

Not all syringes are equal – the comparative performance of syringes in propofol target-controlled infusions

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Background: Syringe infusion pumps are used for target-controlled infusions (TCI) and total intravenous anaesthesia (TIVA). Modern pumps compatible with third-party syringes require user input for the syringe type loaded. Within public hospitals in Johannesburg, South Africa, the supply of programmed, validated 50/60 ml syringes is inconsistent, with various non-programmed syringes substituted. These syringes are used for infusions when programmed variants are unavailable. This study aimed to compare the TCI propofol volume output of the non-programmed syringes to their programmed counterparts.

Methods: A contextual, quasi-experimental study was performed. The study site consisted of four academic anaesthesiology hospital departments in Johannesburg, South Africa. A syringe audit, description, and estimation of their measurements were performed, along with an assessment of syringe options across the available infusion pumps. An experimental bench test assessing the gravimetric propofol output of TCIs was conducted. The non-programmed syringes' propofol output was compared to four different, named, programmed syringes.

Results: Five different TCI-enabled syringe pumps and four different non-programmed syringes were found across the hospitals. The three non-programmed variants were Luer-slip types and one Luer-lock type. Non-programmed syringes using the BD Plastipak™ option delivered between 17.6% and 21.3% more than the BD Plastipak™ syringe. The B. Braun Original-Perfusor® Syringe (OPS®) option breached the 5% cut-off for overdosage with two non-programmed syringes. Inappropriate infusion end-alarms and premature infusion cessation occurred with all four non-programmed syringes using the B. Braun OPS® option. All four non-programmed syringes delivered volumes within $\pm 2\%$ when using two programmed syringe options (Injectomat® and Terumo®).

Conclusions: Over-delivery of propofol may have significant sequelae, such as cardiac instability, inappropriate anaesthesia depth, and rarely, propofol-related infusion syndrome (PRIS). Inappropriate alarms and infusion cessation could lead to accidental awareness during TCI/TIVA. Recommendations were made for programmed syringe procurement and the safe use of non-programmed syringes.

Keywords: propofol, medication errors, target-controlled infusion, syringe infusion pump, patient safety

Introduction

The modern syringe pump is an electromechanical, micro-infusion positive-pressure pump.¹ They are noted to be some of the most accurate pumps, with reported accuracies of $\pm 2-5\%$.¹⁻⁴ In anaesthesia, they are used to deliver either constant flow rate infusions or variable rate infusions, such as target-controlled infusions (TCIs).⁵

Once mounted, the sensor at the barrel clamp measures the syringe chamber.⁶ A list of programmed syringes is displayed, with user confirmation required. At this point, incorrect syringes can be chosen.^{6,7} Modern pumps are designed to allow the use of third-party syringes, contrary to the original Diprifusor® TCI system, which was only compatible with Diprivan® (propofol) and a proprietary radiolabelled, prefilled syringe.⁷ Current total intravenous anaesthesia (TIVA) practice favours combinations of propofol and remifentanyl TCIs.⁸ Before TCIs, TIVA was achieved by manually controlled infusion protocols, like the "Bristol regime"⁹

Syringe pumps can be prone to errors, including the syphon effect and free flow, backflow into infusion lines, inadvertent boluses, occlusions, and post-occlusion boluses.¹⁰ Modern pumps have safety mechanisms (i.e. pre-alarms and alarms).³ Tooke and Howell described the necessity for the use of and under- and overdosage seen with non-programmed syringes, as well as other alarm errors.⁶ Pump manufacturers, as well as the United States Food and Drug Administration, note that only dedicated validated syringes should be used, as the use of the "non-compatible" syringes may result in insufficient occlusion recognition, inaccurate drug delivery, and other faults.^{3,11,12}

There is no single industry standardisation for syringe measurements, and manufacturers produce syringes with metrics that are unique to their branded products.^{6,7} The supply of syringes to public hospitals is primarily governed by contracting and procurement processes.⁶ These syringes are not always the programmed variants, with many non-programmed syringes substituted. Third-party consumables ultimately reduce cost, thus increasing pump accessibility.^{1,6} A study by Chae et al.⁷ in 2013 investigated the impact of the incorrect syringe choice

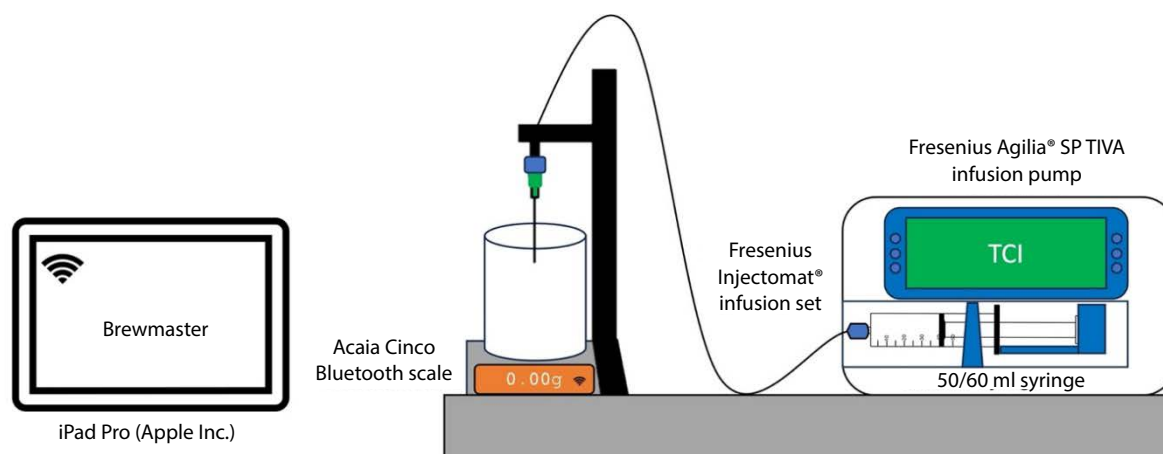


Figure 1: Schematic of the study setup

Note: Brewmaster is a proprietary application of Acaia (Acaia Corp.) that connects via Bluetooth to the Acaia Cinco Bluetooth scale. The application was designed by the scale manufacturer as a companion application for the scale, allowing the recording of mass data points in relation to their time measured for each infusion. TCI – target-controlled infusion, TIVA – total intravenous anaesthesia

during propofol TCIs, highlighting the possibility of incorrect syringe selection.

In Johannesburg, South Africa, using available non-programmed syringes for TCIs is a common practice when the programmed variants are unavailable. The ramifications of this practice are unknown and potentially concerning for patient safety. The study aimed to describe the pump and syringe populations and to estimate the potential under- and overdosage of non-programmed syringes compared to programmed syringes by assessing the volume of propofol output during standardised TCIs.

Methods

Ethical clearance (reference number: W-CBP-230712-02) for this study was granted as a waiver from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand. This study design and manuscript was prepared following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.¹³

An initial audit was conducted, outlining the TCI-enabled syringe pumps and available 50/60 ml syringes in the four central academic hospitals affiliated with the University of the Witwatersrand, Johannesburg, South Africa. All syringes were measured, and their metrics were tabulated.

Definitions of terms:

- **Programmed syringes:** These are syringes used as “control” syringes for the study. They are named, manufacturer-validated variants whose metrics are programmed into the pump databases and are user-selectable options for syringe choice.
- **Non-programmed syringes:** These syringes are not validated for use by the pump manufacturer, and their metrics are not programmed into the pump databases. They are used as “study” syringes.

Syringes were inspected for expiry dates and defects. New syringes were used for every infusion run. Propofol was carefully drawn up with a wide-bore (14 G) needle to the maximum reported volume and attached to the infusion line. A new Fresenius Injectomat® infusion line with an anti-syphon valve was connected to an 18 G intravenous catheter.¹⁴ The line was primed until no bubbles were visible in the syringe or infusion set. Propofol was inspected for bubbles and splitting. The infusion set priming volume was ~ 1.4 ml, according to the manufacturer.¹⁴ Syringe starting volume after priming was visually inspected at ~ 58 ml for 60 ml syringes and ~ 48 ml for 50 ml syringes.

A bench test was set up using an Acaia Cinco Bluetooth scale (Acaia Corp.), chosen for its accuracy to 1/100th of a gram and Bluetooth technology. Gravimetric analysis of pump output was described by Chae et al.,⁷ and a similar study method was designed. The scale was charged, set up, calibrated per the manufacturer, and placed on a level workstation. Propofol (Fresenius Propoven 1%, Fresenius Kabi SA [Pty] Ltd.) was used for the study. The average mass of the propofol used each day was measured in a calibrated volumetric flask, and the average was used to derive a conversion factor for volume (i.e. 1.0 ml = 1.00969 g).

A 100 ml borosilicate glass beaker was prepared with an adhesive clear film cover to prevent evaporation and spillage. For each infusion, the scale was tared and connected to the Brewmaster (Acaia Corp.) application, installed on an iPad Pro (Apple Inc.). Raw mass data points were recorded and exported as a CSV file to Microsoft® Excel.

A recently serviced Fresenius Agilia® SP TIVA syringe pump was used for all infusion runs. A schematic of the experimental study setup is depicted in Figure 1. The pump was selected because it was compatible with all four programmed control syringes when loaded with all four non-programmed syringes, as seen in Figure 2. The pump was connected to a main power source throughout the study and was set up on an identical workstation adjacent



Figure 2: Syringe population

* Denotes programmed "control" syringe.

† Denotes non-programmed "study" syringe.

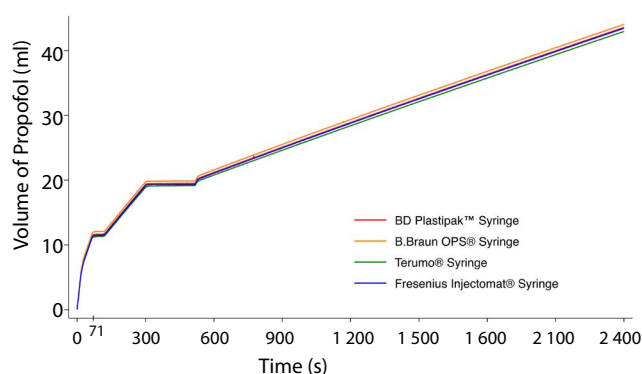


Figure 3: Volume versus time plots of the named control-syringe infusion

to the scale. Recording of mass data points only began once the scale registered a change in mass.

For every infusion, the pump was programmed with the same TCI model using standard patient parameters (i.e. Schnider effect-site TCI, propofol 10 mg/ml, age (years): 40, weight (kg): 70, height (cm): 170, and gender: male). The infusion was started with the initial C_{et} (effect-site target concentration) = 7 $\mu\text{g/ml}$. At the five-minute (300 seconds) mark, as recorded by the Brewmaster application, the C_{et} was decreased to 3 $\mu\text{g/ml}$. The pump was then allowed to run for 35 minutes to the 40-minute mark. Two infusions were run for each syringe variant and syringe pump setting. Datasets were imported into Microsoft® Excel, averaged, and converted to millilitres.

At the end of each day of testing, all hazardous consumables (propofol, infusion sets, glass ampoules, and needles) were disposed of in an appropriate pharmaceutically safe manner for incineration.

Propofol, Injectomat® syringes, and infusion sets were donated by Fresenius Kabi SA (Pty) Ltd. Named syringes were donated by both B. Braun Medical SA (Pty) Ltd. and Becton Dickinson SA

(Pty) Ltd. Terumo® syringes were purchased privately. Figures 3 and 4A–D were plotted using Stata® SE 18 (StataCorp LLC).

Results

Table I summarises the syringe and pump audits and syringe metrics. Four different non-programmed syringes met the inclusion criteria across the study site. No programmed variants of any type were available across the study site during the study period.

For control syringe (programmed variant) selection, the four non-programmed study syringes were each loaded into the different syringe pumps found across the study site. A total of 30 distinct user-selectable syringe choices were found as possible options across all five syringe pumps when mounting each of the non-programmed syringes. Prefilled syringes and enteral feeding syringes were excluded. The four most commonly occurring syringes were chosen as the control syringes for the study. The average of the paired infusions for each of the four control syringes chosen above is plotted as the control infusions in Figure 3. Paired study infusions using the non-programmed syringes were run using each of the control syringe choices on the pump, and their averages are plotted in Figure 4A–D. While plotting the infusions, two distinct plateaus were noted. The initial plateau occurred 71 seconds into the infusion and the second at 300 seconds. The average volumes delivered at these time points, and at 2400 seconds, are summarised in Table IIA. Table IIB details the segmental flow rates for each infusion study.

During the infusions using the B. Braun Original-Perfusor® Syringe(OPS)® pump setting and all four of the non-programmed syringes, the pump alarmed between the 31st and 34th minutes during the infusion, displaying the "Near end infusion !!" pre-alarm. The pump ceased delivery between 36 and 39 minutes and alarmed "End of infusion !!". To complete the study, a second, new and identical, filled and primed syringe was mounted as quickly as possible to continue the infusion to the 40-minute mark. The residual propofol in the first syringes for each infusion was weighed.

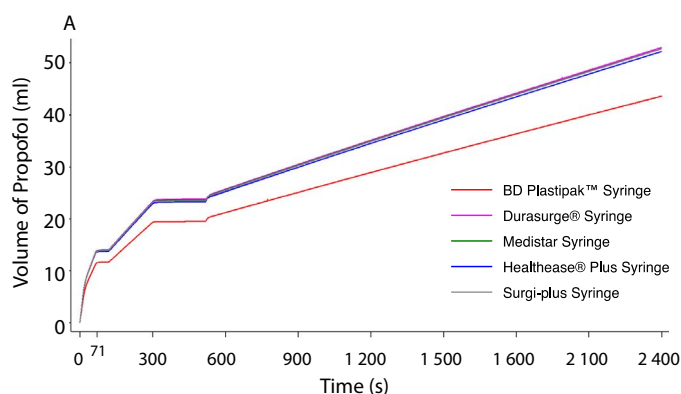


Figure 4A: Volume versus time plot of non-programmed syringes versus BD Plastipak™ option

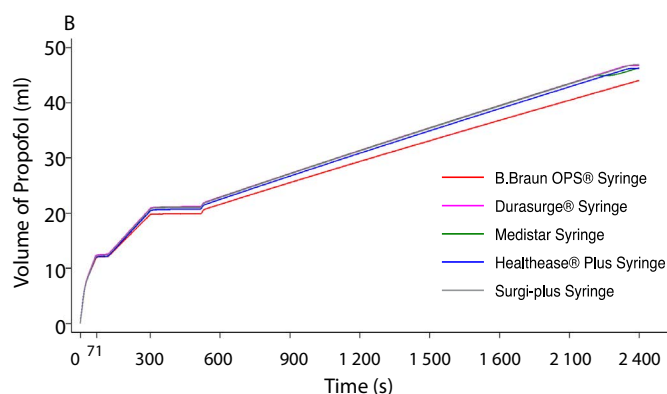


Figure 4B: Volume versus time plot of non-programmed syringes versus B. Braun OPS® option

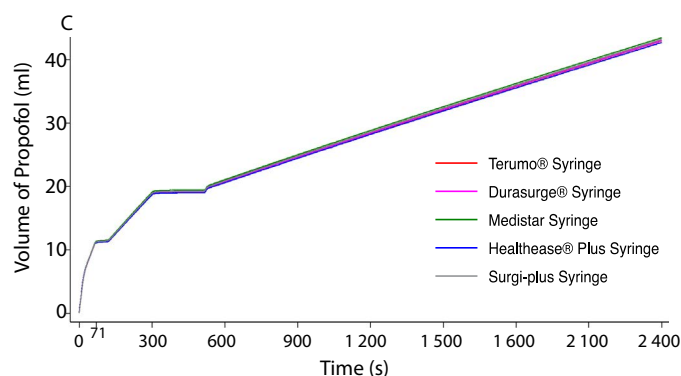


Figure 4C: Volume versus time plot of non-programmed syringes versus Terumo® option

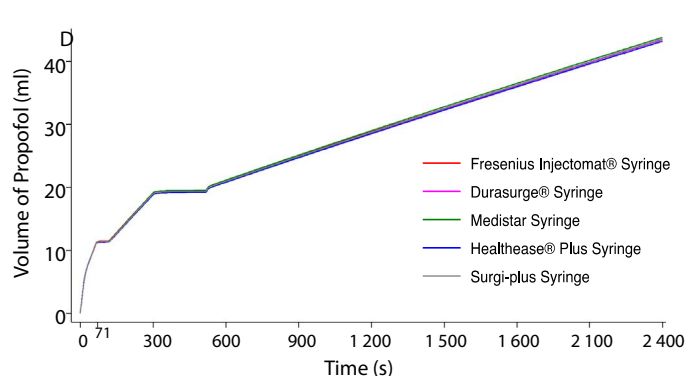


Figure 4D: Volume versus time plot of non-programmed syringes versus Fresenius Injectomat® option

Table I: Syringe audit and measurements and pump audit

Syringe	Internal diameter (mm)	Barrel wall thickness (mm)	External diameter (mm)	Length of plunger at 0 ml, measured from outside flange to inside plunger (mm)	Rubber plunger height (mm)	Scale length from 0 ml to maximal reported volume (mm)	Scale length (10 ml = x mm)	Maximum reported volume (ml)	Luer-lock or Luer-slip nozzle
Non-programmed syringes									
MediStar Luer-Slip 50/60 ml	29.2	1.1	30.8	16.2	8.8	90.0	15.0	60.0	Slip
Neomed Healthease® Plus 60 ml	29.1	1.1	30.5	20.2	8.4	89.3	14.5	60.0	Slip
DuraSurge® Disposable Syringe 50 ml	30.0	1.0	30.6	18.8	8.4	89.5	14.9	60.0	Slip
SurgiPlus 3-Part Syringe 50/60 ml	28.8	1.3	31.0	18.8	8.8	90.5	14.8	60.0	Lock
Programmed syringes									
BD Plastipak™ 50 ml	26.4	1.6	29.2	13.1	6.2	109.9	18.3	60.0	Lock
B. Braun OPS® 50 ml	27.7	1.5	30.2	32.8	7.7	80.6	16.0	50.0	Lock
B. Braun® Omnifix® 50 ml	27.7	1.5	30.2	15.5	7.7	97.5	16.0	60.0	Lock
Terumo® 50 ml	29.6	1.6	31.6	19.2	10.8	88.0	14.5	60.0	Lock
Fresenius Injectomat® Spritze 50 ml	28.9	1.3	31.5	15.2	12.1	89.3	14.8	60.0	Lock
Pumps found across the study site									

- MedCaptain™ HP TCI
- BD/CareFusion Alaris™ PK
- B. Braun Perfusor® Space TCI
- Fresenius TIVA Agilia® SP
- Fresenius Orchestra® Base Primea with DPS and Visto modules

OPS® – Original-Perfusor® Syringe, TCI – target-controlled infusion, TIVA – total intravenous anaesthesia

Note: Syringes are named by the manufacturer, and maximal reported volumes differ from the name on the packaging.

Table IIA: Average volumes and per cent differences for each infusion permutation

		Vol. (ml) at T = 71 s [SD]	% difference	Vol. (ml) at T = 300 s [SD]	% difference	Vol. (ml) at T = 2 400 s [SD]	% difference
Study syringe	Syringe control – BD Plastipak™	11.6*	[0.09]	19.3*	[0.13]	43.7*	[0.27]
	DuraSurge® Disposable Syringe	13.9	[0.02]	23.3	[0.09]	53.0	[0.11]
	MediStar Luer-Slip	13.8	[0.01]	23.2	[0.04]	52.7	[0.06]
	Neomed Healthease® Plus	13.6	[0.59]	22.9	[0.58]	52.2	[0.59]
	SurgiPlus 3-Part Syringe	13.8	[0.56]	23.2	[0.49]	52.7	[0.56]
Study syringe	Syringe control – B. Braun OPS®	12.0*	[0.17]	19.7*	[0.18]	44.2*	[0.12]
	DuraSurge® Disposable Syringe	12.4	[0.21]	20.8	[0.19]	46.7	[0.41]
	MediStar Luer-Slip	12.2	[0.02]	20.7	[0.02]	46.3	[0.00]
	Neomed Healthease® Plus	12.0	[0.22]	20.4	[0.08]	46.3	[0.24]
	SurgiPlus 3-Part Syringe	12.2	[0.10]	20.7	[0.00]	47.0	[0.23]
Study syringe	Syringe control – Injectomat®	11.4*	[0.03]	19.2*	[0.01]	43.6*	[0.11]
	DuraSurge® Disposable Syringe	11.2	[0.24]	18.9	[0.22]	43.5	[0.23]
	MediStar Luer-Slip	11.3	[0.01]	19.1	[0.02]	43.8	[0.02]
	Neomed Healthease® Plus	11.2	[0.37]	18.8	[0.26]	43.2	[0.17]
	SurgiPlus 3-Part Syringe	11.3	[0.08]	19.0	[0.11]	43.6	[0.01]
Study syringe	Syringe control – Terumo®	11.1*	[0.44]	18.8*	[0.48]	43.0*	[0.34]
	DuraSurge® Disposable Syringe	11.2	[0.48]	18.8	[0.35]	43.0	[0.36]
	MediStar Luer-Slip	11.3	[0.10]	19.1	[0.04]	43.5	[0.07]
	Neomed Healthease® Plus	11.1	[0.29]	18.7	[0.27]	42.7	[0.16]
	SurgiPlus 3-Part Syringe	11.3	[0.24]	18.9	[0.21]	43.2	[0.19]

Vol. – volume, SD – standard deviation, OPS® – Original-Perfusor® Syringe

Note: All volumes in Table IIA are averages of the two infusions run for the permutations.

* Values are derived from infusions where the pump was programmed with the named syringe and the correctly matched syringe (i.e. the control).

† Value was rounded.

Table IIB: Segmental flow rates

		Segmental flow rates (ml/hr)		
		Time = 0–71 s	Time = 72–300 s	Time = 301–2 400 s
Study syringe	Syringe control – BD Plastipak™	587.0*	122.1*	41.7*
	DuraSurge® Disposable Syringe	704.2	148.3	50.8
	MediStar Luer-Slip	699.8	148.2	50.6
	Neomed Healthease® Plus	690.4	146.3	50.2
	SurgiPlus 3-Part Syringe	697.5	148.0	50.6
Study syringe	Syringe control – B. Braun OPS®	607.7*	121.8*	41.9*
	DuraSurge® Disposable Syringe	628.7	132.4	44.4
	MediStar Luer-Slip	617.2	133.6	44.0
	Neomed Healthease® Plus	610.5	130.6	44.4
	SurgiPlus 3-Part Syringe	620.5	133.3	45.0
Study syringe	Syringe control – Injectomat®	578.5*	122.4*	41.8*
	DuraSurge® Disposable Syringe	567.5	121.4	42.1
	MediStar Luer-Slip	572.1	123.6	42.3
	Neomed Healthease® Plus	568.3	119.7	41.8
	SurgiPlus 3-Part Syringe	570.6	121.6	42.2
Study syringe	Syringe control – Terumo®	563.9*	121.3*	41.5*
	DuraSurge® Disposable Syringe	567.0	119.5	41.6
	MediStar Luer-Slip	575.4	122.1	41.8
	Neomed Healthease® Plus	563.7	119.0	41.2
	SurgiPlus 3-Part Syringe	570.6	120.8	41.6

OPS® – Original-Perfusor® Syringe

* Values are derived from infusions where the pump was programmed with the named syringe and the correctly matched syringe (i.e. the control).

After volume conversion, it was found that between 11.2 and 13.9 ml remained in each syringe. No other syringe pump settings displayed premature alarms or infusion cessation when used with the non-programmed syringes.

Other observations noted during the study included the propofol “slipping” behind the plunger during the filling of all the non-programmed syringes, as well as “damage” (in the form of stress marks) to the syringe chamber. The “damage” occurred when loading two non-programmed (Healthease® Plus and DuraSurge®) syringes into the BD/CareFusion Alaris™ PK pump at the barrel mounting clamp while conducting the syringe choice audit. This did not occur with the programmed variants.

Discussion

This study showed that heterogeneity exists for available syringes and TCI pumps within four academic anaesthesiology hospital departments in Johannesburg, South Africa. Five different syringe pumps were described, with 30 different user-programmable syringe choices for the non-programmed syringes. This contributes to incorrect syringe choice of both programmed and non-programmed syringes.⁶

The study’s main objective was to compare the volume output of the non-programmed syringes to their programmed counterparts. A volume variation > 5% was considered overdosage, as the syringe pump’s reported accuracies fall within a range of ± 2 –5% when using validated syringes.^{1–4}

When non-programmed syringes were used, the BD Plastipak™ pump setting showed the highest overdosage of 17.6–21.3%, followed by the B. Braun OPS® setting and two syringes overdosing. Notably, the four non-programmed syringes delivered infusions closely matching (within $\pm 2\%$) the Terumo® and Injectomat® options. This over-delivery of propofol is attributed to their differing barrel diameters, as seen in Table 1 and Figure 2.

The BD Plastipak™ has the smallest cross-sectional diameter, followed by the B. Braun OPS® and Omnifix® syringes. This translates to greater horizontal displacement of the plunger to deliver equal volumes. The non-programmed syringes exhibited tight agreement to their controls when used with the Terumo® and Fresenius Injectomat® options, as their cross-sectional diameters were similar.

The non-programmed syringes in this study population had thinner barrel wall thicknesses. This was relevant for two non-programmed syringes being damaged when loaded in the BD/CareFusion Alaris™ PK pump during the audit. If the clamp cracked the syringe barrel, an air leak could occur, allowing the free flow or syphoning of propofol when used with sets without anti-syphon valves.¹⁰ The ramifications of undetected free flow of propofol are potentially severe.

Inappropriate alarms occurred with the B. Braun OPS® setting, with premature termination of the infusion. This is seen in Figure 4B, where there is a change in the graph gradients towards the

end. During these infusions, the first syringe also ended with a “large” residual volume. This is worrisome as it provides a visual false sense of security that the syringe will not empty soon and may catch the clinician off guard. Further, inappropriate termination of the TCI is concerning as changes in the depth of anaesthesia can occur.

Inappropriate alarms are attributed to the differing plunger lengths at “empty” for each syringe, as shown in Table 1. At a volume of 0 ml (i.e. “empty”), the B. Braun OPS® syringe had the longest plunger length of 32.8 mm, which is > 12 mm greater than all of the non-programmed syringes.

The pump uses the horizontal displacement of the plunger to calculate residual volumes. The non-programmed variants are truly “empty” at shorter plunger lengths compared to the B. Braun OPS® syringe, explaining why the pump ceased delivery with the B. Braun OPS® syringe choice despite residual propofol in the syringes. As TCIs are variable rate infusions, clinicians would potentially not notice a syringe emptying quicker than it should, as with the BD Plastipak™ setting and non-programmed syringes.⁵

Only one of the non-programmed syringes was a Luer-lock type. A joint guideline for the practice and provision of TIVA recommended that Luer-lock connectors be used to prevent inadvertent detachment.¹⁵ Infusion sets used for TCIs and TIVA should also include anti-syphon and anti-reflux valves.^{2,15} These inclusions increase the pressure developed within the line. Luer-locks provide secure, pressure-resistant connections between the syringe, infusion set, and patient. Without them, disconnection and, ultimately, awareness is risked, as infusion to the patient would stop.

The implications of propofol overdose during a TCI/TIVA are broad. The Schnider TCI model accounts for age during infusion rate calculations and delivers lower doses, such that cardiac instability in the elderly is less likely.¹⁶ Therefore, the over-delivering syringe has the potential to cause haemodynamic instability in the elderly, even with appropriate targets set.

In the bench test, using the standard patient parameters and the BD Plastipak™ syringe choice, the control infusion delivered ~ 116 mg (~ 11.6 ml) of propofol during the first 71 seconds of the infusion (i.e. the induction period). The non-programmed syringes delivered ~ 136–139 mg (13.6–13.9 ml) of propofol. The clinical impact of the extra 2.0–2.3 ml of propofol is uncertain and likely minimal. However, one can surmise that with a higher patient body mass index, the absolute amount of propofol infused would increase, along with the risk of cardiac instability. Of note, in the same study set, each infusion over-delivered ~ 10 ml (~ 100 mg) of propofol throughout the study. The implication of this would be more frequent syringe changes during TCIs, potential inappropriate depth of anaesthesia, accumulation of propofol, and potentially unnecessary propofol waste with increased costs.

Inappropriate depth of anaesthesia may occur with propofol over-delivery. The 5th National Audit Project (NAP5) report states that increasing the dose of an anaesthetic agent will prevent awareness; however, at the cost of adverse events, like delayed recovery and postoperative confusion.¹⁷ Deep anaesthesia is one of many precipitating factors for perioperative neurocognitive disorders (NCD).¹⁸ Therefore, the over-delivering syringe can be partially implicated in the aetiology of NCDs. The rare but pertinent complication of propofol-related infusion syndrome (PRIS) with prolonged infusions also requires consideration.¹⁵ With propofol infusions being used in the intensive care unit (ICU) setting, over-delivery of propofol for extended periods may precipitate PRIS in the at-risk.^{15,19}

The idea that a pump can over-deliver by a factor of 20% throughout the infusion is worrisome, especially when used for extremely long infusions, or with more potent or concentrated vasoactive drugs. The context in which the studied departments function is also important, as cost may limit the procurement of “brand name” consumables. A patient safety statement was drafted, with recommendations on using these pump syringe choices with the specific study population of pumps and syringes.

Previous recommendations have been made for a standardised device and consumable procurement approach within departments.^{10,15} Authors advise that individual departments keep only one type of device.^{10,15} Nimmo et al.,¹⁵ along with Tooke and Howell, further recommend one syringe type. Study results showed that more than one type of TCI pump was present in individual hospital departments.⁶ During the study period, no programmed syringes were found in any of the departments, highlighting and confirming the use of non-programmed syringes instead of programmed variants.⁶

Strengths of this study included the use of actual propofol lipid emulsions, allowing the pump to behave in a realistic and clinically relevant manner (compared to the use of water with assumed differences in viscosity and flow characteristics), as well as the elucidation of inappropriate alarms. This study was limited by only assessing the syringes in the TCI pathway, along with relatively short infusion durations, which were designed for study feasibility. Another limitation is the variable syringe availability; syringes currently available may differ from those studied, limiting the scope of recommendations.

The scope of broader applicability is also limited because three of the four non-programmed syringes were Luer-slip variants, which are explicitly advised against in TCI and TIVA use.¹⁵ However, this study highlights the real-world necessity for practitioners to use consumables that are not ideal (i.e. non-programmed Luer-slip syringes). Thus, the audit component of this study describes current clinical practices and adds important data to the broader literature on TCIs, especially as they become more prevalent in this setting.

As the use of TCIs/TIVA increases, we emphasise the recommendations of Nimmo et al.¹⁵ for using anaesthesia depth

monitors, like processed electroencephalograms (EEG), when using TCIs/TIVA wherever possible. This is especially important for concomitant neuromuscular blockade under TIVA.¹⁵ Utilising the depth of anaesthesia monitors when using non-programmed syringes will allow the clinician to safely titrate the depth of anaesthesia, even when over-delivering non-programmed syringes are used, to avoid both awareness and inappropriate depth.

Therefore, we recommend the procurement and use of only validated, programmed Luer-lock syringes, as per the pump manufacturers. However, in their absence, the specific non-programmed syringes studied should only be used if absolutely necessary, and only using the Terumo® or Injectomat® options for the provision of TCIs, as these two syringe choices showed tight agreement ($\pm 2\%$ difference) compared to the controls. Lastly, we reaffirm the recommendations made by Tooke and Howell, Keay and Callander, and Nimmo et al.¹⁵ for the safe provision of TCIs and TIVA.^{6,10}

The clinical significance of the overdosage found is not clear at this point but warrants future investigation. We further recommend that a similar study be conducted with any new non-programmed variants to identify “best fit” syringe pump options in this setting.

Conclusion

This study found heterogeneity in the syringe and pump populations within the study site. Most non-programmed syringes available offer thinner barrel thicknesses and lack the Luer-lock connector. The absence of programmed syringes for TCIs has the potential for propofol overdosage when non-programmed syringes are used instead.

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Conflict of interest

DJ Miller declares that the study was undertaken as a partial requirement for the completion of the Masters of Medicine in Anaesthesia at the University of the Witwatersrand. The other authors declare no conflict of interest.

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Ethical approval

Ethical approval was granted as a waiver from the University of the Witwatersrand Human Research Ethics Council (Medical), reference number: W-CBP-230712-02. The authors declare that this submission follows the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010. This article does not contain any studies with human or animal subjects.

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References

1. Kan K, Levine WC. Infusion pumps. In: Ehrenwerth J, Eisenkraft JB, Berry JM, editors. *Anaesthesia equipment: principles and applications*. 3rd ed. St. Louis: Elsevier; 2021. p. 351-67. <https://doi.org/10.1016/B978-0-323-67279-5.00016-9>.
2. Aston D, Rivers A, Dharmadasa A. Infusion pumps. In: *Equipment in anaesthesia and critical care: a complete guide for the FRCA*. Banbury: Scion Publishing; 2014. p. 315-6.
3. B. Braun Melsungen AG [Internet]. Perfusor® space and accessories [user guide]. Melsungen: B. Braun Medical Inc.; 2015. Available from: <https://www.bbraunusa.com/content/dam/catalog/bbraun/bbraunProductCatalog/S/AEM2015/en-us/b3/perfusor-space-syringepump-nextgenerationsoftwareu.pdf>. Accessed 13 February 2023.
4. Fresenius Kabi [Internet]. Agilia syringe infusion pumps [technical manual]. Fresenius Kabi; 2017. Available from: https://www.fresenius-kabi.com/no/documents/TM_Agilia_Connect_SP.pdf. Accessed 23 March 2023.
5. Doh I, Lee SH, Lee Y-H, et al. Accuracy assessment of a PION TCI pump based on international standards. *Anesth Pain Med* (Seoul). 2019;14(4):407-11. <https://doi.org/10.17085/apm.2019.14.4.407>.
6. Tooke LJ, Howell L. Syringe drivers: incorrect selection of syringe type from the syringe menu may result in significant errors in drug delivery. *Anaesth Intensive Care*. 2014;42(4):467-72. <https://doi.org/10.1177/0310057X1404200407>.
7. Chae Y-J, Kim J-Y, Kim D-W, Moon B-K, Min S-K. False selection of syringe-brand compatibility and the method of correction during target-controlled infusion of propofol. *Korean J Anesthesiol*. 2013;64(3):251-6. <https://doi.org/10.4097/kjae.2013.64.3.251>.
8. Al-Rifai Z, Mulvey D. Principles of total intravenous anaesthesia: practical aspects of using total intravenous anaesthesia. *BJA Educ*. 2016;16(8):276-80. <https://doi.org/10.1093/bjaed/mkv074>.
9. Meyer B, Milner A, Möhr D, et al. Applied pharmacokinetics. In: Milner A, Welch E, editors. *Applied pharmacology in anaesthesiology and critical care*. 2nd ed. Milner and Welch; 2019. p. 1-36.
10. Keay S, Callander C. The safe use of infusion devices. *BJA Educ*. 2004;4(3):81-5. <https://doi.org/10.1093/bjaeaccp/mkh022>.
11. Becton, Dickinson and Company. A validated syringe is critical for patient safety [Internet]. BD; 2021. Available from: <https://www.praxisdienst.com/out/media/138426-bd-plastipak-luer-lock-syringes-becton-dickinson-information-sheet.pdf>. Accessed 16 February 2024.
12. United States Food and Drug Administration. Syringe pump problems with fluid flow continuity at low infusion rates can result in serious clinical consequences: FDA safety communication [Internet]. Available from: <https://www.fda.gov/oc/2016/08/25-16-pumpsafetynotice.pdf>?1520631923. Accessed 23 March 2023.
13. Cuschieri S. The STROBE guidelines. *Saudi J Anaesth*. 2019;13(Suppl 1):S31-4. https://doi.org/10.4103/sja.SJA_543_18.
14. Fresenius Kabi AG [Internet]. Fresenius Kabi medical devices - disposables information. Available from: https://www.fresenius-kabi.com/no/documents/Disposables_TIVA_TWIN_TIVA_TWIN_Y-Sets.pdf. Accessed 19 March 2023.
15. Nimmo AF, Absalom AR, Bagshaw O, et al. Guidelines for the safe practice of total intravenous anaesthesia (TIVA): joint guidelines from the Association of Anaesthetists and the Society for Intravenous Anaesthesia. *Anaesthesia*. 2019;74(2):211-24. <https://doi.org/10.1111/anae.14428>.
16. Absalom AR, Mani V, De Smet T, Struys MMR. Pharmacokinetic models for propofol - defining and illuminating the devil in the detail. *Br J Anaesth*. 2009;103(1):26-37. <https://doi.org/10.1093/bja/aep143>.
17. Pandit JJ, Cook TM, editors. *Accidental awareness during general anaesthesia in the United Kingdom and Ireland* [Internet]. The Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland; 2014. Available from: <https://www.rcoa.ac.uk/sites/default/files/documents/2023-02/NAP5%20full%20report.pdf>. Accessed 15 February 2024.
18. Kong H, Xu L-M, Wang D-X. Perioperative neurocognitive disorders: a narrative review focusing on diagnosis, prevention, and treatment. *CNS Neurosci Ther*. 2022;28(8):1147-67. <https://doi.org/10.1111/cns.13873>.
19. Szederjesi J. Target controlled infusion: an anaesthetic technique brought in ICU. *J Crit Care Med* (Targu Mures). 2022;8(1):3-5. <https://doi.org/10.2478/jccm-2022-0001>.