Drug waste of ready-to-administer syringes in the intensive care unit: Aseptically prepared syringes versus prefilled sterilized syringes

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ABSTRACT

Background: The availability of ready-to-administer (RTA) syringes for intravenous (IV) drugs facilitates rapid and safe administration in emergency and intensive care situations. Hospital pharmacies can prepare RTA syringes through aseptic batchwise filling. Due to excess production of these RTA syringes for sufficient availability for patient care and their limited (microbiological) shelf-life, waste is unavoidable, which contributes to environmental pollution. RTA prefilled sterilized syringes (PFSSs) have much longer shelf-lives than aseptically prepared RTA syringes and might contribute to reducing drug waste.

Aim: This study aimed to evaluate the difference in drug waste between RTA syringes that were prepared through aseptic batchwise filling and RTA PFSSs in the Intensive Care Unit (ICU).

Methods: We measured drug waste of RTA syringes over an 8-year time period from August 2015 to May 2023 in the 32-bed ICU of the University Medical Center Utrecht. We distinguished between RTA syringes prepared through aseptic batchwise filling by our hospital pharmacy ("*RTA aseptic syringes",* shelf-life of 31 days) and RTA PFSSs (shelf-life of 18 months). An intervention group of three drug products that were replaced by PFSSs was compared to a control group of five drug products that were not replaced by PFSSs during the study period. We then defined four different periods within the total study period, based on quarantine time of the RTA aseptic syringes and time of PFSS introduction: 1) no quarantine, 2) 3-day quarantine, 3) 7-day quarantine and 4) PFSS introduction. Our primary endpoint was the number of RTA syringes that was wasted, expressed as the percentage of the total number of syringes dispensed to the ICU in each of these four periods. We used a Kruskall-Wallis test to test if waste percentages differed between time periods in the control and intervention groups, with a post-hoc Dunn's test for pairwise comparisons. Furthermore, we applied two interrupted time series (ITS) analyses to visualize and test the effect of introducing different quarantine times and the PFSSs on waste percentage.

Results: Introduction of PFSSs significantly decreased drug waste of RTA syringes irrespective of drug type in the intervention group, from 31% during the 7-day quarantine period to 5% after introduction of the PFSS ($p<0.001$). The control group showed no significant decrease in drug waste over the same time periods (from 20% to 16%; $p=0.726$). We observed a significant difference in the total drug waste of RTA aseptic syringes between time periods, which may be attributed to the implementation of different quality control quarantine procedures. The ITS model of the intervention group showed a direct decrease of 17.7% in waste percentage after the introduction of PFSSs ($p=0.083$).

Conclusion: Drug waste of RTA syringes for the ICU can be significantly decreased by introducing PFSSs, supporting hospitals to enhance environmental sustainability. Furthermore, the waste percentage of RTA syringes prepared through aseptic batchwise filling is significantly impacted by duration of quarantine time.

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1. Introduction

Bedside preparation of intravenous (IV) drugs by critical care nurses in the Intensive Care Unit (ICU) is a time-consuming procedure which carries the risk of both medication errors and microbiological contamination of the parenteral product (Carter, 2020; Keers et al., 2013; Larmené-Beld et al., 2019). The use of ready-to-administer (RTA) syringes that are premixed to standardized concentrations (in accordance with Good Manufacturing Practice (GMP) guidelines) as provided by the hospital pharmacy department can reduce these risks (Larmené-Beld et al., 2019; Malik et al., 2022; Council of Europe 2016). Also, it enables critical care nurses to spend more time at the bedside of the patient.

In Dutch hospitals, RTA syringes are prepared by *aseptic handling*, a procedure characterized by a range of measures aimed at minimizing the risk of product contamination (Council of Europe 2016; Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022; Boom et al., 2022; Boom et al., 2021; Boom et al., 2023). The microbiological shelf-life of the RTA syringes depends on where aseptic handling takes place. When prepared in the clinical area ("bedside preparation"), shelf-life can be as short as 8 h (Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022). In contrast, when RTA syringes are produced in a laminar airflow (LAF) cabinet (GMP Grade A) placed in a GMP grade D environment in the hospital pharmacy, shelf-life can be up to 31 days in the refrigerator (Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022). In addition, preparation in the hospital pharmacy allows for aseptic *batchwise filling*, a procedure where a large number (up to 200) of RTA syringes are prepared at once, followed by pharmaceutical quality control (QC), during which the batches are placed in quarantine. In Dutch hospitals, aseptic batchwise filling of RTA syringes is mostly done for use in the ICU.

Despite the longer shelf-life of RTA syringes prepared by aseptic handling in the hospital pharmacy, the waste can be substantial. This is due to the inherent unpredictability in terms of the quantity and characteristics of patients admitted to the ICU, making it challenging to accurately forecast the precise utilization of RTA syringes over the designated shelf life period of 31 days. Consequently, as a precautionary measure against potential shortages, it is common practice to prepare and dispense a surplus of RTA syringes. A recent multicenter study across 12 hospitals showed a mean drug waste rate of RTA syringes as high as 38% in the operation rooms (ORs) and ICUs (Barbariol et al., 2021). Reducing waste and optimization of drug use are needed to accomplish environmental sustainability goals (McGain et al., 2020). Moreover, in times of drug shortages worldwide due to quality related manufacturing problems, production delays and supply chain challenges, it is necessary to use drugs more efficiently and reduce waste to a minimum (Traynor, 2022).

Recently, RTA prefilled sterilized syringes (PFSSs) were introduced in order to overcome these challenges. These RTA syringes are sterilized after production, which means that the shelf-life is no longer limited by microbiological aspects, but by the physical and chemical stability of the drug. PFSSs of physically and chemically stable drugs can thus have shelf-lives of up to 36 months and do not have to be stored in the refrigerator. The longer shelf-lives facilitate use over longer periods of time, accommodating fluctuations in use and thus a possible reduction in drug waste. The magnitude of this effect has, however, not been estimated before.

This study aimed to evaluate the difference in drug waste between RTA syringes that were prepared through aseptic batchwise filling (with different quarantine times) and RTA PFSSs in the ICU.

2. Methods

2.1. Setting

This observational study was conducted in a 32-mixed bed medical-surgical ICU (with an average of around 2000 admissions and 8000 patient-days per year) from August 2015 to May 2023. The ICU hosts a drug compounding facility consisting of a clean-room with two GMP Grade A LAF cabinets placed in a GMP Grade D environment which was built in 2010. The hospital pharmacy holds a GMP certificate for the production of aseptic preparations (certificate number NL/H 19/2,013,892).

2.2. Ready-to-administer syringes

In this study, we distinguish between two types of RTA syringes used by the ICU.

(1) *RTA aseptic syringes:* RTA syringes prepared by the hospital pharmacy in the drug compounding facility of the ICU by aseptic handling through batchwise filling.
(2) *RTA prefilled sterilized syringes:* commercially available RTA syringes prepared by a large-scale compounding pharmacy that are sterilized after production.

2.2.1. RTA aseptic syringes

The hospital pharmacy of the UMCU prepared different RTA syringes by aseptic handling through batchwise filling for the ICU according to Dutch national guidelines for preparation under aseptic conditions (Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022). Batch sizes differed from 40 syringes (e.g. milrinone 10mg = 50ml) to 200 syringes (e.g. norepinephrine 5mg = 50ml). It is important to acknowledge that the optimization of these batch sizes has been pursued to the best extent possible, considering the inherent unpredictability associated with the usage levels within the ICU setting.

After preparation, the RTA aseptic syringes were placed in quarantine during which pharmaceutical QC testing was done. QC testing of the batches was mandatory according to national GMP (z) guidelines, as the syringes are used for multiple patients and are kept in stock (Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022). Testing included, among other tests, microbiological monitoring of the workspace (with tryptic soy agar (TSA) settle plates) and tryptic soy broth (TSB) fills (Boom et al., 2020; Boom et al., 2022). When the QC results complied to product specifications, the RTA aseptic syringes were authorized for release and made available for the nursing staff of the ICU. The microbiological shelf-life of the RTA aseptic syringes prepared by our hospital pharmacy was 31 days, including the duration of the quarantine period (Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022).

2.2.2. RTA prefilled sterilized syringes

In July 2022, three of the RTA aseptic syringes prepared by our hospital pharmacy were replaced by RTA PFSSs produced by '*Apotheek A15*', a large-scale compounding pharmacy. '*Apotheek A15*' is a collaboration of four Dutch university medical centers and provides expertise, preservation and nationwide distribution of commercially unavailable but medically necessary pharmaceuticals. It is equipped with approximately 2000 m²s of cleanrooms and a fully equipped pharmaceutical and microbiological laboratory. The preparation of the RTA PFSSs takes place in a GMP grade C area, ensuring a controlled environment. Prior to sterilization, a bioburden test is performed to ascertain the microbial count. The syringes are then sterilized using an autoclave for 15 min at 121°C by steam sterilization. To validate the efficiency of the sterilization process, a subsequent test in accordance with the pH. Eur. monograph 2.6.1 is conducted post-sterilization.

We replaced potassium chloride 60mmol = 60ml, midazolam 50mg = 50ml and morphine 50mg = 50ml. These three PFSSs were chosen based on the product range of '*Apotheek A15*' and product use in our ICU. All three PFSSs had a shelf-life of 18 months during the study period.

2.3. Study design

This study is a time-series analysis of two groups of drug products.

2.3.1. Control and intervention drug products

We defined two different groups of drug products in our study: a *control group*, consisting of the five drug products that were only prepared through aseptic batchwise filling by our hospital pharmacy (RTA aseptic syringes) throughout the whole study period (cefazolin 1000mg = 10ml, insulin novorapid 50 IU = 50ml, magnesium chloride 20mmol = 40ml, milrinone 10mg = 5ml an norepinephrine 5mg = 50ml) and an *intervention group*, consisting of the three drug products that were first prepared through aseptic batchwise filling by our hospital pharmacy (RTA aseptic syringes) but replaced by RTA PFSSs in July 2022 (midazolam 50mg = 50ml, morphine 50mg = 50ml and potassium chloride 60mmol = 60ml).

2.3.2. Different time periods

Over the course of the study period, our hospital pharmacy changed the quarantine time of the RTA aseptic syringes twice because of updates in national guidelines (Nederlandse Vereniging van Ziekenhuisapothekers (NVZA) 2022). We hypothesized that quarantine time would impact on the amount of RTA aseptic syringes that were wasted due to microbiological expiry, as a longer quarantine time results in less time available for use. Thus, instead of only defining two time periods (i.e. before and after PFSS introduction), we defined four periods in our study: (1) August 2015 – September 2017 (no quarantine time), (2) October 2017 – January 2019 (3-day quarantine; RTA aseptic syringes made available for use after preliminary results of TSB fills), (3) February 2019 – June 2022 (7-day quarantine; RTA aseptic syringes made available for use after preliminary results of TSB fills and definitive results of TSA settle plate) and (4) July 2022 – May 2023 (introduction of three RTA PFSS products; 7-day quarantine still in place for the control group).

Table 1 visualizes the design of the study with the effective time of use of the drug products in the control and intervention group per time period.

Table 1
Study design with the effective time of use of the drug products in the control and intervention group per time period. RTA = Ready to administer, PFSS = Prefilled sterilized syringe, MgCl = Magnesium chloride, KCl = Potassium chloride.

	RTA aseptic syringes *shelf-life 31 days*			
	No quarantine Aug 2015 – Sep 2017	3-day quarantine Oct 2017 – Jan 2019	7-day quarantine Feb 2019 – June 2022	7-day quarantine July 2022 – May 2023
Effective time of use in control group of drug products *Cefazolin, insulin, MgCl, milrinone, norepinephrine*	31 days	28 days	24 days	24 days
	RTA aseptic syringes *shelf-life 31 days*			RTA PFSSs *shelf-life 18 months* July 2022 – May 2023
	No quarantine Aug 2015 – Sep 2017	3-day quarantine Oct 2017 – Jan 2019	7-day quarantine Feb 2019 – June 2022	
Effective time of use in intervention group of drug products *Midazolam, morphine, KCl*	31 days	28 days	24 days	18 months

2.4. Drug waste

The primary endpoint of this study was the number of RTA syringes that was wasted, expressed as the percentage of the total number of syringes dispensed to the ICU per time period. Our ICU uses the medication management system ServeRx® (3AM Technologies, 2023). The ServeRx® system registers every transaction type of the RTA syringes: replenishment/refill of the medicine refrigerators by staff of the hospital pharmacy, removal by the nursing staff of the ICU for patient use and removal by the pharmacy staff due to expiry of the RTA syringe. All ServeRx® transactions are registered in a Microsoft SQL-server and made available through Microsoft Access. All ServeRx® transactions from August 2015 to May 2023 were used for this study. Data of transactions before August 2015 were not available due to a server migration at that time.

2.5. Statistical analysis

We used a Kruskal-Wallis test to examine whether the waste percentages differed significantly between time periods within the control and intervention groups. This non-parametric test was selected because the data were not normally distributed. To determine which specific periods exhibited significant differences, we conducted a post-hoc Dunn's test for pairwise comparisons with Bonferroni adjustment. We performed two interrupted time series (ITS) analyses to visualize and test the effect of introducing longer quarantine time (control group) and of introducing longer quarantine time as well as introducing the RTA PFSS (intervention group) on waste percentage. The ITS analyses comprised linear regression models with waste percentage as the dependent variable and time as the independent variable. For each time period we introduced two dummy predictor variables in the models: one binary variable indicating if the time period had elapsed or not and one dummy variable indicating the number of days since the new time period (Wagner et al., 2002).

All statistical analyses were 2-sided using a significance level of 0.05. Data handling as well as statistical analyses were performed in R version 4.0.3 (The R Foundation for Statistical Computing, 2020; including 'dplyr', 'tidyr', 'lubridate' and 'ggplot2' packages).

3. Results

During the study period of almost 8 years, a total of 312,352 RTA aseptic syringes were dispensed by our hospital pharmacy. From July 2022 to May 2023, we dispensed 7269 RTA PFSSs produced by '*Apotheek A15*'. A total of 246,422 RTA syringes (including both types) were used by the ICU nursing staff during the study period, with a mean number of used products of 2650 per month (standard deviation 500; see Appendix Fig. A1).

Table 2 shows the waste percentage per time period for all different drug products within the control and intervention groups. In the control group, total waste percentages differed significantly across the different time periods ($p<0.001$), and was driven by the prevailing quarantine time: 5% waste when no period of quarantine was implemented, versus 17% (3-day quarantine), 20% (7-day quarantine, Feb 2019 – June 2022) and 16% (7-day quarantine, July 2022 – May 2023) when microbiology QC testing preceded RTA aseptic syringe release. Post-hoc testing showed no significant difference between the last two time periods of the control group (20% and 16% waste respectively, $p=0.726$). Highest waste percentages were seen for the cefazolin 1000mg = 10ml and milrinone 10mg = 50ml syringes, with waste percentages as high as 39% during the 7-day quarantine period (Feb 2019 – June 2022) and 36% during the 3-day quarantine period respectively.

The intervention group showed a similar trend across all different time periods ($p<0.001$) with a total waste of 4% with no quarantine, 27% with 3-day quarantine and 31% with 7-day quarantine, but showed a significant drop to 5% waste after introduction of the RTA PFSS, which

Table 2
Waste percentage of all RTA drug products across different time periods.

CONTROL GROUP		No quarantine Aug 2015 – Sep 2017			3-day quarantine Oct 2017 – Jan 2019			7-day quarantine Feb 2019 – June 2022			7-day quarantine July 2022 – May 2023		
Drug	Syringe dilution	Prepared (n)	Expired (n)	Waste (%)	Prepared (n)	Expired (n)	Waste (%)	Prepared (n)	Expired (n)	Waste (%)	Prepared (n)	Expired (n)	Waste (%)
Cefazolin*	1000mg = 10 ml	7437	28	0	6385	2439	38	13,589	5283	39	2090	449	21
Insulin Novorapid	50 IU = 50 ml	13,943	698	5	7777	471	6	27,187	4962	18	5002	1451	29
Magnesium chloride	20mmol = 40 ml	8072	20	0	5925	408	7	17,259	4218	24	3976	367	9
Milrinone	10mg = 50 ml	3154	239	8	3696	1335	36	8103	2424	30	1826	369	20
Norepinephrine	5mg = 50 ml	27,369	1771	6	18,747	2485	13	42,502	5087	12	10,472	1125	11
Total:		59,975	2756	5	42,530	7138	17	108,640	21,974	20	23,366	3761	16
INTERVENTION GROUP		No quarantine Aug 2015 – Sep 2017			3-day quarantine Oct 2017 – Jan 2019			7-day quarantine Feb 2019 – June 2022			Introduction PFSS July 2022 – May 2023		
Midazolam	50mg = 50 ml	7703	421	5	3493	953	27	24,706	6874	28	3761	203	5
Morphine	50mg = 50 ml	5766	170	3	2947	976	33	11,300	4384	39	1520	97	6
Potassium chloride	60mmol = 60 ml	6238	243	4	3776	842	22	11,912	3528	30	1988	43	2
Total:		19,707	834	4	10,216	2771	27	47,918	14,786	31	7269	343	5

* The shelf life of cefazolin changed from 21 days to 31 days during the 7-day quarantine period.
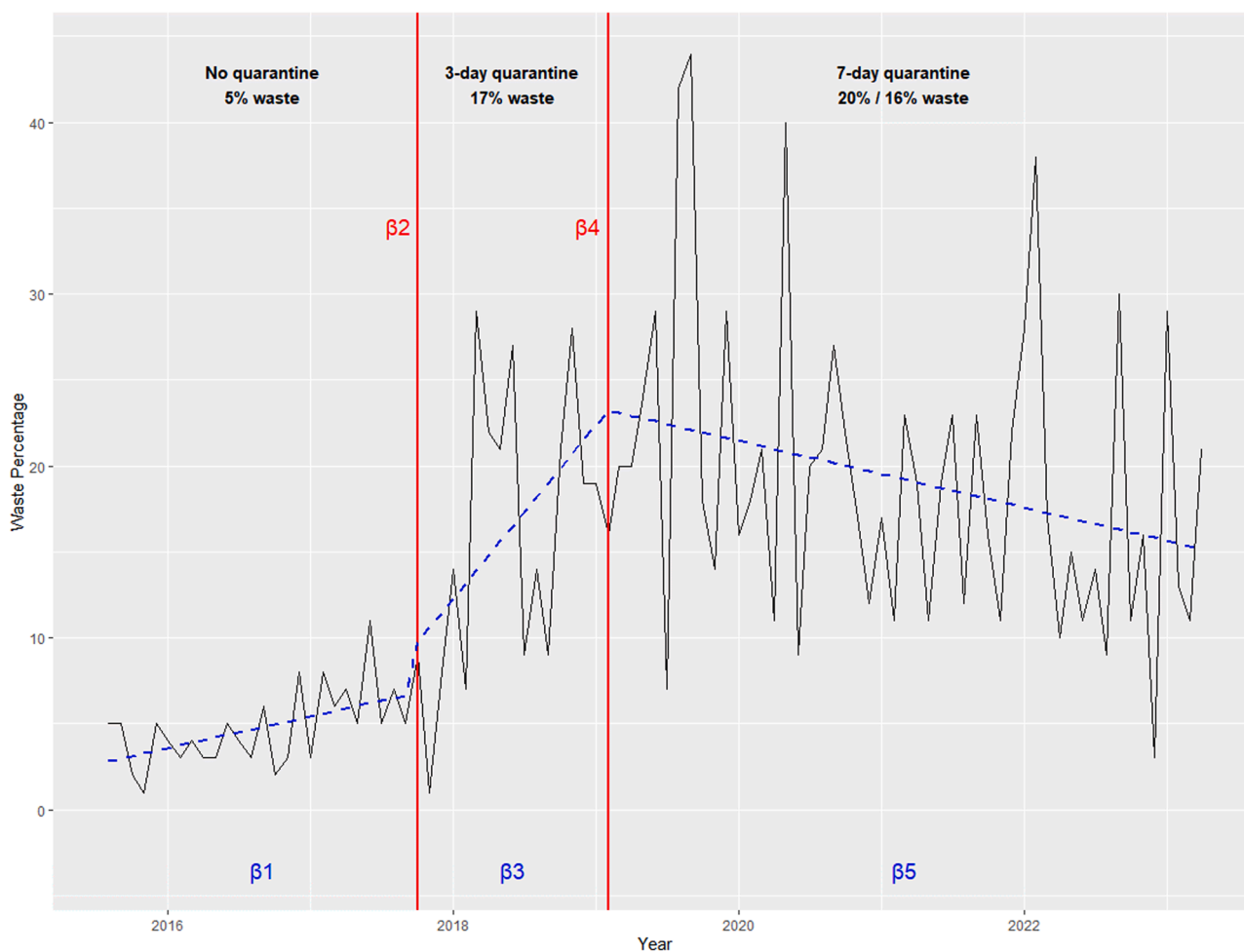

Fig. 1. Cumulative waste percentage of the five RTA aseptic syringes (cefazolin, insulin novorapid, magnesium chloride, milrinone and norepinephrine) that were not replaced by RTA PFSSs over time. Red vertical lines represent the start of a new time period; blue dotted line represents the interrupted time series model. β0 2.7 (p=0.369; 95% confidence interval (CI) −3.2 to 8.5), β1 0.2 (p=0.423; 95% CI −0.2 to 0.5), β2 2.3 (p=0.635; 95% CI −7.1 to 11.6), β3 0.7 (p=0.120; 95% CI −0.2 to 1.6), β4 1.0 (p=0.800; −7.0 to 9.1), β5 −1.0 (p=0.014; 95% CI −1.8 to −0.2).

differed significantly with the preceding period (*p*<0.001 in post-hoc testing). Of the three drug products in the intervention group, morphine 50mg = 50ml had the highest waste percentages over time, with 3%, 33%, 39% and 6% waste during the different time periods.

The ITS model for the control group (Fig. 1) shows a non-significant direct increase of 2.3% (*p*=0.635) in waste percentage after introducing the 3-day quarantine and a non-significant direct decrease of 1.0% (*p*=0.800) after introducing the 7-day quarantine. Introduction of the RTA PFSS in the ITS model of the intervention group (Fig. 2) showed a direct absolute decrease of 17.7% in waste percentage (*p*=0.083).

4. Discussion

In this study, we measured the amount of wasted RTA syringes in an ICU over a period of almost 8 years. We observed a significant difference in both the control and intervention group in total drug waste of RTA syringes between time periods, which may be attributed to the implementation of different microbiological QC procedures. The introduction of RTA PFSSs in the intervention group significantly reduced the amount of wasted RTA syringes from 31% during the 7-day quarantine period to only 5% during the PFSS period. To the best of our knowledge, this is the first study to measure the effect of introducing RTA PFSSs on drug waste.

Barbariol et al (2021) found drug waste percentages of RTA syringes as high as 86% for epinephrine, with a mean drug waste percentage of 38% during 1 month, corresponding to 4978 prepared syringes thrown away untouched (Barbariol et al., 2021). This study measured drug waste in the ICU as well as in the OR however, which makes a direct comparison to the outcomes in our study less appropriate. In the OR, syringes are prepared for every procedure to use in case of emergency situations. These products are not produced through aseptic batchwise filling followed by pharmaceutical QC, which gives them even shorter shelf-lives, possibly explaining the higher waste percentages than in the current study. Weinger (2001) collected 157 syringes prepared for 166 operating procedures and found that products like atropine, ephedrine, epinephrine, naloxone and phenylephrine had waste percentages of more than 50% (Weinger, 2001). These percentages are related solely to waste in the OR, which might explain the higher percentages.

The cefazolin 1000mg = 10ml drug product showed the highest waste percentage over the study period. This might be explained by the fact that this product is not used as much within the designated shelf-life compared to the batch size, which is 100 syringes. It should be noted that the preparation of this RTA aseptic syringe necessitates the dissolution of 100 gs of cefazolin, thereby precluding the possibility of producing smaller batch sizes for this specific product. Furthermore, the relatively short shelf-life of 21 days during the initial two time periods further restricted the effective time of use, thereby increasing the likelihood of waste.

Waste percentages fluctuated significantly in the first three time periods in which RTA syringes were prepared through aseptic batchwise filling with different quarantine times. This reflects the highly
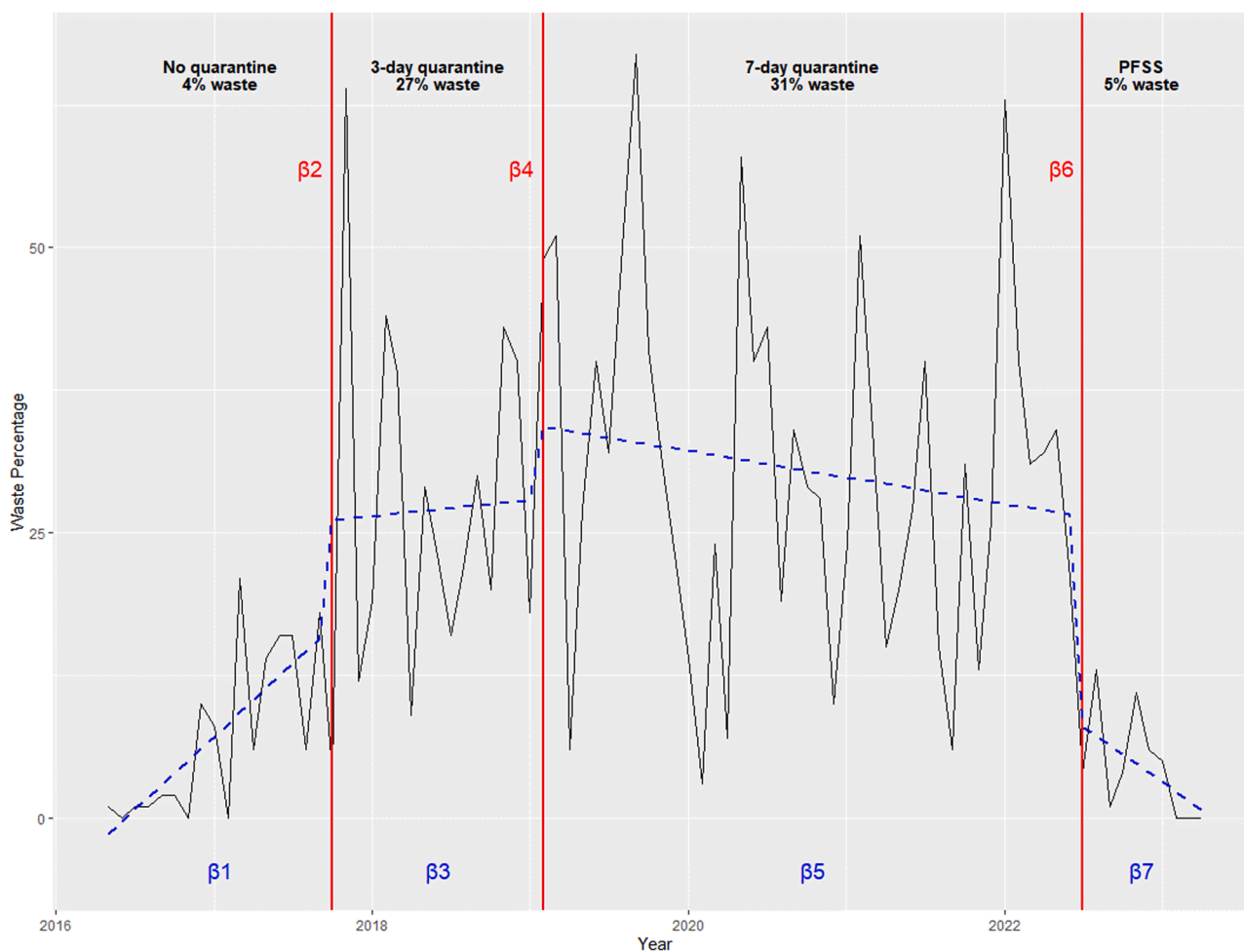

Fig. 2. Cumulative waste percentage of the three RTA aseptic syringes (morphine, midazolam and potassium chloride) that were replaced by RTA PFSSs in July 2022 over time. Red vertical lines represent the start of a new time period; blue dotted line represents the interrupted time series model. $\beta 0$ −2.4 (*p*=0.725; 95% confidence interval (CI) −16.1 to 11.2), $\beta 1$ 1.1 (*p*=0.115; 95% CI −0.3 to 2.4), $\beta 2$ 10.3 (*p*=0.280; 95% CI −8.5 to 29.1), $\beta 3$ −0.9 (*p*=0.342; 95% CI −2.9 to 1.0), $\beta 4$ 6.6 (*p*=0.395; 95% CI −8.8 to 22.1), $\beta 5$ −0.3 (*p*=0.682; 95% CI −1.8 to 1.2), $\beta 6$ −17.7 (*p*=0.083; −37.9 to 2.4), $\beta 7$ 0.6 (*p*=0.680; −3.6 to 2.4).

unpredictable nature of drug use in the ICU. Because of this nature, a surplus of aseptic syringes is prepared every month to ensure availability. However, when drug usage is lower than expected, a significant amount of aseptic syringes is wasted due to their one-month shelf-life. The additional time period in which RTA PFSSs were used, showed that PFSSs can be introduced to diminish drug waste due to overproduction.

One may question the justification for extending quarantine time if it results in a high percentage of waste for RTA syringes prepared through aseptic batchwise filling. It is crucial to acknowledge that although the risk of microbial contamination of RTA syringes produced through aseptic batchwise filling in hospital pharmacies is lower than preparing RTA syringes in the clinical area, the consequences can be severe since the syringes are intended for use by multiple patients. Further investigation could explore the frequency with which QC results on day 7 fail to confirm previous QC results on day 3, indicating the potential for incorrect release of batches based on day 3 QC results.

Remarkably, waste percentages of the three RTA PFSSs, which all have shelf-lives of 18 months, were higher than 0% during the period of their introduction (July 2022 – May 2023). This has two explanations. First, the initial RTA PFSS batches of morphine and potassium chloride we received from *'Apotheek A15'* expired at the end of August 2022, as they were manufactured by *'Apotheek A15'* well in advance of their actual utilization, resulting in limited remaining shelf-lives. Second, hospital pharmacy staff that replenishes the ServeRx® refrigerators also rectify any discrepancies in stock levels. These discrepancies arise when the ServeRx® system indicates a different quantity of stock compared to the actual amount present. The hospital pharmacy staff may occasionally utilize incorrect commands within the ServeRx® system while addressing these variations, leading to a misperception that RTA syringes were discarded due to expiration when, in fact, the discrepancy originated from an inaccurate recording of the stock quantity. We anticipate that the waste percentages of RTA PFSSs will approach 0% when new RTA PFSSs are produced on demand.

The results of the ITS model of the intervention group (Fig. 2) showed a direct decrease in waste percentage of 17.7% after PFSS introduction, but this effect did not reach statistical significance ($p=0.083$). However, it is important to note that the waste percentages of the RTA PFSSs were only measured over a relatively short period of 10 months, within a total study period of almost 8 years. This limited data on the waste percentages of the RTA PFSSs may have contributed to the lack of statistical significance of the intervention effect in the ITS model.

To reduce drug waste of RTA aseptic syringes even further, it would be interesting to replace more products by PFSSs. Good candidates for this replacement are drugs of which the use is hard to predict (i.e. higher waste because of excess production), which have a low degradation rate and which are physically and chemically stable enough to endure sterilization. For instance, drugs such as insulin and milrinone are unsuitable for sterilization by heat due to their susceptibility to degradation at elevated temperatures.

Introduction of RTA PFSSs does not only help achieve environmental sustainability goals by directly reducing drug waste, but also by less workforce waste. A recent workflow time study showed that nursing staff time was associated with the waste disposal process. Nursing staff time spent by preparing the syringes by themselves totaled 14 h during a study period of 15 days (Hertig et al., 2021). The time that is won by using PFSSs thus also offers a solution for labor market tightness in healthcare.

The main strength of this study is the very large amount of data collected and robust method of data collection, giving high data validity and reliability. As the refrigerators in which the RTA syringes are stocked are only opened by actual registrations by hospital pharmacy staff or critical care nurses in the ServeRx® medication management system, the numbers presented in this study are a very accurate representation of clinical practice. The main limitation of this study is that we only looked at the transaction data of the syringes and that no other data was included in the ITS model. Possible elements that could have impacted on drug waste over time were thus not taken into account.

5. Conclusion

Drug waste percentage of RTA syringes for the ICU can be substantially decreased by introducing RTA PFSSs, supporting hospitals to enhance environmental sustainability. Furthermore, the waste percentage of RTA syringes prepared through aseptic batchwise filling by the hospital pharmacy is significantly impacted on by quarantine time.

CRediT authorship contribution statement

Thomas G. van Gelder: Conceptualization, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Arief Lalmohamed:** Methodology, Formal analysis, Writing – review & editing, Supervision. **Kim D. Dorst-Mooiman:** Methodology, Writing – review & editing. **Jan C. Dekker:** Resources, Writing – review & editing. **Marcel J. Schinkel:** Conceptualization, Resources. **Maaike A. Sikma:** Writing – review & editing. **Esther V. Uijtendaal:** Methodology, Writing – review & editing. **Toine C.G. Egberts:** Conceptualization, Resources, Supervision, Project administration.

Declaration of Competing Interest

None.

Data availability

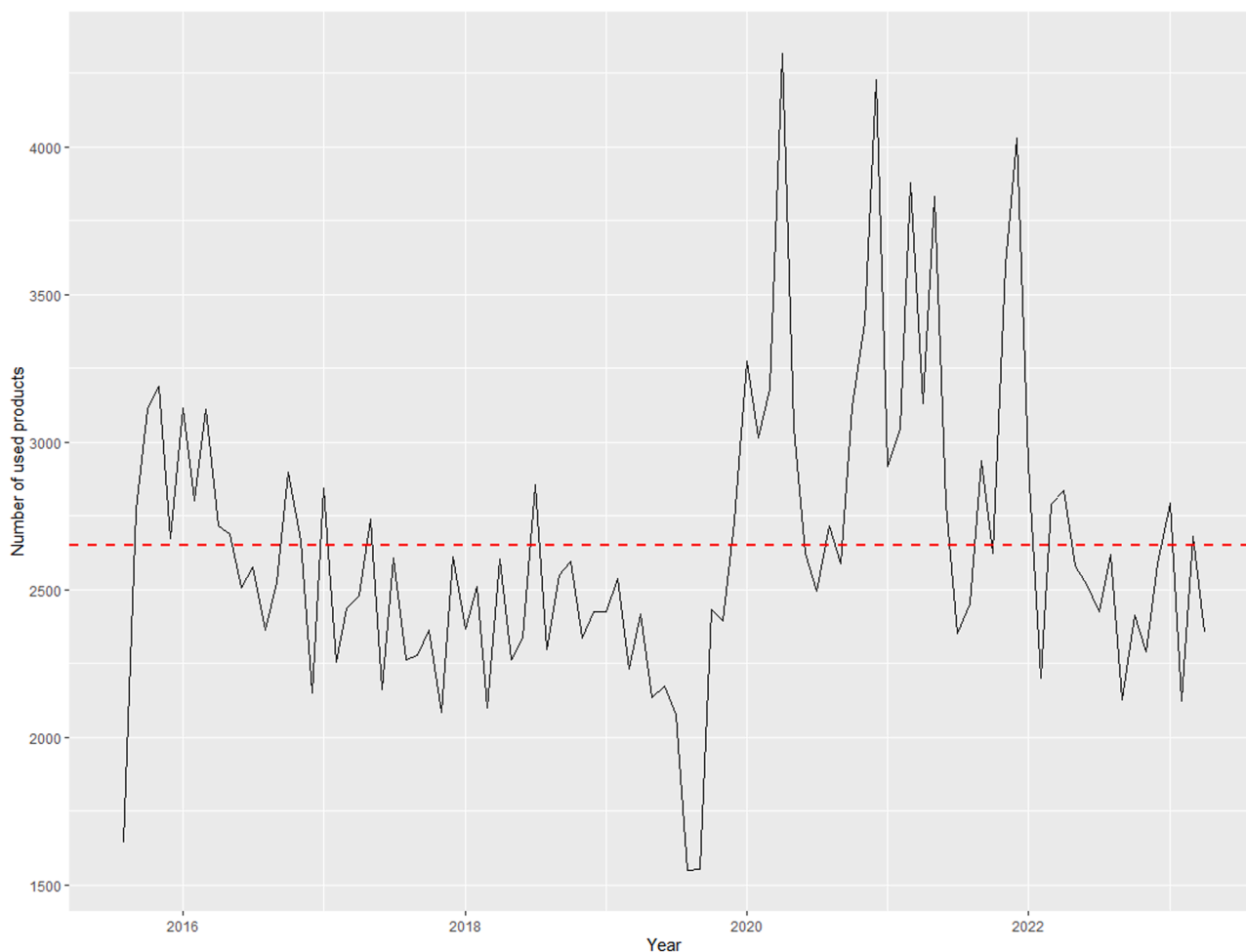Data will be made available on request.

Appendix

Fig. A1

Fig. A1. Number of drug products used by the ICU nursing staff per month; red dotted line represents mean number of used products per month.

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