Staff mentioned that they found DCA to be a positive and unique aspect of our intervention.

44 271

45
46
47 272 *“So, you are no longer administering intervention for one. You sort of trying to be*
48
49 273 *specific ...to a person and offer them care in their in their specific sort of situations.*
50
51 274 *So, I think that is a positive thing because you don’t assume everyone is the same.*
52
53 275 *You don’t assume everyone’s situation is the same. You understand that you are*
54
55 276 *dealing with ... individuals. That’s ... what I think is positive about this differentiated*
56
57 277 *model of care.” – Male, study staff*
58
59

60 278

1
2
3 279 *“... yah, I think I think the differentiated model of care ... is a very positive thing, that*
4
5 280 *it works to an extent because it’s not a blanket approach. You don’t, you don’t think*
6
7 281 *of every patient as the same...you sort of attend to each person in their context and*
8
9 282 *... try to understand what they are going through.” – Male, study staff*
10
11
12 283

13 284 The staff also felt that the counselling they provided as part of the DCA helped them to
14
15 285 understand their patients’ reasons for not taking their treatment thus allowing them to
16
17 286 manage them better as they supported them on their treatment journey.
18
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20 287

21
22 288 *“This whole approach I feel like it’s a great initiative because it assists in managing*
23
24 289 *the patient - like fully. Like if I can say wholly, not just managing the patient, taking*
25
26 290 *the medication. You could also like... with the counselling you actually find that the*
27
28 291 *problem is that the participant is facing beyond treatment intake.”- Female, study staff*
29
30 292

31
32 293 Phone calls to PWTB allowed for clarification on any issues that may not have been clear to
33
34 294 the patient while at the clinic.
35
36 295

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38
39 296 *“...he didn’t understand but when I called him and I was speaking to him over the*
40
41 297 *phone to understand how they’re taking the treatment, I find that ... yeah there was*
42
43 298 *mistake ... one of the best things about this intervention because some of them are*
44
45 299 *able to even call me up, I don’t always now have to call patients.”*
46

47 300 *– Male, study staff*
48
49 301

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51 302 Home visits allowed the staff to have better interaction with their patients and to build trust
52
53 303 with them making them feel like someone cares about them.
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2
3 305 *"It's not bad. It's nice to do home visits. It's whereby ... you contact with the patients,*
4
5 306 *know each other ... where the patient has got the problem, it's with the ... problem*
6
7 307 *with the box or she wanted to ask me something that she forget to ask at the clinic."*

8
9 308 *– Female, study staff*
10

11 309
12
13 310 *"... I think the participant at least get that thing when you do home visits, or you*
14
15 311 *phone them when they are not taking the treatment they feel as if they are cared of,*
16
17 312 *someone is care is cared for me when I am not taking the treatment because I would*
18
19 313 *get a call, or I will get a home visit"- Female, study staff*
20

21 314
22
23
24 315 Some providers described DCA as more of a journey of supporting the patients and helping
25
26 316 build trust between the staff and the PWTB.
27

28 317
29
30 318 *"... that is really good part of the intervention. I think it ... continue to build that*
31
32 319 *trust...And that support for the patients ... so I- I think that was impressive."*

33
34 320 *- Female, DOH stakeholder (District level)*
35

36 321
37
38
39 322 *"I thought it was only about the box... it's more than them just using the box. It's their*
40
41 323 *treatment journey and being supported to adhere to the treatment and get healed*
42
43 324 *from the TB." – Female, study staff*
44

45 325
46
47 326 **Major Theme 2: Intervention challenges within the adoption system and broad context**

48
49 327 Some staff felt that the trust they built with the PWTB could be threatened by human
50
51 328 resource shortages and a dedicated cadre was needed to ensure successful
52
53 329 implementation.
54

55
56 330 *"However, when we find at once the research study stop and we over onto*
57
58 331 *implementation, ... the constraints is always HR resources and at the operational*
59
60 332 *level, if that initial education isn't framed correctly. There could be a*

1
2
3 333 *misunderstanding about the purpose of the box.” - Female, DOH stakeholder (District*
4
5 334 *level)*

6
7 335
8
9 336 Challenges that were encountered with the device or the network resulted in delays in the
10
11 337 system updating that the box was opened which staff felt created trust issues between them
12
13 338 and the participant.
14

15 339
16
17 340 *“Now it’s creating a trust issue between you and the patient, because you phoning*
18
19 341 *regarding treatment that was not taken because ... Wisepill says treatment was not*
20
21 342 *taken, while the patient on the other side did take the medication.” - Female, study*
22
23 343 *staff*

24 344
25
26 345 Health care workers reported that some patients received incorrect SMS’s due to delays in
27
28 346 the system.

29
30 347 *“ Especially when it has been a weekend and then they will not ... send out the data*
31
32 348 *of... the weekend like ... if there were any missed or any ... intakes. Sometimes they*
33
34 349 *will show that they missed the weekend and they did not take the medication, but in*
35
36 350 *three days down the line... the correct information will show. That’s where we will see*
37
38 351 *that there were no missed doses.”- Female, study staff*

39 352
40
41 353 Staff also felt that that the device would not work for some group of patients such as those
42
43 354 who abuse substances.
44

45 355
46
47 356 *“The patient that are on substance abuse, yoh! You know, when they come here,*
48
49 357 *they are ok. At a later stage, once they’ve started treatment, you realise that this*
50
51 358 *patient is using substances...With those patients, they the device- ya. It’s not good.*
52
53 359 *Won’t- won’t work. Won’t- won’t help.” – Female, facility staff*

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60 360

1
2
3 361 *“He took the evriMED box device and the TB meds. That was the last time we saw*
4
5 362 *him on the clinic. He run away from home apparently. He was on drugs. But*
6
7 363 *then...he is back. He’s here in the TB room. He’s got TB again. So I was asking him*
8
9 364 *the other day: “are you still interested in joining this study?”. And he was like: “you*
10
11 365 *know what I did with the first box? I sold it”. - Female, study staff*

12 366

16 367 **Sub-theme 3: Provider perceptions of stigma related to use of the evriMED device and**

18 368 **DCA**

20 369 Staff perceived that some of the features of the box such as the alarm and the size of the
21
22 370 box may have been a concern to some PWTB in trying to conceal their TB status so they
23
24 371 would opt to leave their devices behind when travelling on holiday or going to work for fear of
25
26 372 disclosure of their TB status.

27 373

31 374 *“The thing that is common, especially in December ... an example is person*
32
33 375 *supposed to take it at 8, they take it at 8 but they not taking it at 8 from the box... I*
34
35 376 *think they went for holidays ... This person is taking treatment and the putting it... in*
36
37 377 *a purse. Whereby you’ll take in the morning without this alarm ringing.”- Male, study*
38
39 378 *staff*

40 379

44 380 *“So some will come to us and say: “what if the pill box doesn’t make so much noise?*
45
46 381 *It will be easier for me to carry around- or if it was a bit ... smaller, then it will be*
47
48 382 *easier for me to carry it. But now it’s big, I don’t want ... people seeing me like with*
49
50 383 *this pill box in the taxi or at work.”- Female, study staff*

51 384

54 385 *“I haven’t disclosed to my partner that I’m on TB medication and imagine if I had to*
55
56 386 *carry this box and the box would be ringing in the morning and it would cause*
57
58 387 *unnecessary fights.” - Female, study staff.*

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4
5 389 Providers perceived that stigma was more of an issue outside the PWTB household as often
6
7 390 they would not disclose their TB status to members outside their homes.

9 391

10
11 392 *“So, I noticed that it’s comfortable for them to use this box when they are at home*
12
13 393 *with the people that actually know what is going on with them but when they are*
14
15 394 *going to other people that are not aware that they are sick or anything, it seems as if*
16
17 395 *they don’t want to carry the boxes.” - Female, study staff.*

19 396

20
21
22 397 Staff perceived that stigma related to DCA existed in the community and some of them
23
24 398 witnessed the PWTB fear of being stigmatized when conducting home visits. PWTB would
25
26 399 often ask staff not to wear their uniforms when they visit their homes.

28 400

29
30 401 *“Uhm they hate it when we wear our TB MATE t-shirts, because they are saying:*
31
32 402 *“due to stigma”. When we go visit their homes, we must not wear something that will*
33
34 403 *be written ‘TB’ or ‘HIV’. So we wear our normal clothes...”- Female, study staff.*

36 404

37
38
39 405 *“Then I took off my jacket, and then the participant saw that TB MATE on my t-shirt.*
40
41 406 *And then the patient told me that I must wear my jacket because what if someone*
42
43 407 *walks in and sees the TB MATE on my t-shirt. So I wasn’t aware that the participant*
44
45 408 *didn’t disclose... She told me that she’s got fear that- because she will be judged*
46
47 409 *because she was drinking alcohol a lot. But now she’s got TB. They will say she must*
48
49 410 *go and stay in the back room.”- Female, study staff*

51 411

52
53
54 412 Staff perceived that some stigma could have been internalised and not actually experienced
55
56 413 by PWTB.

57
58
59
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1
2
3 414 *"It's their thoughts because the person would feel like it did not want to be seen*
4
5 415 *carrying the box. Because people will think- so he sees all their thoughts. It's not*
6
7 416 *something that really happened."- Female, facility staff*
8

9 417
10
11 418 *"But in the clinic, there wasn't really anything that contributed to the stigma but*
12
13 419 *maybe with now giving the pill box... some of the patients would say that maybe it's*
14
15 420 *gonna show. Maybe with their ARV's they could take it in private. Now we have them*
16
17 421 *having this pill box that is gonna ring even, that is gonna beep and remind them to*
18
19 422 *take treatment..." – Female, study staff*
20
21

22 423

23
24 424 **Major Theme 3: Ensuring intervention sustainability through constant training of staff**
25
26 425 **and education of PWTB**

27
28 426 Education on the intervention emerged as one of the major themes that stakeholders and
29
30 427 staff placed emphasis on as a means of managing their patients in a holistic way leading to
31
32 428 successful treatment outcomes. Education and training should emphasize the importance of
33
34 429 adhering to treatment and should be strengthened at various levels – with the PWTB
35
36 430 themselves, those who would be involved in implementation such as community health
37
38 431 workers (CHWs) and also to the community at large.
39
40

41 432

42
43 433 *"My experience was that as the community we need to need to educate the*
44
45 434 *community the importance of complying to medication...we need to educate and*
46
47 435 *educate and educate."- Female, facility staff*
48

49 436

50
51 437 *"But I definitely think it's... strengthening that interface between the patient and the*
52
53 438 *staff... it's an important interface. And- and of course that too- the 'how' of- of the*
54
55 439 *contact, if it is about 'why you didn't- why you aren't taking your treatment' rather than*
56
57 440 *saying 'how are you doing'- you know- 'are you ok', uhm 'how can I help you'. When*
58
59 441 *we start off with those different conversations, it can lead to different outcomes."*
60

1
2
3 442 – *Female, DOH stakeholder (District level)*
4
5 443

6
7 444 The staff felt that constant education and reinforcement would ultimately lead to behaviour
8
9 445 change and treatment adherence.
10

11 446

12
13 447 *“I think the intervention even though we are the one offering the intervention but we*
14
15 448 *sort of gave patients the power to understand the... reasons why they are taking*
16
17 449 *treatment, why is it important for them to...adhere to the treatment...we were actually*
18
19 450 *able to make patients to take their treatment journey into their own hands ... it’s*
20
21 451 *almost like we were empowering patients...”- Male, study staff*
22
23

24 452

25
26
27 453 **DISCUSSION**

28
29 454 Using the Wisepill evriMED device to support adherence to TB treatment appears to be a
30
31 455 feasible option in South Africa. Providers were supportive of the evriMED device and the
32
33 456 differentiated care approach, as they felt it had a positive impact on the TB patient’s
34
35 457 programme. Stakeholders were supportive despite their involvement being limited to
36
37 458 approval of the study and providing oversight of the TB programme.
38
39

40 459

41
42 460 This study has shown that DATs is an innovative approach that might improve the
43
44 461 management of PWTB by allowing individual differentiated support. Early notification of
45
46 462 missed doses from the device allowed staff to intervene through SMS messaging and phone
47
48 463 calls, thus reducing the need for a home visit. This freed up time for staff to focus on other
49
50 464 duties. These findings are similar to other studies where differentiated care models used in
51
52 465 HIV treatment delivery have addressed challenges such as overcrowded facilities,
53
54 466 overburdened staff and long waiting times in countries like Uganda, Swaziland, Mozambique
55
56 467 and South Africa(6, 16-18).
57
58

59 468
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1
2
3 469 Staff noted that the differentiated care allowed a journey of educating and supporting PWTB.
4
5 470 Through adherence and motivational counselling, staff empowered patients to understand
6
7 471 the importance of adhering to treatment and to empower them to take their treatment journey
8
9 472 into their own hands. For scale-up, the real time monitoring feature of the device is important
10
11 473 so that the correct individuals are promptly identified for further support before they become
12
13 474 lost to follow-up. This also allows for the efficient utilisation of resources to those in most
14
15 475 need, as seen in various studies(4, 19, 20). More attention should also be given to
16
17 476 relationship training as the sustainability of the intervention depends on a sound provider-
18
19 477 patient relationship. Correct framing of the intervention as a support tool would also help
20
21 478 ensure that the intervention is well perceived once scaled-up. Training needs to be constant
22
23 479 and not once-off to reinforce their understanding of the intervention.
24
25
26 480

27
28 481 Some challenges with the technology were cited such as alarm malfunction, incorrectly sent
29
30 482 SMS's and short battery lifespan. These challenges created distrust from PWTB, and the
31
32 483 device would therefore need to be of the highest quality to ensure sustainability of the
33
34 484 intervention. A systematic review of DAT for the management of tuberculosis therapy found
35
36 485 similar feasibility challenges remain in low- and middle-income settings(9).Once the
37
38 486 intervention is scaled up, the shortage of human resources (HR) could serve as a barrier to
39
40 487 ensuring that providers receive the correct information. For successful scale-up, some staff
41
42 488 recommended that a dedicated cadre should be in place to follow-up PWTB to ensure that
43
44 489 they understand the importance of taking treatment. However, since the support system had
45
46 490 reduced the need for home visits and follow up calls, the current TB cadres, clerical staff and
47
48 491 community-based teams were also seen as being sufficient. Despite any challenges
49
50 492 experienced within the adoption system and broad context, the staff were all very supportive
51
52 493 of the intervention and even recommended that it should be used for all TB and chronic
53
54 494 patients as well as in other facilities.
55
56
57
58 495

1
2
3 496 Fear of stigma and the disclosure of one's TB status has the potential to act as a barrier to
4
5 497 scale-up and sustainability of the intervention, if not well addressed. Stigma and fear of
6
7 498 disclosure resulting in lower acceptance of DAT technologies amongst multi-drug resistant
8
9 499 TB patients have also been reported in India(21), with improvements recommended on the
10
11 500 design. Disease-related stigma may be more difficult to address, and screening should be
12
13 501 used to identify upfront those patients whom stigma and fear of disclosure may limit the use
14
15 502 of the MERM(21).
16
17
18 503

19
20 504 A limitation of the study was that interviews had to be conducted virtually on Microsoft
21
22 505 teams, due to the Covid-19 pandemic, and to allow for effective social distancing for both the
23
24 506 researchers and the study providers. This new mode of conducting interviews had setbacks
25
26 507 such as network and connectivity challenges which interrupted the flow of some of the
27
28 508 interviews. The interviewers mitigated this challenge through re-iterating what the participant
29
30 509 had said to ensure that the correct message had been captured. Through the consenting
31
32 510 process, we were able to ensure confidentiality and that the participant was relaxed. A
33
34 511 second limitation is that some of the interviews were conducted by a member of the study
35
36 512 management team, although this was limited to senior stakeholders who were unlikely to feel
37
38 513 reluctant to freely express their views and to withhold some of their opinions. We conducted
39
40 514 the study in three provinces with different health service characteristics, TB epidemiology
41
42 515 and population characteristics which allowed us to understand feasibility of implementation
43
44 516 from a broader perspective. Another strength was that the study was done in a routine
45
46 517 setting with limited resources and without the use of incentives to providers to increase
47
48 518 uptake.
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51
52 519

53 54 520 **CONCLUSION**

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56
57 521 Digital adherence technology (DAT) such as medication monitors have a huge potential to
58
59 522 improve tuberculosis treatment adherence. However, to ensure successful scale-up and
60

1
2
3 523 sustainability of the intervention, the differentiated care approach should be used as a
4
5 524 platform to constantly educate PWTB and the community at large on TB and the importance
6
7 525 of adhering to treatment since technology on its own will not solve treatment adherence
8
9 526 issues especially those related to stigma and lack of support. Sound communication
10
11 527 between PWTB and providers serves as a key tool to improving treatment outcomes thus
12
13 528 more attention should be given to relationship training to ensure that the provider-patient
14
15 529 relationships provide the necessary support to those who need it most.

530 **ABBREVIATIONS**

20	COVID	Corona Virus Disease
21	DCA	Differentiated Care Approach
22	DOH	Department of Health
23	DS-TB	Drug-sensitive TB
24	DATs	Digital Adherence Technologies
25	DOTs	Directly Observed Treatment Short Course
26	ICFs	Informed Consent Forms
27	IDI	In-depth Interview
28	MDR-TB	Multidrug-resistant TB
29	PWTB	People With TB
30	SA	South Africa
31	SMS	Short Message Service
32	TB	Tuberculosis
33	TB MATE	TB Monitoring Adherence to Treatment Endpoints

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52 540 RM, NM, LJ, MTM, KLF, SC and CMCM conceptualized the study. RM and CMCM analysed
53
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55
56 542 revised subsequent versions of the manuscript. SC and CMCM provided guidance on earlier
57
58 543 versions of the manuscript. NM, CO, LJ, PN, MTM, KV, KLF, SC and CMCM reviewed and

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2
3
4 544 edited previous versions. RM, SC and CMCM are responsible for the overall content of the
5
6 545 manuscript. The authors read and approved the final manuscript.
7
8

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10 547 The authors declare that they have no competing interests.
11
12

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20 553 manuscript for publication.
21
22

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24 555 No additional data available.
25
26

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28 557 The parent study received ethics approval from the three district and provincial ethics
29 558 committees where the trial sites were located. This qualitative study was approved by the
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BMJ Open

“It’s more than them just using the box” A qualitative study exploring the feasibility of using medication monitors and a differentiated care approach to support adherence among people receiving TB treatment in South Africa

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2
3 1 Title: ***“It’s more than them just using the box”*** A qualitative study exploring the feasibility
4 of using medication monitors and a differentiated care approach to support adherence
5
6 2
7 3 among people receiving TB treatment in South Africa
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9 4

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50 29 Digital Adherence Technology, Differentiated Care Approach, treatment adherence support,
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1
2
3 37 **ABSTRACT**

4
5 38 **Objectives**

6
7 39 The TB MATE study evaluated whether a differentiated care approach (DCA) based on
8
9 40 tablet-taking data from Wisepill evriMED digital adherence technology could improve
10
11 41 tuberculosis treatment adherence. The DCA entailed a stepwise increase in adherence
12
13 42 support starting from short message service (SMS) to phone calls, followed by home visits
14
15 43 and motivational counselling. We explored feasibility of this approach with providers in
16
17 44 implementing clinics.

18
19
20 45 **Design**

21
22 46 Between June 2020 to February 2021, In-depth interviews were conducted in the provider's
23
24 47 preferred language, audio recorded, transcribed verbatim and translated. The interview
25
26 48 guide included three categories: feasibility, system-level challenges and sustainability of the
27
28 49 intervention. We assessed saturation and used thematic analysis.

30
31 50 **Setting**

32
33 51 Primary healthcare clinics in three provinces of South Africa.

34
35 52 **Participants**

36
37 53 We conducted 25 interviews with 18 staff and seven stakeholders.

38
39 54 **Results**

40
41 55 Three major themes emerged: Firstly, providers were supportive of the intervention being
42
43 56 integrated into the TB programme and were eager to be trained on the device as it helped to
44
45 57 monitor treatment adherence. Secondly, there were challenges in the adoption system such
46
47 58 as shortage of human resources which could serve as a barrier to information provision once
48
49 59 the intervention is scaled-up. Health care workers reported that some patients received
50
51 60 incorrect SMS's due to delays in the system that contributed to distrust. Thirdly, DCA was
52
53 61 considered as a key aspect of the intervention by some staff and stakeholders since it
54
55 62 allowed for support based on individual needs.

63 **Conclusions**

64 It was feasible to monitor tuberculosis treatment adherence using the evriMED device and
65 DCA. To ensure successful scale-up of the adherence support system, emphasis will need
66 to be placed on ensuring that the device and the network operate optimally and continued
67 support on adhering to treatment which will enable people with TB to take ownership of their
68 treatment journey and help overcome TB related stigma.

70 **Strengths and limitations of this study**

- 71 • We conducted the study in three provinces with different health service characteristics,
72 TB epidemiology and population characteristics which allowed us to understand
73 feasibility of implementation from a broader perspective.
- 74 • Another strength was that the study was done in a routine setting with limited resources
75 and without the use of incentives to providers to increase uptake.
- 76 • One limitation is that some of the interviews were conducted by a member of the study
77 management team, although this was limited to senior stakeholders who were unlikely to
78 feel reluctant to freely express their views and to withhold some of their opinions.

80 **INTRODUCTION**

81 Globally the treatment success rate for new and relapse drug-sensitive TB (DS-TB), is 86%
82 while in South Africa (SA) this is much lower at 79% [1]. Amongst those who are HIV
83 positive with TB, the treatment success rate is 78% and 67% for those previously treated
84 with TB [1]. Treatment failure is often a result of non-adherence to treatment, loss to follow-
85 up or unevaluated outcomes [2]. Typical reasons that people with TB (PWTB) might not
86 adhere to treatment include false perceptions of being cured once they feel better, stigma,
87 forgetfulness, lack of social network support, and poor user experience of accessing care at
88 clinics [3]. Traditional methods such as Directly Observed Treatment Short course (DOTs),
89 pill counts and self-report have limitations and have not been shown to improve treatment

1
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3 90 adherence in PWTB especially where DOTs programs are not designed and implemented
4
5 91 appropriately [4-6]. The effectiveness of DOTs is influenced by higher DOTs coverage where
6
7 92 cure rates have been found to be higher amongst those DOTs supporters with fewer patients
8
9 93 allocated to them [5]. Digital adherence technology (DAT) including medication monitors may
10
11 94 overcome challenges to monitoring tuberculosis treatment adherence through remotely
12
13 95 documenting dosing patterns of PWTB [7].
14
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16 96

17
18 97 Both globally and in South Africa, there is limited information on the value of DATs in TB
19
20 98 treatment. A study done in KwaZulu-Natal SA amongst drug resistant TB-HIV co-infected
21
22 99 inpatients using an older version of the Wisepill device, the RT2000 3G, showed that
23
24 100 feasibility challenges for digital pillboxes may include battery failure, device malfunction and
25
26 101 problems related to cellular networks [8]. Previous studies have found that other DAT such
27
28 102 as SMS reminders for TB treatment were insufficient to improve treatment adherence alone.
29
30 103 Barriers included frequent changing of phone numbers and uncertainty whether patients
31
32 104 were taking their tablets immediately after they received the SMS or not [9]. Another study
33
34 105 done in Uganda for HIV treatment showed that challenges for cellphone-based strategies
35
36 106 included: use of shared cell phones, technical failures preventing receipt of SMS texts,
37
38 107 electricity outages and changing phone numbers [10, 11]. Another DAT known as 99 DOTs
39
40 108 also has the potential to improve treatment adherence as the PWTB is required to call a
41
42 109 hidden phone number within the blister pack so as to indicate when a dose was taken [10].
43
44 110 However, 99 DOTs is limited in its ability to accurately report if a dose was taken since the
45
46 111 PWTB may dial the number without actually taking any medication [10, 12]. This challenge
47
48 112 has been overcome by DATs methods like Video DOT (VOT) which allow HCWs to watch
49
50 113 the PWTB taking treatment over video-conferencing hence it is considered a more accurate
51
52 114 method to ensure that PWTB adhere to treatment [13]. In addition, VOT can be a source of
53
54 115 support to those who lack family and friends to support them during their TB illness [14].
55
56 116 However, VOT requires a smartphone, data plan and sufficient bandwidth making it a less
57
58 117 affordable method in low and middle income countries such as SA [13].
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5 119 Most DATs have focused on monitoring adherence and few studies have used DATs to
6
7 120 differentiate between those patients who are struggling and need individual support, and
8
9 121 those who are doing well. Given this gap in knowledge, we evaluated the feasibility of using
10
11 122 the Wisepill evriMED DAT to monitor TB treatment adherence while using a differentiated
12
13 123 care approach (DCA) with a stepwise increase in adherence support for PWTB in South
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15
16 124 Africa.

19 125 **METHODS**

21 126 **Study design and study setting**

23 127 This qualitative study was embedded within a cluster-randomized trial (CRT) that took place
24
25 128 in six clinics in each of three provinces of South Africa: Gauteng (Ekurhuleni district);
26
27 129 Western Cape (Klipfontein and Mitchell's Plain districts); and Kwa-Zulu Natal (eThekweni
28
29 130 district), the details of which have been published elsewhere [15]. In the intervention arm of
30
31 131 the CRT, PWTB received medication monitors with reminders triggering differentiated care
32
33 132 approach (DCA) in response to adherence data uploads, carried out from a central database
34
35 133 [15]. The DCA was implemented in a progressive manner depending on the number of
36
37 134 doses a participant missed [15]. If one dose was missed, then a short message service
38
39 135 (SMS) reminder was sent to the participant [15]. If a second or third dose was missed, then
40
41 136 study staff would make a telephone call to the participant and once the fourth dose was
42
43 137 missed then a home visit was conducted during which motivational counselling took place
44
45 138 [15]. We describe the *feasibility* of implementing Wisepill evriMED device and differentiated
46
47 139 care from a stakeholder perspective.
48
49

50
51 140

53 141 **Site selection**

55 142 There were a total of nine intervention clinics, three in each province. Clinics were selected
56
57 143 based on location, HIV prevalence and numbers of patients starting TB treatment per month
58
59 144 [15].
60

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4
5 146**Study population**

7 147 The study population consisted of seven purposively selected stakeholders from the
8
9 148 Department of Health (DOH): one national, one provincial and five district-level
10
11 149 representatives, who worked closely with the facilities using the electronic device (Wisepill
12
13 150 evriMED DAT). From each intervention facility, we interviewed one facility staff (government
14
15 151 employee) and one study staff member. All study staff worked on the project for at least
16
17 152 three months. Facility staff-initiated patients on TB treatment and monitored patients for their
18
19 153 scheduled monthly follow-up visits while study staff offered PWTB the device, followed-up on
20
21 154 those who had missed doses and provided motivational and adherence counselling.
22
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25

26

Patient and public involvement

27 156
28
29 157 Patients or the public were not involved in the design, or conduct, or reporting, or
30
31 158 dissemination plans of our research.
32
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35

36

Conceptual framework and themes explored

37 160
38 161 Using the feasibility framework suggested by Bowen et al [16], we developed an in depth
39
40 162 interview (IDI) guide that covered the following topics; (i) the relative ease of implementation
41
42 163 and operation of the technology within existing health systems, technology infrastructure and
43
44 164 supply chain; (ii) system level challenges of delivering, sustaining and integrating the
45
46 165 intervention into the existing TB programme. We used the framework on the 'Integration and
47
48 166 sustainability of interventions into health systems' [17] to organize the data.
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52

Data collection

53 168
54
55 169 We conducted a total of 25 in-depth interviews. The sample was representative of providers
56
57 170 involved in the intervention while also considering saturation where themes usually start to
58
59 171 converge after 15 interviews. The IDI guide was piloted with one stakeholder, two facility and
60

1
2
3 172 one study staff between January to February 2020. The probing questions were adapted
4
5 173 after the pilot. These interviews were conducted face-to-face, and the data was included in
6
7 174 the analysis. Data collection continued between June 2020 to January 2021 with each
8
9 175 interview lasting between 45 – 90 minutes. The interviews were all conducted in the
10
11 176 providers preferred language by a female PhD student (RM) and a female study coordinator
12
13 177 who was a PhD student with qualitative experience (VM). Both researchers established a
14
15 178 prior relationship with the providers enabling them to understand the reasons for the study.
16
17 179 The interviews were digitally recorded with the providers consent and transcribed verbatim
18
19 180 by trained research assistants (Masters students). The transcripts were not returned to the
20
21 181 providers for comment or correction. Due to the impact of COVID-19 and the national
22
23 182 lockdown that took place, these interviews were conducted virtually over Microsoft Teams.
24
25 183 No one else was present in the interviews besides the providers and the researchers and
26
27 184 field notes were made during the interviews. Saturation was assessed during data collection
28
29 185 through asking the same question in different ways and reviewing a sample of the recordings
30
31 186 until no new information was obtainable. No repeat interviews were carried out.
32
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36

37 188 **Data analysis**

38
39 189 Thematic analysis was used with deductive and inductive approaches [18, 19]. At least 10%
40
41 190 of the transcripts were coded inductively by two independent researchers so as to reduce
42
43 191 bias and improve reliability [18]. A codebook of emerging themes was developed, guided by
44
45 192 the framework on the 'Integration and sustainability of interventions into health systems'
46
47 193 [17], with discrepancies being resolved through discussion. Where there was no inter-rater
48
49 194 agreement, the theme was dropped [18]. The final codebook was used to code the
50
51 195 remaining transcripts and any new codes that emerged were also included in this codebook.
52
53 196 MAXQDA qualitative software was used for the coding process. We highlight the major
54
55 197 themes (overarching theme) and sub-themes (specific themes) that emerged and use
56
57 198 supportive direct quotations from providers. Providers did not provide feedback on the
58
59 199 findings.
60

200 RESULTS

201 We conducted 25 interviews in total with 18 staff (9 facility staff and 9 study staff) and 7
202 stakeholders (1 national, 1 provincial and 5 at district-level) across 3 provinces. Majority of
203 the providers (23 out of 25) were female. None of the approached providers declined to
204 participate. Major themes included (1) Providers were supportive of the intervention, (2)
205 Intervention challenges within the adoption system and broad context, and (3) Ensuring
206 intervention sustainability through constant training of staff and education of PWTB

208 Major Theme 1: Providers were supportive of the intervention

209 There was buy-in from staff who felt involved and were supportive of the intervention.
210 Stakeholders were also very supportive of the intervention despite their limited involvement.

212 *“... to me it was a very good idea and it was working very well ... it improved our cure
213 rate because we had a lot of patients who were defaulting and who and to be
214 referred to the hospital because they developed multi, MDR. So since we had ...this
215 intervention, at least we had less patients who developed multi-drug resistance.”
216 - FFS_019_7*

218 *“...I think...it’s magnificent. I think it’s... a tool box, it’s really a way for us to see
219 what’s really happening at the point of ... TB treatment, where the patient take... the
220 medication when they open the box. So I think it’s really innovation that can be used.
221 ... I think it also is a reminder for the patient. You know? That ... “I need to take my
222 medication”. And it’s a way to ...to ensure the quality of the programme, that patients
223 are adhering to the ... medication...I think it is a critical intervention.” – FDS_WC_008
224 (District level)*

226 Both facility and study staff found the device easy to learn and facility staff who had received
227 a briefing on the study were eager to receive the complete training to support the study staff.

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3 2284
5 229 *“Because sometimes she (referring to study staff) [might not be here and it happens*6
7 230 *that she’s not here, either she is sick or she’s gone on holiday for December. She*8
9 231 *says: “...we can show you and then you do this things when we are not here”. I said:*10
11 232 *“... it will be easy... As long as you show us, we can do that device”.*12
13 233 *- FFS_762_003*14
15 23416
17 235 The staff described the activities of the intervention such as issuing devices, phone calls and18
19 236 making home visits as being well integrated into the TB programme. Providers had strong20
21 237 support for the device for two main reasons that we classified as sub-themes in our analysis:22
23 23824
25 239 **Sub-theme 1: Device as a useful reminder and early notification tool**26
27 240 Most providers found the alarm that was fitted on the device to be a useful reminder to28
29 241 patients to take their treatment on time and to attend their clinic visits. The device also30
31 242 alerted providers to PWTB who were not using the device and not taking treatment.32
33 24334
35 244 *“I feel like it assists with the real time monitoring because now if you check on the*36
37 245 *system, you would be able to check instead of waiting like someone waiting for their*38
39 246 *appointment that is months after, you can actually check now on the system that this*40
41 247 *person there’s no activity, let me call and you would actually find that the person has*42
43 248 *died or maybe the person has- is in hospital is admitted..”- FSS_762_006*44
45 24946
47 250 *“So, it will help us because ...sometimes we notice the other patient...didn’t take their*48
49 251 *medication and start to recall all of them and then the other just default ... With the*50
51 252 *box, someone is getting ... a notification that this person is not taking her*52
53 253 *treatment...” - FFS_524_006*54
55 25456
57 255 However, some staff distrusted that opening of the device meant that PWTB took their pills.

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5 257 *"...some patients do that when they open the pill box and ... show an adherence of*
6
7 258 *100%, but still they... have not been taking their medications. So we would try to*
8
9 259 *motivate them, counsel them, explain the disadvantages of not of them not taking the*
10
11 260 *medication." - FSS_519_001*

12
13
14 261

15 262 *"I think because you know patients always find a way to find loopholes within the*
16
17 263 *health system, so at some point they will understand that you're recording the*
18
19 264 *opening and the closing of the box not necessarily them actively taking the*
20
21 265 *medications. So they can easily open and close the box without really taking the*
22
23 266 *medication." - FDS_GP_008 (District level)*

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26 267
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28 268 **Sub-theme 2: Differentiated Care Approach allows for patient-centred care**

29 269 Staff mentioned that they found DCA to be a positive and unique aspect of our intervention.

30
31 270

32
33 271 *"So, you are no longer administering intervention for one. You sort of trying to be*
34
35 272 *specific ...to a person and offer them care in their in their specific sort of situations.*
36
37 273 *So, I think that is a positive thing because you don't assume everyone is the same.*
38
39 274 *You don't assume everyone's situation is the same. You understand that you are*
40
41 275 *dealing with ... individuals. That's ... what I think is positive about this differentiated*
42
43 276 *model of care." - MSS_732_005*

44
45
46 277
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48
49 278 *"... yah, I think I think the differentiated model of care ... is a very positive thing, that*
50
51 279 *it works to an extent because it's not a blanket approach. You don't, you don't think*
52
53 280 *of every patient as the same...you sort of attend to each person in their context and*
54
55 281 *... try to understand what they are going through." - MSS_732_005*

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3 283 The staff also felt that the counselling they provided as part of the DCA helped them to
4
5 284 understand their patients' reasons for not taking their treatment thus allowing them to
6
7 285 manage them better as they supported them on their treatment journey.
8

9
10 286

11 287 *"This whole approach I feel like it's a great initiative because it assists in managing*
12
13 288 *the patient - like fully. Like if I can say wholly, not just managing the patient, taking*
14
15 289 *the medication. You could also like... with the counselling you actually find that the*
16
17 290 *problem is that the participant is facing beyond treatment intake."*- FSS_762_006
18

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20 291

21
22 292 Phone calls to PWTB allowed for clarification on any issues that may not have been clear to
23
24 293 the patient while at the clinic.
25

26 294

27
28 295 *"...he didn't understand but when I called him and I was speaking to him over the*
29
30 296 *phone to understand how they're taking the treatment, I find that ... yeah there was*
31
32 297 *mistake ... one of the best things about this intervention because some of them are*
33
34 298 *able to even call me up, I don't always now have to call patients."*
35

36
37 299 *- MSS_732_005*
38

39 300

40
41 301 Home visits allowed the staff to have better interaction with their patients and to build trust
42
43 302 with them making them feel like someone cares about them.
44

45 303

46
47 304 *"It's not bad. It's nice to do home visits. It's whereby ... you contact with the patients,*
48
49 305 *know each other ... where the patient has got the problem, it's with the ... problem*
50
51 306 *with the box or she wanted to ask me something that she forget to ask at the clinic."*
52

53 307 *- FSS_522_002*
54

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56 308

57
58 309 *"... I think the participant at least get that thing when you do home visits, or you*
59
60 310 *phone them when they are not taking the treatment they feel as if they are cared of,*

1
2
3 311 *someone is care is cared for me when I am not taking the treatment because I would*
4
5 312 *get a call, or I will get a home visit”- FSS_524_003*
6

7 313
8
9 314 Some providers described DCA as more of a journey of supporting the patients and helping
10
11 315 build trust between the staff and the PWTB.
12

13 316
14
15 317 *“... that is really good part of the intervention. I think it ... continue to build that*
16
17 318 *trust...And that support for the patients ... so I- I think that was impressive.”*
18
19 319 *- FDS_WC_008 (District level)*
20

21 320
22
23 321 *“I thought it was only about the box... it’s more than them just using the box. It’s their*
24
25 322 *treatment journey and being supported to adhere to the treatment and get healed*
26
27 323 *from the TB.” - FSS_762_006*
28
29 324

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31
32
33 325 **Major Theme 2: Intervention challenges within the adoption system and broad context**
34
35 326 **of South Africa**

36
37 327 Some staff felt that the trust they built with the PWTB could be threatened by human
38
39 328 resource shortages and a dedicated cadre was needed to ensure successful
40
41 329 implementation.

42
43 330 *“However, when we find at once the research study stop and we over onto*
44
45 331 *implementation, ... the constraints is always HR resources and at the operational*
46
47 332 *level, if that initial education isn’t framed correctly. There could be a*
48
49 333 *misunderstanding about the purpose of the box.” - FDS_WCR_008 (District level)*
50

51 334
52
53 335 Challenges that were encountered with the device or the network resulted in delays in the
54
55 336 system updating that the box was opened which staff felt created trust issues between them
56
57 337 and the participant.
58
59 338

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2
3 339 *“Now it’s creating a trust issue between you and the patient, because you phoning*
4
5 340 *regarding treatment that was not taken because ... Wisepill says treatment was not*
6
7 341 *taken, while the patient on the other side did take the medication.”- FSS_516_002*
8
9 342

10
11 343 Heath care workers reported that some patients received incorrect SMS’s due to delays in
12
13 344 the system.

14
15 345 *“ Especially when it has been a weekend and then they will not ... send out the data*
16
17 346 *of... the weekend like ... if there were any missed or any ... intakes. Sometimes they*
18
19 347 *will show that they missed the weekend and they did not take the medication, but in*
20
21 348 *three days down the line... the correct information will show. That’s where we will see*
22
23 349 *that there were no missed doses.”- FSS_519_001*
24
25 350

26
27 351 Staff also felt that that the device would not work for some group of patients such as those
28
29 352 who abuse substances.
30
31 353

32
33 354 *“The patient that are on substance abuse, yoh! You know, when they come here,*
34
35 355 *they are ok. At a later stage, once they’ve started treatment, you realise that this*
36
37 356 *patient is using substances...With those patients, they the device- ya. It’s not good.*
38
39 357 *Won’t- won’t work. Won’t- won’t help.” - FFS_762_003*
40
41 358

42
43 359 *“He took the evriMED box device and the TB meds. That was the last time we saw*
44
45 360 *him on the clinic. He run away from home apparently. He was on drugs. But*
46
47 361 *then...he is back. He’s here in the TB room. He’s got TB again. So I was asking him*
48
49 362 *the other day: “are you still interested in joining this study?”. And he was like: “you*
50
51 363 *know what I did with the first box? I sold it”. - FSS_521_001*
52
53 364

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3 365 **Sub-theme 1: Provider perceptions of stigma related to use of the evriMED device and**
4
5 366 **DCA**
6

7 367 Staff perceived that some of the features of the box such as the alarm and the size of the
8
9 368 box may have been a concern to some PWTB in trying to conceal their TB status so they
10
11 369 would opt to leave their devices behind when travelling on holiday or going to work for fear of
12
13 370 disclosure of their TB status.
14
15

16 371
17
18 372 *“The thing that is common, especially in December ... an example is person*
19
20 373 *supposed to take it at 8, they take it at 8 but they not taking it at 8 from the box... I*
21
22 374 *think they went for holidays ... This person is taking treatment and the putting it... in*
23
24 375 *a purse. Whereby you’ll take in the morning without this alarm ringing.”-*
25

26 376 *MSS_019_002*
27

28 377
29
30 378 *“So some will come to us and say: “what if the pill box doesn’t make so much noise?*
31
32 379 *It will be easier for me to carry around- or if it was a bit ... smaller, then it will be*
33
34 380 *easier for me to carry it. But now it’s big, I don’t want ... people seeing me like with*
35
36 381 *this pill box in the taxi or at work.”- FSS_519_001*
37
38

39 382
40
41 383 *“I haven’t disclosed to my partner that I’m on TB medication and imagine if I had to*
42
43 384 *carry this box and the box would be ringing in the morning and it would cause*
44
45 385 *unnecessary fights.” - FSS_762_006*
46
47

48 386
49
50 387 Providers perceived that stigma was more of an issue outside the PWTB household as often
51
52 388 they would not disclose their TB status to members outside their homes.
53

54 389
55
56 390 *“So, I noticed that it’s comfortable for them to use this box when they are at home*
57
58 391 *with the people that actually know what is going on with them but when they are*
59
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3 392 *going to other people that are not aware that they are sick or anything, it seems as if*
4
5 393 *they don't want to carry the boxes.” - FSS_762_006*
6
7 394

8
9 395 Staff perceived that stigma related to DCA existed in the community and some of them
10
11 396 witnessed the PWTB fear of being stigmatized when conducting home visits. PWTB would
12
13 397 often ask staff not to wear their uniforms when they visit their homes.
14
15

16 398
17
18 399 *“Uhm they hate it when we wear our TB MATE t-shirts, because they are saying:*
19
20 400 *“due to stigma”. When we go visit their homes, we must not wear something that will*
21
22 401 *be written ‘TB’ or ‘HIV’. So we wear our normal clothes...”- FSS_521_001*
23
24 402

25
26 403 *“Then I took off my jacket, and then the participant saw that TB MATE on my t-shirt.*
27
28 404 *And then the patient told me that I must wear my jacket because what if someone*
29
30 405 *walks in and sees the TB MATE on my t-shirt. So I wasn't aware that the participant*
31
32 406 *didn't disclose... She told me that she's got fear that- because she will be judged*
33
34 407 *because she was drinking alcohol a lot. But now she's got TB. They will say she must*
35
36 408 *go and stay in the back room.”- FSS_521_001*
37
38

39 409
40
41 410 Staff perceived that some stigma could have been internalised and not actually experienced
42
43 411 by PWTB.
44

45 412 *“It's their thoughts because the person would feel like it did not want to be seen*
46
47 413 *carrying the box. Because people will think- so he sees all their thoughts. It's not*
48
49 414 *something that really happened.”- FFS_732_001*
50
51

52 415
53
54 416 *“But in the clinic, there wasn't really anything that contributed to the stigma but*
55
56 417 *maybe with now giving the pill box... some of the patients would say that maybe it's*
57
58 418 *gonna show. Maybe with their ARV's they could take it in private. Now we have them*
59
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2
3 419 *having this pill box that is gonna ring even, that is gonna beep and remind them to*
4
5 420 *take treatment...*” - FSS_732_005
6

7 421

9 422 **Major Theme 3: Ensuring intervention sustainability through constant training of staff**
11 **and education of PWTB**

12 423
13
14 424 Education on the intervention emerged as one of the major themes that stakeholders and
15
16 425 staff placed emphasis on as a means of managing their patients in a holistic way leading to
17
18 426 successful treatment outcomes. Education and training should emphasize the importance of
19
20 427 adhering to treatment and should be strengthened at various levels – with the PWTB
21
22 428 themselves, those who would be involved in implementation such as community health
23
24 429 workers (CHWs) and also to the community at large.
25

26 430

28 431 *“My experience was that as the community we need to need to educate the*
29
30 432 *community the importance of complying to medication...we need to educate and*
31
32 433 *educate and educate.”*- FFS_019_007
33
34

35 434

36
37 435 *“But I definitely think it’s... strengthening that interface between the patient and the*
38
39 436 *staff... it’s an important interface. And- and of course that too- the ‘how’ of- of the*
40
41 437 *contact, if it is about ‘why you didn’t- why you aren’t taking your treatment’ rather than*
42
43 438 *saying ‘how are you doing’- you know- ‘are you ok’, uhm ‘how can I help you’. When*
44
45 439 *we start off with those different conversations, it can lead to different outcomes.”*
46
47 440 *- FDS_WC_008 (District level)*
48

49 441

51 442 The staff felt that constant education and reinforcement would ultimately lead to behaviour
52
53 443 change and treatment adherence.
54

55 444

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57
58 445 *“I think the intervention even though we are the one offering the intervention but we*
59
60 446 *sort of gave patients the power to understand the... reasons why they are taking*

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3 447 *treatment, why is it important for them to...adhere to the treatment...we were actually*
4
5 448 *able to make patients to take their treatment journey into their own hands ... it's*
6
7 449 *almost like we were empowering patients..."- MSS_732_005*
8
9
10 450

11 12 451 **DISCUSSION**

13
14 452 Using the Wisepill evriMED device to support adherence to TB treatment appears to be a
15
16 453 feasible option in South Africa. Providers were supportive of the evriMED device and the
17
18 454 differentiated care approach, as they felt it had a positive impact on the TB patient's
19
20 455 programme. Stakeholders were supportive despite their involvement being limited to
21
22 456 approval of the study and providing oversight of the TB programme.
23
24

25 457

26
27 458 This study has shown that DATs is an innovative approach that might improve the
28
29 459 management of PWTB by allowing individual differentiated support. Early notification of
30
31 460 missed doses from the device allowed staff to intervene through SMS messaging and phone
32
33 461 calls, thus reducing the need for a home visit. This freed up time for staff to focus on other
34
35 462 duties. These findings are similar to other studies where differentiated care models used in
36
37 463 HIV treatment delivery have addressed challenges such as overcrowded facilities,
38
39 464 overburdened staff and long waiting times in countries like Uganda, Swaziland, Mozambique
40
41 465 and South Africa [7, 20-22].
42
43

44 466

45
46 467 Staff noted that the differentiated care allowed a journey of educating and supporting PWTB.
47
48 468 Through adherence and motivational counselling, staff empowered patients to understand
49
50 469 the importance of adhering to treatment and to empower them to take their treatment journey
51
52 470 into their own hands. For scale-up, the real time monitoring feature of the device is important
53
54 471 so that the correct individuals are promptly identified for further support before they become
55
56 472 lost to follow-up. This also allows for the efficient utilisation of resources to those in most
57
58 473 need, as seen in various studies [6, 23, 24]. More attention should also be given to
59
60

1
2
3 474 relationship training as the sustainability of the intervention depends on a sound provider-
4
5 475 patient relationship. Correct framing of the intervention as a support tool would also help
6
7 476 ensure that the intervention is well perceived once scaled-up. Training needs to be constant
8
9 477 and not once-off to reinforce their understanding of the intervention. In a routine TB program
10
11 478 setting, training of healthcare providers could be conducted by sub-district co-ordinators
12
13 479 since they visit facilities on a regular basis for monitoring purposes.
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17
18 481 Some challenges with the technology were cited such as alarm malfunction, incorrectly sent
19
20 482 SMS's and short battery lifespan. These challenges created distrust from PWTB, and the
21
22 483 device would therefore need to be of the highest quality to ensure sustainability of the
23
24 484 intervention. A systematic review of DAT for the management of tuberculosis therapy found
25
26 485 similar feasibility challenges remain in low- and middle-income settings [10]. Once the
27
28 486 intervention is scaled up, the shortage of human resources (HR) could serve as a barrier to
29
30 487 ensuring that providers receive the correct information. For successful scale-up, some staff
31
32 488 recommended that a dedicated cadre should be in place to follow-up PWTB to ensure that
33
34 489 they understand the importance of taking treatment. However, since the support system had
35
36 490 reduced the need for home visits and follow up calls, the current TB cadres, clerical staff and
37
38 491 community-based teams were also seen as being sufficient. Despite any challenges
39
40 492 experienced within the adoption system and broad context, the staff were all very supportive
41
42 493 of the intervention and even recommended that it should be used for all TB and chronic
43
44 494 patients as well as in other facilities.
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48
49 496 Fear of stigma and the disclosure of one's TB status has the potential to act as a barrier to
50
51 497 scale-up and sustainability of the intervention, if not well addressed. Stigma and fear of
52
53 498 disclosure resulting in lower acceptance of DAT technologies amongst multi-drug resistant
54
55 499 TB patients have also been reported in India [25], with improvements recommended on the
56
57 500 design. Disease-related stigma may be more difficult to address, and screening should be
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3 501 used to identify upfront those patients whom stigma and fear of disclosure may limit the use
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5 502 of the MERM [25].
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7 503
8

9 504 A limitation of the study was that interviews had to be conducted virtually on Microsoft
10
11 505 teams, due to the Covid-19 pandemic, and to allow for effective social distancing for both the
12
13 506 researchers and the study providers. This new mode of conducting interviews had setbacks
14
15 507 such as network and connectivity challenges which interrupted the flow of some of the
16
17 508 interviews. The interviewers mitigated this challenge through re-iterating what the participant
18
19 509 had said to ensure that the correct message had been captured. Through the consenting
20
21 510 process, we were able to ensure confidentiality and that the participant was relaxed. A
22
23 511 second limitation is that some of the interviews were conducted by a member of the study
24
25 512 management team, although this was limited to senior stakeholders who were unlikely to feel
26
27 513 reluctant to freely express their views and to withhold some of their opinions. Patients were
28
29 514 not included in this study which is a limitation since their views would have added a broader
30
31 515 understanding on feasibility. We conducted the study in three provinces with different health
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33 516 service characteristics, TB epidemiology and population characteristics which allowed us to
34
35 517 understand feasibility of implementation from a broader perspective. Another strength was
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37 518 that the study was done in a routine setting with limited resources and without the use of
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39 519 incentives to providers to increase uptake.
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45 46 521 **CONCLUSION**

47
48 522 Digital adherence technology (DAT) such as medication monitors have a huge potential to
49
50 523 improve tuberculosis treatment adherence. However, to ensure successful scale-up and
51
52 524 sustainability of the intervention, the differentiated care approach should be used as a
53
54 525 platform to constantly educate PWTB and the community at large on TB and the importance
55
56 526 of adhering to treatment since technology on its own will not solve treatment adherence
57
58 527 issues especially those related to stigma and lack of support. Sound communication
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3 528 between PWTB and providers serves as a key tool to improving treatment outcomes thus
4
5 529 more attention should be given to relationship training to ensure that the provider-patient
6
7 530 relationships provide the necessary support to those who need it most.
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10 531 **ABBREVIATIONS**

11	COVID	Corona Virus Disease
12	DCA	Differentiated Care Approach
13	DOH	Department of Health
14	DS-TB	Drug-sensitive TB
15	DATs	Digital Adherence Technologies
16	DOTs	Directly Observed Treatment Short Course
17	ICFs	Informed Consent Forms
18	IDI	In-depth Interview
19	MDR-TB	Multidrug-resistant TB
20	PWTB	People With TB
21	SA	South Africa
22	SMS	Short Message Service
23	TB	Tuberculosis
24	TB MATE	TB Monitoring Adherence to Treatment Endpoints
25		
26		
27		

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43
44 541 RM, NM, LJ, MTM, KLF, SC and CMCM conceptualized the study. RM and CMCM analysed
45
46 542 the data. RM, NM, CO, SC and CMCM interpreted the data. RM wrote the original draft and
47
48 543 revised subsequent versions of the manuscript. SC and CMCM provided guidance on earlier
49
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51
52 545 edited previous versions. RM, SC and CMCM are responsible for the overall content of the
53
54 546 manuscript. The authors read and approved the final manuscript.

55
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57 548 The authors declare that they have no competing interests.
58
59
60

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561 and the University of Cape Town (Ref 452/2018). We obtained written informed consent for
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COREQ (CONsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
<i>Personal characteristics</i>			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	
Occupation	3	What was their occupation at the time of the study?	
Gender	4	Was the researcher male or female?	
Experience and training	5	What experience or training did the researcher have?	
<i>Relationship with participants</i>			
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
<i>Theoretical framework</i>			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
<i>Participant selection</i>			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	
Sample size	12	How many participants were in the study?	
Non-participation	13	How many people refused to participate or dropped out? Reasons?	
<i>Setting</i>			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	
<i>Data collection</i>			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	
Field notes	20	Were field notes made during and/or after the interview or focus group?	
Duration	21	What was the duration of the interviews or focus group?	
Data saturation	22	Was data saturation discussed?	
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	
Software	27	What software, if applicable, was used to manage the data?	
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	
Clarity of major themes	31	Were major themes clearly presented in the findings?	
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

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A qualitative study exploring the feasibility of using medication monitors and a differentiated care approach to support adherence among people receiving TB treatment in South Africa

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3 1 Title: A qualitative study exploring the feasibility of using medication monitors and a
4 2 differentiated care approach to support adherence among people receiving TB treatment in
5 3 South Africa
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49 **Keywords**

50 29 Digital Adherence Technology, Differentiated Care Approach, treatment adherence support,
51 30 Tuberculosis, Feasibility
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1
2
3 37 **ABSTRACT**
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5 38 **Objectives**
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7 39 The TB MATE study evaluated whether a differentiated care approach (DCA) based on
8 40 tablet-taking data from Wisepill evriMED digital adherence technology could improve
9 41 tuberculosis treatment adherence. The DCA entailed a stepwise increase in adherence
10 42 support starting from short message service (SMS) to phone calls, followed by home visits
11 43 and motivational counselling. We explored feasibility of this approach with providers in
12 44 implementing clinics.
13

14 45 **Design**
15

16 46 Between June 2020 to February 2021, In-depth interviews were conducted in the provider's
17 47 preferred language, audio recorded, transcribed verbatim and translated. The interview
18 48 guide included three categories: feasibility, system-level challenges and sustainability of the
19 49 intervention. We assessed saturation and used thematic analysis.
20

21 50 **Setting**
22

23 51 Primary healthcare clinics in three provinces of South Africa.
24

25 52 **Participants**
26

27 53 We conducted 25 interviews with 18 staff and seven stakeholders.
28

29 54 **Results**
30

31 55 Three major themes emerged: Firstly, providers were supportive of the intervention being
32 56 integrated into the TB programme and were eager to be trained on the device as it helped to
33 57 monitor treatment adherence. Secondly, there were challenges in the adoption system such
34 58 as shortage of human resources which could serve as a barrier to information provision once
35 59 the intervention is scaled-up. Health care workers reported that some patients received
36 60 incorrect SMS's due to delays in the system that contributed to distrust. Thirdly, DCA was
37 61 considered as a key aspect of the intervention by some staff and stakeholders since it
38 62 allowed for support based on individual needs.
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63 **Conclusions**

64 It was feasible to monitor tuberculosis treatment adherence using the evriMED device and
65 DCA. To ensure successful scale-up of the adherence support system, emphasis will need
66 to be placed on ensuring that the device and the network operate optimally and continued
67 support on adhering to treatment which will enable people with TB to take ownership of their
68 treatment journey and help overcome TB related stigma.

70 **Strengths and limitations of this study**

- 71 • We conducted the study in three provinces with different health service characteristics,
72 TB epidemiology and population characteristics which allowed us to understand
73 feasibility of implementation from a broader perspective.
- 74 • Another strength was that the study was done in a routine setting with limited resources
75 and without the use of incentives to providers to increase uptake.
- 76 • One limitation is that some of the interviews were conducted by a member of the study
77 management team, although this was limited to senior stakeholders who were unlikely to
78 feel reluctant to freely express their views and to withhold some of their opinions.

80 **INTRODUCTION**

81 Globally the treatment success rate for new and relapse drug-sensitive TB (DS-TB), is 86%
82 while in South Africa (SA) this is much lower at 79% [1]. Amongst those who are HIV
83 positive with TB, the treatment success rate is 78% and 67% for those previously treated
84 with TB [1]. Treatment failure is often a result of non-adherence to treatment, loss to follow-
85 up or unevaluated outcomes [2]. Typical reasons that people with TB (PWTB) might not
86 adhere to treatment include false perceptions of being cured once they feel better, stigma,
87 forgetfulness, lack of social network support, and poor user experience of accessing care at
88 clinics [3]. Traditional methods such as Directly Observed Treatment Short course (DOTs),
89 pill counts and self-report have limitations and have not been shown to improve treatment

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3 90 adherence in PWTB especially where DOTs programs are not designed and implemented
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5 91 appropriately [4-6]. The effectiveness of DOTs is influenced by higher DOTs coverage where
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7 92 cure rates have been found to be higher amongst those DOTs supporters with fewer patients
8
9 93 allocated to them [5]. Digital adherence technology (DAT) including medication monitors may
10
11 94 overcome challenges to monitoring tuberculosis treatment adherence through remotely
12
13 95 documenting dosing patterns of PWTB [7].
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17
18 97 Both globally and in South Africa, there is limited information on the value of DATs in TB
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20 98 treatment. A study done in KwaZulu-Natal SA amongst drug resistant TB-HIV co-infected
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22 99 inpatients using an older version of the Wisepill device, the RT2000 3G, showed that
23
24 100 feasibility challenges for digital pillboxes may include battery failure, device malfunction and
25
26 101 problems related to cellular networks [8]. Previous studies have found that other DAT such
27
28 102 as SMS reminders for TB treatment were insufficient to improve treatment adherence alone.
29
30 103 Barriers included frequent changing of phone numbers and uncertainty whether patients
31
32 104 were taking their tablets immediately after they received the SMS or not [9]. Another study
33
34 105 done in Uganda for HIV treatment showed that challenges for cellphone-based strategies
35
36 106 included: use of shared cell phones, technical failures preventing receipt of SMS texts,
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38 107 electricity outages and changing phone numbers [10, 11]. Another DAT known as 99 DOTs
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40 108 also has the potential to improve treatment adherence as the PWTB is required to call a
41
42 109 hidden phone number within the blister pack so as to indicate when a dose was taken [10].
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44 110 However, 99 DOTs is limited in its ability to accurately report if a dose was taken since the
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46 111 PWTB may dial the number without actually taking any medication [10, 12]. This challenge
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48 112 has been overcome by DATs methods like Video DOT (VOT) which allow HCWs to watch
49
50 113 the PWTB taking treatment over video-conferencing hence it is considered a more accurate
51
52 114 method to ensure that PWTB adhere to treatment [13]. In addition, VOT can be a source of
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54 115 support to those who lack family and friends to support them during their TB illness [14].
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56 116 However, VOT requires a smartphone, data plan and sufficient bandwidth making it a less
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58 117 affordable method in low and middle income countries such as SA [13].
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5 119 Most DATs have focused on monitoring adherence and few studies have used DATs to
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7 120 differentiate between those patients who are struggling and need individual support, and
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9 121 those who are doing well. Given this gap in knowledge, we evaluated the feasibility of using
10
11 122 the Wisepill evriMED DAT to monitor TB treatment adherence while using a differentiated
12
13 123 care approach (DCA) with a stepwise increase in adherence support for PWTB in South
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16 124 Africa.

17 18 19 125 **METHODS**

20 21 126 **Study design and study setting**

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23 127 This qualitative study was embedded within a cluster-randomized trial (CRT) that took place
24
25 128 in six clinics in each of three provinces of South Africa: Gauteng (Ekurhuleni district);
26
27 129 Western Cape (Klipfontein and Mitchell's Plain districts); and Kwa-Zulu Natal (eThekweni
28
29 130 district), the details of which have been published elsewhere [15]. In the intervention arm of
30
31 131 the CRT, PWTB received medication monitors with reminders triggering differentiated care
32
33 132 approach (DCA) in response to adherence data uploads, carried out from a central database
34
35 133 [15]. The DCA was implemented in a progressive manner depending on the number of
36
37 134 doses a participant missed [15]. If one dose was missed, then a short message service
38
39 135 (SMS) reminder was sent to the participant [15]. If a second or third dose was missed, then
40
41 136 study staff would make a telephone call to the participant and once the fourth dose was
42
43 137 missed then a home visit was conducted during which motivational counselling took place
44
45 138 [15]. We describe the *feasibility* of implementing Wisepill evriMED device and differentiated
46
47 139 care from a stakeholder perspective.
48
49
50

51 140

52 53 141 **Site selection**

54
55 142 There were a total of nine intervention clinics, three in each province. Clinics were selected
56
57 143 based on location, HIV prevalence and numbers of patients starting TB treatment per month
58
59 144 [15].
60

1
2
3 145
4**146 Study population**

147 The study population consisted of seven purposively selected stakeholders from the
148 Department of Health (DOH): one national, one provincial and five district-level
149 representatives, who worked closely with the facilities using the electronic device (Wisepill
150 evriMED DAT). From each intervention facility, we interviewed one facility staff (government
151 employee) and one study staff member. All study staff worked on the project for at least
152 three months. Facility staff-initiated patients on TB treatment and monitored patients for their
153 scheduled monthly follow-up visits while study staff offered PWTB the device, followed-up on
154 those who had missed doses and provided motivational and adherence counselling.

155

156 Patient and public involvement

157 Patients or the public were not involved in the design, or conduct, or reporting, or
158 dissemination plans of our research.

159

160 Conceptual framework and themes explored

161 Using the feasibility framework suggested by Bowen et al [16], we developed an in depth
162 interview (IDI) guide (Appendix I) that covered the following topics; (i) the relative ease of
163 implementation and operation of the technology within existing health systems, technology
164 infrastructure and supply chain; (ii) system level challenges of delivering, sustaining and
165 integrating the intervention into the existing TB programme. We used the framework on the
166 'Integration and sustainability of interventions into health systems' [17] to organize the data.

167

168 Data collection

169 We conducted a total of 25 in-depth interviews. The sample was representative of providers
170 involved in the intervention while also considering saturation where themes usually start to
171 converge after 15 interviews. The IDI guide (Appendix I) was piloted with one stakeholder,

1
2
3 172 two facility and one study staff between January to February 2020. The probing questions
4
5 173 were adapted after the pilot. These interviews were conducted face-to-face, and the data
6
7 174 was included in the analysis. Data collection continued between June 2020 to January 2021
8
9 175 with each interview lasting between 45 – 90 minutes. The interviews were all conducted in
10
11 176 the providers preferred language by a female PhD student (RM) and a female study
12
13 177 coordinator who was a PhD student with qualitative experience (VM). Both researchers
14
15 178 established a prior relationship with the providers enabling them to understand the reasons
16
17 179 for the study. The interviews were digitally recorded with the providers consent and
18
19 180 transcribed verbatim by trained research assistants (Masters students). The transcripts were
20
21 181 not returned to the providers for comment or correction. Due to the impact of COVID-19 and
22
23 182 the national lockdown that took place, these interviews were conducted virtually over
24
25 183 Microsoft Teams. No one else was present in the interviews besides the providers and the
26
27 184 researchers and field notes were made during the interviews. Saturation was assessed
28
29 185 during data collection through asking the same question in different ways and reviewing a
30
31 186 sample of the recordings until no new information was obtainable. No repeat interviews were
32
33 187 carried out.
34
35
36
37
38

39 189 **Data analysis**

40
41 190 Thematic analysis was used with deductive and inductive approaches [18, 19]. At least 10%
42
43 191 of the transcripts were coded inductively by two independent researchers so as to reduce
44
45 192 bias and improve reliability [18]. A codebook of emerging themes was developed, guided by
46
47 193 the framework on the 'Integration and sustainability of interventions into health systems'
48
49 194 [17], with discrepancies being resolved through discussion. Where there was no inter-rater
50
51 195 agreement, the theme was dropped [18]. The final codebook was used to code the
52
53 196 remaining transcripts and any new codes that emerged were also included in this codebook.
54
55 197 MAXQDA qualitative software was used for the coding process. We highlight the major
56
57 198 themes (overarching theme) and sub-themes (specific themes) that emerged and use
58
59
60

199 supportive direct quotations from providers. Providers did not provide feedback on the
200 findings.

201 RESULTS

202 We conducted 25 interviews in total with 18 staff (9 facility staff and 9 study staff) and 7
203 stakeholders (1 national, 1 provincial and 5 at district-level) across 3 provinces. Majority of
204 the providers (23 out of 25) were female. None of the approached providers declined to
205 participate. Major themes included (1) Providers were supportive of the intervention, (2)
206 Intervention challenges within the adoption system and broad context, and (3) Ensuring
207 intervention sustainability through constant training of staff and education of PWTB

209 Major Theme 1: Providers were supportive of the intervention

210 There was buy-in from staff who felt involved and were supportive of the intervention.

211 Stakeholders were also very supportive of the intervention despite their limited involvement.

213 *“... to me it was a very good idea and it was working very well ... it improved our cure
214 rate because we had a lot of patients who were defaulting and who and to be
215 referred to the hospital because they developed multi, MDR. So since we had ...this
216 intervention, at least we had less patients who developed multi-drug resistance.”*

217 *- FFS_019_7*

219 *“...I think...it’s magnificent. I think it’s... a tool box, it’s really a way for us to see
220 what’s really happening at the point of ... TB treatment, where the patient take... the
221 medication when they open the box. So I think it’s really innovation that can be used.
222 ... I think it also is a reminder for the patient. You know? That ... “I need to take my
223 medication”. And it’s a way to ...to ensure the quality of the programme, that patients
224 are adhering to the ... medication...I think it is a critical intervention.” – FDS_WC_008
225 (District level)*

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2
3 226
4

5 227 Both facility and study staff found the device easy to learn and facility staff who had received
6
7 228 a briefing on the study were eager to receive the complete training to support the study staff.
8

9 229
10

11 230 *“Because sometimes she (referring to study staff) [might not be here and it happens*
12
13 231 *that she’s not here, either she is sick or she’s gone on holiday for December. She*
14
15 232 *says: “...we can show you and then you do this things when we are not here”. I said:*
16
17 233 *“... it will be easy... As long as you show us, we can do that device”.*
18

19
20 234 *- FFS_762_003*
21

22 235
23

24 236 The staff described the activities of the intervention such as issuing devices, phone calls and
25
26 237 making home visits as being well integrated into the TB programme. Providers had strong
27
28 238 support for the device for two main reasons that we classified as sub-themes in our analysis:
29

30 239
31

32 240 **Sub-theme 1: Device as a useful reminder and early notification tool**

33 241 Most providers found the alarm that was fitted on the device to be a useful reminder to
34
35 242 patients to take their treatment on time and to attend their clinic visits. The device also
36
37 243 alerted providers to PWTB who were not using the device and not taking treatment.
38
39

40 244
41

42
43 245 *“I feel like it assists with the real time monitoring because now if you check on the*
44
45 246 *system, you would be able to check instead of waiting like someone waiting for their*
46
47 247 *appointment that is months after, you can actually check now on the system that this*
48
49 248 *person there’s no activity, let me call and you would actually find that the person has*
50
51 249 *died or maybe the person has- is in hospital is admitted..”- FSS_762_006*
52

53 250
54

55
56 251 *“So, it will help us because ...sometimes we notice the other patient...didn’t take their*
57
58 252 *medication and start to recall all of them and then the other just default ... With the*
59
60

1
2
3 253 *box, someone is getting ... a notification that this person is not taking her*
4
5 254 *treatment...” - FFS_524_006*
6

7 255
8

9 256 However, some staff distrusted that opening of the device meant that PWTB took their pills.
10

11 257
12

13 258 *“...some patients do that when they open the pill box and ... show an adherence of*
14
15 259 *100%, but still they... have not been taking their medications. So we would try to*
16
17 260 *motivate them, counsel them, explain the disadvantages of not of them not taking the*
18
19 261 *medication.” - FSS_519_001*
20
21

22 262
23

24 263 *“I think because you know patients always find a way to find loopholes within the*
25
26 264 *health system, so at some point they will understand that you’re recording the*
27
28 265 *opening and the closing of the box not necessarily them actively taking the*
29
30 266 *medications. So they can easily open and close the box without really taking the*
31
32 267 *medication.” - FDS_GP_008 (District level)*
33
34

35 268
36

37 269 **Sub-theme 2: Differentiated Care Approach allows for patient-centred care**

38
39 270 Staff mentioned that they found DCA to be a positive and unique aspect of our intervention.
40

41 271
42

43 272 *“So, you are no longer administering intervention for one. You sort of trying to be*
44
45 273 *specific ...to a person and offer them care in their in their specific sort of situations.*
46
47 274 *So, I think that is a positive thing because you don’t assume everyone is the same.*
48
49 275 *You don’t assume everyone’s situation is the same. You understand that you are*
50
51 276 *dealing with ... individuals. That’s ... what I think is positive about this differentiated*
52
53 277 *model of care.” - MSS_732_005*
54
55

56 278
57

58 279 *“... yah, I think I think the differentiated model of care ... is a very positive thing, that*
59
60 280 *it works to an extent because it’s not a blanket approach. You don’t, you don’t think*

1
2
3 281 *of every patient as the same...you sort of attend to each person in their context and*
4
5 282 *... try to understand what they are going through.” - MSS_732_005*
6

7 283
8
9 284 The staff also felt that the counselling they provided as part of the DCA helped them to
10
11 285 understand their patients' reasons for not taking their treatment thus allowing them to
12
13 286 manage them better as they supported them on their treatment journey.
14

15 287
16
17 288 *“This whole approach I feel like it's a great initiative because it assists in managing*
18
19 289 *the patient - like fully. Like if I can say wholly, not just managing the patient, taking*
20
21 290 *the medication. You could also like... with the counselling you actually find that the*
22
23 291 *problem is that the participant is facing beyond treatment intake.”- FSS_762_006*
24

25 292
26
27 293 Phone calls to PWTB allowed for clarification on any issues that may not have been clear to
28
29 294 the patient while at the clinic.
30

31 295
32
33 296 *“...he didn't understand but when I called him and I was speaking to him over the*
34
35 297 *phone to understand how they're taking the treatment, I find that ... yeah there was*
36
37 298 *mistake ... one of the best things about this intervention because some of them are*
38
39 299 *able to even call me up, I don't always now have to call patients.”*
40

41 300 *- MSS_732_005*
42

43 301
44
45 302 Home visits allowed the staff to have better interaction with their patients and to build trust
46
47 303 with them making them feel like someone cares about them.
48

49 304
50
51 305 *“It's not bad. It's nice to do home visits. It's whereby ... you contact with the patients,*
52
53 306 *know each other ... where the patient has got the problem, it's with the ... problem*
54
55 307 *with the box or she wanted to ask me something that she forget to ask at the clinic.”*
56
57 308 *- FSS_522_002*
58
59
60

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3 309
4

5 310 *"... I think the participant at least get that thing when you do home visits, or you*
6
7 311 *phone them when they are not taking the treatment they feel as if they are cared of,*
8
9 312 *someone is care is cared for me when I am not taking the treatment because I would*
10
11 313 *get a call, or I will get a home visit"- FSS_524_003*

12
13
14 314

15
16 315 Some providers described DCA as more of a journey of supporting the patients and helping
17
18 316 build trust between the staff and the PWTB.

19
20 317

21
22 318 *"... that is really good part of the intervention. I think it ... continue to build that*
23
24 319 *trust...And that support for the patients ... so I- I think that was impressive."*
25
26 320 *- FDS_WC_008 (District level)*

27
28 321

29
30 322 *"I thought it was only about the box... it's more than them just using the box. It's their*
31
32 323 *treatment journey and being supported to adhere to the treatment and get healed*
33
34 324 *from the TB." - FSS_762_006*

35
36 325

37
38
39 326 **Major Theme 2: Intervention challenges within the adoption system and broad context**
40
41 327 **of South Africa**

42
43 328 Some staff felt that the trust they built with the PWTB could be threatened by human
44
45 329 resource shortages and a dedicated cadre was needed to ensure successful
46
47 330 implementation.

48
49 331 *"However, when we find at once the research study stop and we over onto*
50
51 332 *implementation, ... the constraints is always HR resources and at the operational*
52
53 333 *level, if that initial education isn't framed correctly. There could be a*
54
55 334 *misunderstanding about the purpose of the box." - FDS_WCR_008 (District level)*

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57
58 335
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1
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3 336 Challenges that were encountered with the device or the network resulted in delays in the
4
5 337 system updating that the box was opened which staff felt created trust issues between them
6
7 338 and the participant.
8

9 339

10
11 340 *“Now it’s creating a trust issue between you and the patient, because you phoning*
12
13 341 *regarding treatment that was not taken because ... Wisepill says treatment was not*
14
15 342 *taken, while the patient on the other side did take the medication.”- FSS_516_002*
16
17

18 343

19
20 344 Health care workers reported that some patients received incorrect SMS’s due to delays in
21
22 345 the system.

23
24 346 *“ Especially when it has been a weekend and then they will not ... send out the data*
25
26 347 *of... the weekend like ... if there were any missed or any ... intakes. Sometimes they*
27
28 348 *will show that they missed the weekend and they did not take the medication, but in*
29
30 349 *three days down the line... the correct information will show. That’s where we will see*
31
32 350 *that there were no missed doses.”- FSS_519_001*
33

34 351

35
36
37 352 Staff also felt that that the device would not work for some group of patients such as those
38
39 353 who abuse substances.
40

41 354

42
43 355 *“The patient that are on substance abuse, yoh! You know, when they come here,*
44
45 356 *they are ok. At a later stage, once they’ve started treatment, you realise that this*
46
47 357 *patient is using substances...With those patients, they the device- ya. It’s not good.*
48
49 358 *Won’t- won’t work. Won’t- won’t help.” - FFS_762_003*
50

51 359

52
53
54 360 *“He took the evriMED box device and the TB meds. That was the last time we saw*
55
56 361 *him on the clinic. He run away from home apparently. He was on drugs. But*
57
58 362 *then...he is back. He’s here in the TB room. He’s got TB again. So I was asking him*
59
60

1
2
3 363 *the other day: "are you still interested in joining this study?". And he was like: "you*
4
5 364 *know what I did with the first box? I sold it". - FSS_521_001*
6

7 365

8
9
10 366 **Sub-theme 1: Provider perceptions of stigma related to use of the evriMED device and**
11
12 367 **DCA**

13
14 368 Staff perceived that some of the features of the box such as the alarm and the size of the
15
16 369 box may have been a concern to some PWTB in trying to conceal their TB status so they
17
18 370 would opt to leave their devices behind when travelling on holiday or going to work for fear of
19
20 371 disclosure of their TB status.
21

22 372

23
24
25 373 *"The thing that is common, especially in December ... an example is person*
26
27 374 *supposed to take it at 8, they take it at 8 but they not taking it at 8 from the box... I*
28
29 375 *think they went for holidays ... This person is taking treatment and the putting it... in*
30
31 376 *a purse. Whereby you'll take in the morning without this alarm ringing."-*
32
33 377 *MSS_019_002*
34

35 378

36
37 379 *"So some will come to us and say: "what if the pill box doesn't make so much noise?*
38
39 380 *It will be easier for me to carry around- or if it was a bit ... smaller, then it will be*
40
41 381 *easier for me to carry it. But now it's big, I don't want ... people seeing me like with*
42
43 382 *this pill box in the taxi or at work."- FSS_519_001*
44

45 383

46
47
48 384 *"I haven't disclosed to my partner that I'm on TB medication and imagine if I had to*
49
50 385 *carry this box and the box would be ringing in the morning and it would cause*
51
52 386 *unnecessary fights." - FSS_762_006*
53

54 387

55
56 388 Providers perceived that stigma was more of an issue outside the PWTB household as often
57
58 389 they would not disclose their TB status to members outside their homes.
59
60

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4
5 391 *“So, I noticed that it’s comfortable for them to use this box when they are at home*
6
7 392 *with the people that actually know what is going on with them but when they are*
8
9 393 *going to other people that are not aware that they are sick or anything, it seems as if*
10
11 394 *they don’t want to carry the boxes.” - FSS_762_006*

12
13
14 395

15
16 396 Staff perceived that stigma related to DCA existed in the community and some of them
17
18 397 witnessed the PWTB fear of being stigmatized when conducting home visits. PWTB would
19
20 398 often ask staff not to wear their uniforms when they visit their homes.

21
22 399

23
24 400 *“Uhm they hate it when we wear our TB MATE t-shirts, because they are saying:*
25
26 401 *“due to stigma”. When we go visit their homes, we must not wear something that will*
27
28 402 *be written ‘TB’ or ‘HIV’. So we wear our normal clothes...”- FSS_521_001*

29
30 403

31
32 404 *“Then I took off my jacket, and then the participant saw that TB MATE on my t-shirt.*
33
34 405 *And then the patient told me that I must wear my jacket because what if someone*
35
36 406 *walks in and sees the TB MATE on my t-shirt. So I wasn’t aware that the participant*
37
38 407 *didn’t disclose... She told me that she’s got fear that- because she will be judged*
39
40 408 *because she was drinking alcohol a lot. But now she’s got TB. They will say she must*
41
42 409 *go and stay in the back room.”- FSS_521_001*

43
44 410

45
46
47 411 Staff perceived that some stigma could have been internalised and not actually experienced
48
49 412 by PWTB.

50
51 413 *“It’s their thoughts because the person would feel like it did not want to be seen*
52
53 414 *carrying the box. Because people will think- so he sees all their thoughts. It’s not*
54
55 415 *something that really happened.”- FFS_732_001*

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58 416
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1
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3 417 *“But in the clinic, there wasn’t really anything that contributed to the stigma but*
4
5 418 *maybe with now giving the pill box... some of the patients would say that maybe it’s*
6
7 419 *gonna show. Maybe with their ARV’s they could take it in private. Now we have them*
8
9 420 *having this pill box that is gonna ring even, that is gonna beep and remind them to*
10
11 421 *take treatment...” - FSS_732_005*
12

13 422

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15
16 423 **Major Theme 3: Ensuring intervention sustainability through constant training of staff**
17
18 424 **and education of PWTB**

19
20 425 Education on the intervention emerged as one of the major themes that stakeholders and
21
22 426 staff placed emphasis on as a means of managing their patients in a holistic way leading to
23
24 427 successful treatment outcomes. Education and training should emphasize the importance of
25
26 428 adhering to treatment and should be strengthened at various levels – with the PWTB
27
28 429 themselves, those who would be involved in implementation such as community health
29
30 430 workers (CHWs) and also to the community at large.
31

32 431

33
34
35 432 *“My experience was that as the community we need to need to educate the*
36
37 433 *community the importance of complying to medication...we need to educate and*
38
39 434 *educate and educate.”- FFS_019_007*
40

41 435

42
43 436 *“But I definitely think it’s... strengthening that interface between the patient and the*
44
45 437 *staff... it’s an important interface. And- and of course that too- the ‘how’ of- of the*
46
47 438 *contact, if it is about ‘why you didn’t- why you aren’t taking your treatment’ rather than*
48
49 439 *saying ‘how are you doing’- you know- ‘are you ok’, uhm ‘how can I help you’. When*
50
51 440 *we start off with those different conversations, it can lead to different outcomes.”*
52

53
54 441 *- FDS_WC_008 (District level)*
55

56 442

57
58 443 The staff felt that constant education and reinforcement would ultimately lead to behaviour
59
60 444 change and treatment adherence.

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4
5 446 *"I think the intervention even though we are the one offering the intervention but we*
6
7 447 *sort of gave patients the power to understand the... reasons why they are taking*
8
9 448 *treatment, why is it important for them to...adhere to the treatment...we were actually*
10
11 449 *able to make patients to take their treatment journey into their own hands ... it's*
12
13 450 *almost like we were empowering patients..."- MSS_732_005*
14
15
16 451

19 452 **DISCUSSION**

20
21 453 Using the Wisepill evriMED device to support adherence to TB treatment appears to be a
22
23 454 feasible option in South Africa. Providers were supportive of the evriMED device and the
24
25 455 differentiated care approach, as they felt it had a positive impact on the TB patient's
26
27 456 programme. Stakeholders were supportive despite their involvement being limited to
28
29 457 approval of the study and providing oversight of the TB programme.
30

31 458
32
33 459 This study has shown that DATs is an innovative approach that might improve the
34
35 460 management of PWTB by allowing individual differentiated support. Early notification of
36
37 461 missed doses from the device allowed staff to intervene through SMS messaging and phone
38
39 462 calls, thus reducing the need for a home visit. This freed up time for staff to focus on other
40
41 463 duties. These findings are similar to other studies where differentiated care models used in
42
43 464 HIV treatment delivery have addressed challenges such as overcrowded facilities,
44
45 465 overburdened staff and long waiting times in countries like Uganda, Swaziland, Mozambique
46
47 466 and South Africa [7, 20-22].
48
49

50 467
51
52 468 Staff noted that the differentiated care allowed a journey of educating and supporting PWTB.
53
54 469 Through adherence and motivational counselling, staff empowered patients to understand
55
56 470 the importance of adhering to treatment and to empower them to take their treatment journey
57
58 471 into their own hands. For scale-up, the real time monitoring feature of the device is important
59
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1
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3 472 so that the correct individuals are promptly identified for further support before they become
4
5 473 lost to follow-up. This also allows for the efficient utilisation of resources to those in most
6
7 474 need, as seen in various studies [6, 23, 24]. More attention should also be given to
8
9 475 relationship training as the sustainability of the intervention depends on a sound provider-
10
11 476 patient relationship. Correct framing of the intervention as a support tool would also help
12
13 477 ensure that the intervention is well perceived once scaled-up. Training needs to be constant
14
15 478 and not once-off to reinforce their understanding of the intervention. In a routine TB program
16
17 479 setting, training of healthcare providers could be conducted by sub-district co-ordinators
18
19 480 since they visit facilities on a regular basis for monitoring purposes.
20
21
22 481

23
24 482 Some challenges with the technology were cited such as alarm malfunction, incorrectly sent
25
26 483 SMS's and short battery lifespan. These challenges created distrust from PWTB, and the
27
28 484 device would therefore need to be of the highest quality to ensure sustainability of the
29
30 485 intervention. A systematic review of DAT for the management of tuberculosis therapy found
31
32 486 similar feasibility challenges remain in low- and middle-income settings [10]. Once the
33
34 487 intervention is scaled up, the shortage of human resources (HR) could serve as a barrier to
35
36 488 ensuring that providers receive the correct information. For successful scale-up, some staff
37
38 489 recommended that a dedicated cadre should be in place to follow-up PWTB to ensure that
39
40 490 they understand the importance of taking treatment. However, since the support system had
41
42 491 reduced the need for home visits and follow up calls, the current TB cadres, clerical staff and
43
44 492 community-based teams were also seen as being sufficient. Despite any challenges
45
46 493 experienced within the adoption system and broad context, the staff were all very supportive
47
48 494 of the intervention and even recommended that it should be used for all TB and chronic
49
50 495 patients as well as in other facilities.
51
52 496

53
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55
56 497 Fear of stigma and the disclosure of one's TB status has the potential to act as a barrier to
57
58 498 scale-up and sustainability of the intervention, if not well addressed. Stigma and fear of
59
60 499 disclosure resulting in lower acceptance of DAT technologies amongst multi-drug resistant

1
2
3 500 TB patients have also been reported in India [25], with improvements recommended on the
4
5 501 design. Disease-related stigma may be more difficult to address, and screening should be
6
7 502 used to identify upfront those patients whom stigma and fear of disclosure may limit the use
8
9 503 of the MERM [25].
10

11 504
12
13 505 A limitation of the study was that interviews had to be conducted virtually on Microsoft
14
15 506 teams, due to the Covid-19 pandemic, and to allow for effective social distancing for both the
16
17 507 researchers and the study providers. This new mode of conducting interviews had setbacks
18
19 508 such as network and connectivity challenges which interrupted the flow of some of the
20
21 509 interviews. The interviewers mitigated this challenge through re-iterating what the participant
22
23 510 had said to ensure that the correct message had been captured. Through the consenting
24
25 511 process, we were able to ensure confidentiality and that the participant was relaxed. A
26
27 512 second limitation is that some of the interviews were conducted by a member of the study
28
29 513 management team, although this was limited to senior stakeholders who were unlikely to feel
30
31 514 reluctant to freely express their views and to withhold some of their opinions. Patients were
32
33 515 not included in this study which is a limitation since their views would have added a broader
34
35 516 understanding on feasibility. We conducted the study in three provinces with different health
36
37 517 service characteristics, TB epidemiology and population characteristics which allowed us to
38
39 518 understand feasibility of implementation from a broader perspective. Another strength was
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41 519 that the study was done in a routine setting with limited resources and without the use of
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43 520 incentives to providers to increase uptake.
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50 522 **CONCLUSION**

51 523 Digital adherence technology (DAT) such as medication monitors have a huge potential to
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53 524 improve tuberculosis treatment adherence. However, to ensure successful scale-up and
54
55 525 sustainability of the intervention, the differentiated care approach should be used as a
56
57 526 platform to constantly educate PWTB and the community at large on TB and the importance
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3 527 of adhering to treatment since technology on its own will not solve treatment adherence
4
5 528 issues especially those related to stigma and lack of support. Sound communication
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7 529 between PWTB and providers serves as a key tool to improving treatment outcomes thus
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9 530 more attention should be given to relationship training to ensure that the provider-patient
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11 531 relationships provide the necessary support to those who need it most.
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14 532 **ABBREVIATIONS**

16	COVID	Corona Virus Disease
17	DCA	Differentiated Care Approach
18	DOH	Department of Health
19	DS-TB	Drug-sensitive TB
20	DATs	Digital Adherence Technologies
21	DOTs	Directly Observed Treatment Short Course
22	ICFs	Informed Consent Forms
23	IDI	In-depth Interview
24	MDR-TB	Multidrug-resistant TB
25	PWTB	People With TB
26	SA	South Africa
27	SMS	Short Message Service
28	TB	Tuberculosis
29	TB MATE	TB Monitoring Adherence to Treatment Endpoints
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32		

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49 542 RM, NM, LJ, MTM, KLF, SC and CMCM conceptualized the study. RM and CMCM analysed
50
51 543 the data. RM, NM, CO, SC and CMCM interpreted the data. RM wrote the original draft and
52
53 544 revised subsequent versions of the manuscript. SC and CMCM provided guidance on earlier
54
55 545 versions of the manuscript. NM, CO, LJ, PN, MTM, KV, KLF, SC and CMCM reviewed and
56
57 546 edited previous versions. RM, SC and CMCM are responsible for the overall content of the
58
59 547 manuscript. The authors read and approved the final manuscript.
60

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549 The authors declare that they have no competing interests.

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556 **DATA SHARING STATEMENT**

557 No data are available.

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559 The parent study received ethics approval from the three district and provincial ethics
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APPENDIX I

STUDY NUMBER: -□□□-□□□□□-□

AUR2-1-244**INTERVIEW GUIDE:****DEPARTMENT OF HEALTH KEY STAKEHOLDERS/
FACILITY-BASED STAFF/STUDY STAFF****TB MATE*****Introduction***

Staff to say out loud before starting interview

- Thank you for agreeing to take part in our research
- We are interested in knowing about your perceptions, thoughts and attitude toward the differentiated model of care, especially with regard to implementation of the medication device. There are no right or wrong answers.
- You do not have to answer any questions if you don't want to. Just say pass and I will move to the next question.
- Your answers to these questions may help us improve TB treatment services.
- All of your answers will be kept confidential. Confidential means we will not tell anyone your answers outside the research group.

APPENDIX I

STUDY NUMBER: -□□□-□□□□□-□

AUR2-1-244

INTERVIEW GUIDE:

DEPARTMENT OF HEALTH KEY STAKEHOLDERS/ FACILITY-BASED STAFF/STUDY STAFF

Introduction and Ground Rules

1. Obtain written informed consent first, before any data are collected.
2. Interviewer to introduce self. Thank you for taking the time to meet with us today. Our names are [*insert names*]_____and we would like to talk to you about the feasibility, acceptability and the quality to which the differentiated care model was implemented. We are doing this project to understand your role, thoughts, attitude and perceptions of the differentiated model of care and particularly to see whether the medical device technology could be integrated and sustained within the TB programme. We want you to be as open and honest when answering. There are no right or wrong answers in this discussion. Please feel free to tell us what you think.
 - Interviewer to explain the ground rules and terms of confidentiality for the interview.
 - The participant does not have to answer any question they do not want to.
 - The information you share will be handled in confidence. (in secret)
 - When we report back on the information collected in this discussion, your comments will not be able to be linked to you specifically.
 - We ask that you also agree not to share anything discussed in this room with others.
3. The interview should take about 1 hour
4. Interviewer to inform the interviewee that the in-depth interview will be digitally recorded to make sure that all themes are captured. Turn the audio-recorder on and ask for verbal permission again to digitally record the session. While the audio-recorder is running verbal consent (this is a double check against the written consent) must be captured. We will be recording the session because we don't want to miss any of your comments. Although one of us may take some notes while we talk, we can't write fast enough to get everything down on paper. As we are recording, please try to speak loudly so that we don't miss your comments.

Themes to be explored

- I. Feasibility of implementing the differentiated model of care (motivators and barriers)

Appendix I Interview Guide: DoH Key Stakeholders/ Facility-based staff/study staff

Version 5.0 dated 25 February 2020

APPENDIX I

STUDY NUMBER: -□□□-□□□□□-□

AUR2-1-244

INTERVIEW GUIDE:

DEPARTMENT OF HEALTH KEY STAKEHOLDERS/
FACILITY-BASED STAFF/STUDY STAFF

- II. System level challenges of delivering, sustaining and integrating the intervention into the existing TB programme

Time started (HHMM):

Questions**1. General**

- What is the title of your current position?
- How long have you held this position?
- How are TB services delivered at your level with regard to the intervention? (i.e. District, Provincial, National)
- Please describe your role with the differentiated model of care intervention

2. Feasibility of implementing the differentiated model of care (motivators and barriers)

- *Please describe the cadre of staff that were involved with delivering the differentiated model of care?*
- *What are your thoughts on features of the Evrimed device?*
- *Can you describe your experience of delivering the differentiated model of care?*
- *Can you describe the training and resources that staff received prior to or during delivery of the differentiated model of care? What was your opinion of the training and resources received?*
- *Can you describe the benefits of the differentiated model of care and use of the medication device technology?*
- *How often did you follow the requirements for the differentiated model of care?*
- *Please describe the details of what happens on the phone calls and at the home visits.*
- *What tools do you use for the motivational counselling and for adherence counselling?*

Appendix I Interview Guide: DoH Key Stakeholders/ Facility-based staff/study staff

Version 5.0 dated 25 February 2020

APPENDIX I

STUDY NUMBER: -□□□-□□□□□-□

AUR2-1-244

INTERVIEW GUIDE:

DEPARTMENT OF HEALTH KEY STAKEHOLDERS/ FACILITY-BASED STAFF/STUDY STAFF

- *Can you describe the differences between motivational counselling and adherence counselling?*
- *Under what circumstances were not able to follow the requirements for the differentiated model of care?*
- *How can the differentiated model of care be sustained?*
- *Can you describe challenges of the differentiated model of care and use of the medication device technology?*
- *How can TB treatment be improved using this differentiated model of care and the medication device technology?*
- *What was your experience or suggestions regarding interactions with patients? (Giving instructions, or providing motivational counselling)*

3. System level challenges of delivering the intervention

- *How were patients that were part of the differentiated model of care treated differently from those receiving standard of care?*
- *Please elaborate on the positive changes of the differentiated model of care and use of the medication device technology. How do you think these positive changes could be sustained?*
- *Please elaborate on the negative changes of the differentiated model of care and use of the medication device technology. How do you think the negative changes could be addressed?*
- *Can you describe to us what systems are in place that could monitor the differentiated model of care and use of the medication device technology?*
- *Were there any activities that caused or contributed to patients experiencing stigma at the facility? Please elaborate*
- *What types of resources will facilities need to ensure sustainability of the differentiated model of care?*
- *Please describe to us what system level structures need to be improved in order to integrate the differentiated model of care and medication device technology into the existing TB programme system.*

4. Factors that influence the sustainability of the intervention

- *Please describe to us the expectations that you may have had about the differentiated model of care and use of the medication device technology?*

Appendix I Interview Guide: DoH Key Stakeholders/ Facility-based staff/study staff

Version 5.0 dated 25 February 2020

APPENDIX I

STUDY NUMBER: -□□□-□□□□□-□

AUR2-1-244**INTERVIEW GUIDE:****DEPARTMENT OF HEALTH KEY STAKEHOLDERS/
FACILITY-BASED STAFF/STUDY STAFF**

- *Please describe your positive and negative experience of delivering or implementing the differentiated model of care.*
- *How different is the current intervention model compared to your initial expectations and how do you think this model could be more effective?*
- *For scale-up and sustainability who do you think should set up the Evrimed boxes for patients? What would be the advantages and disadvantages of this cadre of staff setting up the Evrimed boxes as part of their daily responsibilities.*
- *Can you describe any gaps which exist in the way the intervention is being delivered currently?*

Any other comments

Are there any final thoughts you have about the differentiated model of care and use of the medication device technology?

End of session

Now we have come to the end of our discussion. Thank you for your participation. If you have any questions about your study participation, please contact us. Thank you.

Time ended (HHMM):

COREQ (CONsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
<i>Personal characteristics</i>			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	
Occupation	3	What was their occupation at the time of the study?	
Gender	4	Was the researcher male or female?	
Experience and training	5	What experience or training did the researcher have?	
<i>Relationship with participants</i>			
Relationship established	6	Was a relationship established prior to study commencement?	
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: Study design			
<i>Theoretical framework</i>			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
<i>Participant selection</i>			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	
Sample size	12	How many participants were in the study?	
Non-participation	13	How many people refused to participate or dropped out? Reasons?	
<i>Setting</i>			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	
<i>Data collection</i>			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	
Field notes	20	Were field notes made during and/or after the interview or focus group?	
Duration	21	What was the duration of the interviews or focus group?	
Data saturation	22	Was data saturation discussed?	
Transcripts returned	23	Were transcripts returned to participants for comment and/or	

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	
Description of the coding tree	25	Did authors provide a description of the coding tree?	
Derivation of themes	26	Were themes identified in advance or derived from the data?	
Software	27	What software, if applicable, was used to manage the data?	
Participant checking	28	Did participants provide feedback on the findings?	
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
Data and findings consistent	30	Was there consistency between the data presented and the findings?	
Clarity of major themes	31	Were major themes clearly presented in the findings?	
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.