

Results

Fig 1 shows the sampling of facilities, their allocation to intervention and control arms, and the total number of facilities analysed at the end of the study.

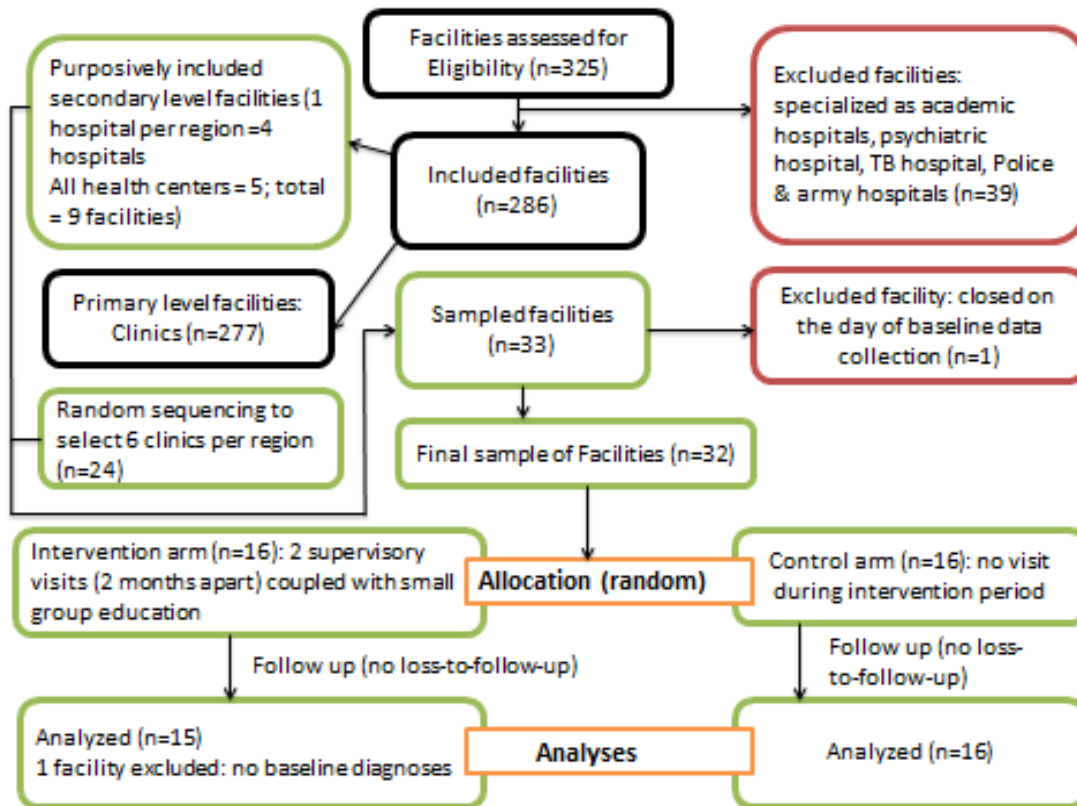


Figure 1: CONSORT diagram showing sampling, allocation, and analyses of facilities.

The intervention arm had 16 facilities: 6 (38%) in the Hhohho region, 1 (6%) in Shiselweni, 3 (19%) in Lubombo, and 6 (38%) in the Manzini region. The control arm also had 16 facilities: 4 (25%) in the Hhohho region, 7 (44%) in Shiselweni, 2 (13%) in Lubombo, and 3 (19%) in the Manzini region. One hundred (100) prescriptions were collected post intervention, and 100 prescriptions post follow-up were collected in each of the 32 facilities making a total of 3200 post intervention and 3200 post follow-up prescriptions analysed at the end of the study. Table 1 shows the mean differences in WHO/INRUD prescribing indicators between intervention and control groups immediately after the intervention and at the end of the follow up period.

Table 1: Regional WHO/INRUD Prescribing Indicators

WHO/INRUD Prescribing Indicators and Timeline	Mean Difference	p-value	95% CI
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Difference in number of drugs between baseline and post intervention	-0.23	0.48	-0.87 - 0.42
Difference in number of drugs between baseline and post follow up	-0.19	0.55	-0.86 - 0.47
Difference in number of drugs between post intervention and post follow up	0.03	0.77	-0.18 - 0.25
Difference in percent of generics between baseline and post intervention	-4.38	0.35	-13.76 - 5
Difference in percent of generics between baseline and post follow up	-3.38	0.42	-11.87 - 5.12
Difference in percent of generics between post intervention and post follow up	1	0.59	-2.77 - 4.77
Difference in percent antibiotics between baseline and post intervention	7.06	0.26	-5.48 - 19.61
Difference in percent antibiotics between baseline and post follow up	-1.25	0.77	-9.94 - 7.44
Difference in percent antibiotics between post intervention and post follow up	-8.31	0.03	-15.74 - -0.89
Difference in percent injections between baseline and post intervention	-0.94	0.71	-6.06 - 4.18
Difference in percent injections between baseline and post follow up	-5.38	0.24	-14.47 - 3.72
Difference in percent injections between post intervention and post follow up	-4.44	0.21	-11.66 - 2.78
Difference in percent EML between baseline and post intervention	-2.75	0.02	-4.99 - -0.51
Difference in percent EML between baseline and post follow up	-2.06	0.06	-4.22 - 0.01
Difference in percent EML between post intervention and post follow up	0.69	0.50	-1.37 - 2.74

*Statistically significant at $p \leq 0.05$

As shown in Table 1, the percentage of prescriptions with antibiotics prescribed decreased from baseline to post-intervention in control facilities though this decrease was statistically insignificant. The percentage of prescriptions with antibiotics increased in control facilities at the end of the follow up period. A statistically significant increase in the percentage of prescriptions with antibiotics in control facilities was observed at the end of the follow-up period (MD = -8.31, $p = 0.03$, 95% CI = -15.74 - -0.89). A statistically significant increase in the percentage of medicines prescribed from the EML was observed in control facilities immediately post intervention (MD = -2.75, $p = 0.02$, 95% CI = -4.99 - -0.51); while the increase in control facilities at the end of the follow up period was not statistically significant. During the follow-up period the percentage of medicines prescribed from the EML increased in intervention facilities.

The average number of medicines per prescription increased in control facilities immediately post intervention and continued to increase at the end of the follow-up period. During the follow-up period, the average number of medicines per prescription increased in intervention facilities. The percentage of medicines prescribed by generic name increased in control facilities immediately post intervention and stayed higher by the end of the follow-up period. During the follow-up period, the percentage of medicines prescribed by generic name increased in intervention facilities. The percentage of prescriptions with injections increased in control facilities throughout the study though these increases were not statistically significant.

WHO/INRUD prescribing indicators by level of care (all facilities)

The sample had nine secondary level facilities (4 hospitals and 5 health centers) and 23 primary level facilities (clinics). Due to the small sample of secondary compared to primary level facilities, analyses were conducted to report on changes that occurred within each level of care during the study but not on changes by intervention or control groups. There were no statistically significant changes on the WHO/INRUD prescribing indicators by level of care that occurred during this study.

The multiple linear regression model analysed at facility level to assess the effect of the intervention over time, while controlling for confounders, showed the following:

a) Average number of medicines:

The interaction between time and intervention was not statistically significant ($p=0.55$), meaning that the change over time in terms of average number of medicines per prescription was not dependent on the intervention. The intervention did not influence the average number of medicines as the intervention group had on average 0.42 more medicines than the control group ($p=0.34$) after adjusting for time, level of care, region, and diagnosis.

b) Generic prescribing

The interaction between time and intervention was not statistically significant ($p=0.86$), meaning that the change over time in terms of average percentage generics prescribed was not dependent on the intervention. The intervention did not influence the average percentage of generics as the intervention group had on average 1.06% less generics than the control group ($p=0.77$) after adjusting for time, level of care, region, and diagnosis. Results also showed that the average percent of generics was similar in the four regions, and level of care at all the time points. The changes in the average percentage of generics over time were significant between baseline and post intervention as well as between baseline and post follow-up. In each case, the percentage of generics increased ($p=0.001$ and $p<0.001$ respectively). There was also a

borderline significantly higher mean percent of generics in chronic vs acute prescriptions ($p=0.05$).

c) Antibiotics prescribing

The interaction between time and intervention was not statistically significant ($p=0.72$), meaning that the change over time in terms of average percentage antibiotics prescribed was not dependent on the intervention. The intervention group had on average 0.62% more antibiotics than the control group ($p=0.88$) after adjusting for time, level of care, region and diagnosis. The average percent of antibiotics was similar in the four regions at all the time points. The second level of care had significantly lower percentage antibiotics than the first ($p=0.02$). The changes in the average percentage of antibiotics over time showed a significant reduction between baseline and post intervention but not between baseline and post follow-up. There was also a highly significantly lower mean percent of antibiotics in chronic vs acute prescriptions ($p<0.001$).

d) Injections prescribing

The logarithm of percent injections was used as the outcome. The interaction between time and intervention was not statistically significant ($p=0.72$). The intervention did not influence the average percentage of injections ($p=0.74$) after adjusting for time, level of care, region, and diagnosis. Results also showed that the average percent of injections was similar in the four regions at all the time points except significantly lower in Manzini than Hhohho ($p=0.03$). The second level of care was not difference from the first ($p=0.17$). The changes in the average percentage of injections over time showed a significant reduction between baseline and post intervention but not between baseline and post follow-up. There was also a highly significantly lower mean percent of injections in chronic vs acute prescriptions ($p<0.001$).

e) Prescribing of EML Medicines

The interaction between time and intervention was not statistically significant ($p=0.14$), meaning that the change over time in terms of average percentage EML prescribed was not dependent on the intervention. The intervention did not influence the average percentage of EMLs ($p=0.32$) after adjusting for time, level of care, region, and diagnosis. Results also showed that the average percent of EML was similar in the four regions at all the time points. The second level of care was not different from the first ($p=0.32$). The changes in the average percentage of EML over time showed a significant reduction between baseline and post intervention but not between baseline and post follow-up. There was also a highly significantly higher mean percent of EML in chronic vs acute prescriptions ($p<0.001$).

Discussion

Study findings showed improvement in all WHO/INRUD prescribing indicators. The positive changes observed in this study could have been due to the small group education aspect of the intervention, where facility staff came together to discuss their prescribing practices as a facility. Literature has shown that peer education on rational use of medicines potentially increases knowledge (Ross-Degnan et al., 1997). Furthermore, this study combined educational and managerial interventions to try and reduce the use of antibiotics – it has been shown that multifaceted, rather than single, interventions often produce desired results (Bbosa et al., 2014).

There was no short-term effect of the intervention on prescribing of antibiotics, but in the long term there seemed to be an effect. Immediately post intervention antibiotics increased in intervention facilities but decreased at the end of study, and even more during the follow-up period, showing that the intervention had positive long-term effects on the prescribing of antibiotics. The decrease however did not reach the WHO recommendation of below 30%. The high use of antibiotics shows that Eswatini, just like other settings reported in literature, is struggling with the appropriate use of antibiotics for non-bacterial infections (Desta et al., 1997; Llor & Bjerrum, 2016; Ncube, Meintjes, & Chola, 2014; Olayemi et al., 2006; Risk et al., 2013). It is also not peculiar to Eswatini that the intervention did not reduce the use of antibiotics to recommended standards. A systematic review conducted in LMICs to assess the effects of interventions implemented to promote rational use of medicines found that antibiotic prescribing increased from 45% to 54% over a 10-year period (Holloway et al., 2013).

Though the overall reduction in use of antibiotics was statistically insignificant, the desired result i.e., a reduction in antibiotics use, seems to have been possible, and this could have been due to the use of a combination of interventions (supervision coupled with small group education in this study). Literature shows that a combination of these interventions is effective in improving prescribing patterns post intervention (Pérez-Cuevas et al., 1996). More research over a longer period needs to be conducted to assess the long-term effect of this intervention in Eswatini. Furthermore, other interventions that have been shown to reduce antibiotic use in literature still need to be explored in Eswatini. These include availability of policies that will advocate for implementation of a national antimicrobial resistance containment strategy; availability of a functional department dedicated to promoting rational use of medicines within

the Ministry of Health which will ensure functional PTCs in health centres, hospitals, and regions; and availability of a medicines information centre (Holloway et al., 2016).

In this study, prescribing of medicines from the EML decreased more in intervention than control facilities. Various changes occurred in the country during the study; including a wide roll-out of the electronic system, CMIS, to 78% of facilities at the end of the follow-up period compared to 6% of facilities at baseline. Client management information systems comes with preloaded medicines. It is possible that most of the preloaded medicines are not from the EML, and this could have resulted in the decrease in prescribing of medicines from the EML observed in this study. However, further studies need to be conducted to validate this assumption. The introduction of CMIS not only affected prescribing of medicines from the EML but also prescribing of medicines by generic name. Generic prescribing increased in both intervention and control facilities. This increase however cannot be solely attributed to the intervention, more so because a greater change was observed in control facilities. The electronic system has most medicines preloaded by generic name. Furthermore, CMIS uses pull down menus for prescribing medicines – forcing people to prescribe by generic name. In both intervention and control facilities the increase did not reach the WHO recommended standard of 100%; though this was the case, the percentage of medicines prescribed by generic name was higher than values reported in Pakistan (71.6%) (Atif et al., 2016) and 11 countries in Africa (68%) (Ofori-Asenso et al., 2016).

Though statistically insignificant immediately post intervention, this study showed a decrease in the use of injections in both the intervention and control arms. At the end of the follow-up period the use of injections increased in both arms with an almost doubled increase in facilities in the control arm. The pattern observed in the use of injection in this study validates literature that support that human behaviour changes during an intervention but the change is not sustained (Dias, 2012). The average number of medicines per prescription decreased more in intervention than control facilities immediately post intervention and at the end of the follow-up period, showing a short- and long-term effect of the intervention on this indicator. The systematically organised education program implemented during each of the two visits to intervention facilities could have resulted in the decrease in the average number of medicines prescribed. Literature highlights that repeated seminars tend to improve prescribing (Bexell et al., 1996).

Findings from the regression analyses to assess the effect of the intervention showed that the intervention had no effect on prescribing indicators after controlling for independent variables and confounders. Changes in the health systems that investigators had no control over could have had negative effects on the intervention. These changes include stock-outs of medicines, changes in the pharmaceutical structure, and introduction of CMIS.