

Intravenous fluid therapy: a randomized controlled trial to investigate the effectiveness of the IV²™ flow medical device

Nesta Fraser MBChB, MPharmMed,
Department of Pharmacology, University of Pretoria, Pretoria, Gauteng, South Africa

Jacques R Snyman MD, MBChB, MPharmMed,
Department of Pharmacology, University of Pretoria, Pretoria, Gauteng, South Africa

Francois Wessels MSc, MTh
Outcomes Consultant, Monumentpark, Pretoria, South Africa

George Nel BSc, MSc
Outcomes Consultant, Monumentpark, Pretoria, South Africa

Abstract

Objectives. To investigate the hypothetical benefits of the IV²™ flow medical device.

Background. Intravenous fluid administration is a standard hospital procedure with assumed inadequacies. The *IV-Event Study* [Fraser N, Nel G, Snyman J & Wessels F (2004) IV-EVENT Study: Intravenous Infusion Therapy – Management and Adverse Events. Data on File: Varori International (Pty) Ltd., Centurion, South Africa] quantified these inadequacies; The ‘*Stargait*’ intervention trial investigated the effectiveness and possible cost-benefit of the IV²™ flow. The IV²™ flow is intended for routine use with gravitational intravenous infusion sets. The IV²™ flow should reduce the incidence rate of adverse events and maintain a set flow rate.

Method. Nursing staff assisted by study assessors captured relevant data. Consented patients were enrolled for the period of their prescribed infusions.

Intervention. The *Stargait* Trial compared the treatment group (standard gravitational sets with the IV²™ flow) with the control group (standard gravitational infusion sets without IV²™ flow). The difference in observed events and the cost benefit derived from this were measured.

Results. A total of 2387 drip hours were observed in 52 patients. The adverse event rates were: Control group (without IV²™ flow) 33.8%. The treatment group (IV²™ flow) 15.4%. This 55% reduction is statistically significant ($p = 0.0069$). Adverse event related monetary wastage (labour and consumables) is reduced by 76% for infusion bags in the intervention group (with IV²™ flow). There was a significant difference between the treatment group and control group as far as deviation in flow rate was concerned ($p = 0.00818$). The mean deviation of the IV²™ flow group was just more than 5 ml per hour. The standard line group had a mean deviation of more than 30 ml per hour.

Conclusion. Gravitational intravenous therapy compromises quality of patient care. The *Stargait* Trial has proven the care-effectiveness and cost-effectiveness of the IV²™ flow.

Relevance to clinical practice. The IV²™ flow improves quality of patient care and reduces associated wastage.

Introduction

New methods and devices for administration of intravenous medications are entering the market. Providers are forced to re-evaluate current methods of delivering services to patients. This decision-making process must include an evaluation of the costs associated with each system as well as an evaluation of system characteristics (Fraser *et al.* 2004).

Physicians are required, on a daily basis, to write orders for administration of intravenous fluid and must be able to justify their choices on clinical grounds (Birdwell 1993). Management of prescribed infusion therapy then becomes the responsibility of attending nursing professionals. Limitations inherent to standard gravitational intravenous infusion (IV) sets routinely used, combined with pressure on nursing time, leads to specific complications that have a negative impact on patient care and resource use (nursing time and consumables).

Deviations in actual vs. prescribed flow rates occur routinely, even if calibration is performed correctly. Flow of intravenous fluid through an IV-line is a gravitational process driven by the fluid volume (pressure) in the container, which constantly declines while the container runs in. This hydraulic mechanism of driving fluid leads to variations in set flow rates. So-called 'creeping of the roller-clamp wheel' further exacerbates this inherent deviation (Makkink 2001).

The second set of complications relates to adverse events (AE). Adverse events (e.g. air emboli, reverse blood flow, clots forming in the line, fluid in tissue, phlebitis, needle dislodge and repriming) can manifest alone or in combination.

The *IV-Event Study* collected time-and-motion data for the gravitational IV-sets currently in use. This exploratory observational study quantified the negative impact of intravenous fluid administration on patient care and resources (Fraser *et al.* 2004). The IV-Event Study established two areas of significance. Firstly, there was a clinically significant (30%) variation in actual vs. prescribed flow rates during IV-fluid administration.

Only 12% of the observed containers were infused within a 10% deviation (72% under infused and 22% over infused). Secondly, AEs were experienced by 53% of patients, with an incidence rate of 25% (one in four bags) (Fraser *et al.* 2004).

The *IV-Event Study* was motivated by a phase 1 clinical trial, the *Clinical validation trial of the IV²™ flow*.

This study established an average deviation in flow rate of 35.2% (Ker 2002) (using standard gravitational infusion sets with a dial type rate control mechanism). The same study confirmed flow rates with IV²™ flow (in line with standard gravitational infusion sets with a dial type rate control mechanism) are accurate within 10% (8.4%) of the calibrated flow rate (Ker 2002). This compares favourably with the standard set by electronic infusion pumps (5% deviation) (Ker 2002) and represents a major technological advance for the gravitational infusion industry.

The IV²™ flow (IVF) medical device was designed to address the inherent shortcomings of standard gravitational IV-sets.

Hypothetically the IVF device closes the IV-line when a container runs empty (See Fig. 1). The line remains free of air and the fluid column is maintained. Reverse blood flow should be limited, formation of blood clots reduced and air emboli prevented. Inclusion of the IVF maintains the set flow rate through creating a new hydraulic head reference point and keeping it constant for the duration of the infusion.

The *Stargait* Trial aimed to quantify possible superiority of standard gravitational sets equipped with the IVF (to those without the IVF).

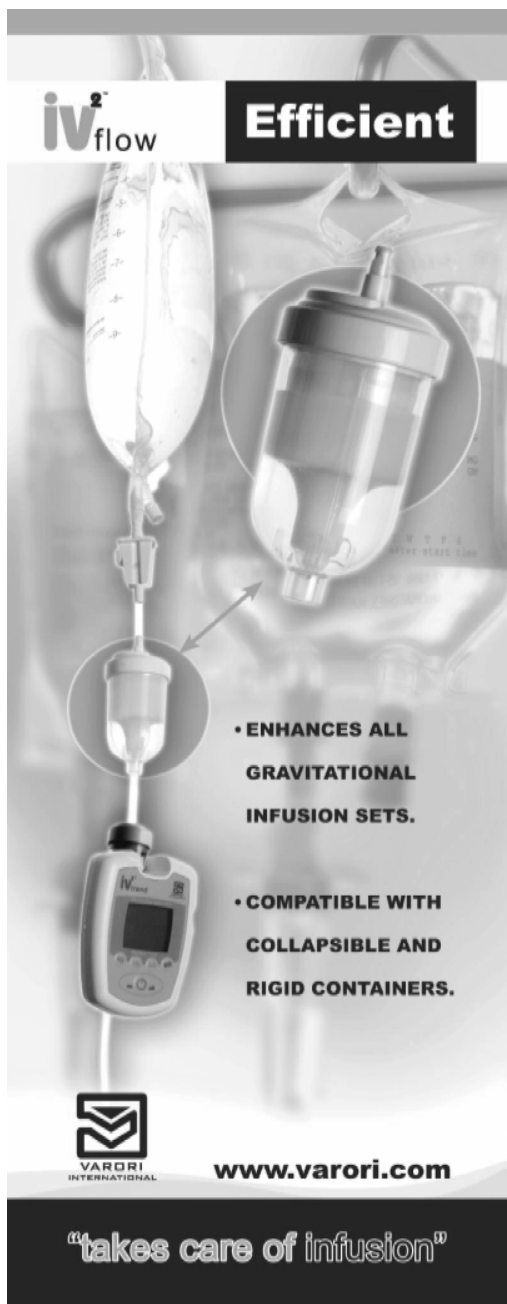


Figure 1 The IV²™ flow medical device illustrated in a typical clinical environment.

Background

Flow rate accuracy is a prerequisite for administration of parenteral fluid. The intention of prescribing physicians is for patients to receive IV fluids as per script for specific clinical indications.

If IV-sets are calibrated accurately and it can be assumed that flow rates will be maintained by the system, a high level of agreement between actual and prescribed flow rates will emerge.

Physiological and pathological factors relevant to intravenous fluid therapy to be emphasized are the following:

The body has a powerful defence against water deficit, but very little against water excess. An increase in serum sodium concentration of 4–5 mmol/l above the usual normal value is a powerful stimulus for thirst.

A conscious patient will demand or drink water until the thirst subsides. On the other hand, hyponatremia does not create feelings of aversion to water. In other words, insufficient water intake will not remain uncorrected in a conscious patient, whereas no effective defence mechanism exists to prevent hyponatremia and fluid overload (Shafiee *et al.* 2003).

Fluid overload can lead to pulmonary congestion, and hyponatremia; the commonest electrolyte abnormality in hospitalized patients (Larson & Hargiss 1984). If the plasma sodium concentration declines to less than 120 mmol/l in 48 hours, brain swelling may result in herniation, with devastating consequences.

The impact of adverse events on quality of patient care and resource wastage should not be underestimated:

- Containers running empty cause air in line, reverse blood flow and blood clot formation. Bag replacements create the potential for air embolism
- In the *IV-Event Study* 53% of subjects experienced one or more adverse event;
- The financial relevance is reflected in the wastage per 24 hours of infusion. Extrapolated to the millions of hours infused per annum, this is an unexplored cost containment measure;
- The total wastage per 24 hours of infusion (as per *IV-Event Study*) is R25·19 (R = ZAR = South African Rand 6·6289 to the US\$ on 31 August 2004), of which 88% can be attributed to consumables and 12% to labour.

Stargait Trial

Patients and methods

Patients

Patients of 18 years and older, managed in a general ward with maintenance IV-fluid without an electronic infusion pump, were recruited into the study. The study was approved by the Research Ethics Committee of the Faculty of Health Science, University of Pretoria and all volunteers signed informed consent.

Study design and treatment

This was a randomized unblinded clinical trial consisting of four study arms:

Control – Roller clamp flow regulator without IVF [STD/RC]

Active – Roller clamp flow regulator with IVF [IVF/RC]

Control – Dial Type regulator without IVF [STD/DF]

Active – Dial Type regulator with IVF [IVF/DF]

Both the Active and Control groups received the same IV-lines (supplied by Varori International (Pty) Ltd., Centurion, South Africa). The medical device (IVF) was incorporated into the main line as well as the added line of the standard gravitational infusion sets of the patients in the treatment (active) groups. Enrolment in the study was in a general ward once a new (full) container was initiated.

Evaluation of patients

The nursing personnel routinely managing the IV-sets captured the study data on the log sheets with assistance from study assessors (SA) if required. Training was performed to ensure correct completion of the log sheets, correct calibration techniques as well as ability to manage the study device with success. The correct use of the IVF device was demonstrated during the trial. The attending SA assisted the nursing professional in changing the infusion lines of the consented patients and at initiation of the new vaculitre ensured that calibration was correctly performed. A note was made of the number of manual adjustments to drip rates in each arm of the study.

Statistics and pharmacoeconomics

The primary variable for this study was *efficiency* as indicated by the reduction in AEs. This is a categorical variable. Secondary variables were *flow rate accuracy* and *cost-implications* (AE related wastage). The sample size calculation was based on the proportions assessed in the exploratory *IV-Event Study* (Fraser *et al.* 2004).

Two proportions were assessed: the adverse event rate and the proportion of the bags infused within acceptable flow specifications. A significance level of 5% is observed while the power of the test is maintained at 80%. The roller clamp flow regulator was used in the treatment arms observed for the primary variable.

The pharmacoeconomic analysis was conducted from a provider's perspective. A cost-effectiveness analysis (CEA) will assist the provider in determining whether the benefits of implementing the routine use of the IVF in IV-sets will exceed cost.

Certain assumptions, based on good clinical practice, limit the amount of data to be captured. These assumptions apply to labour time spent and consumables used. [Extracted from the *IV-Event Study* (Fraser *et al.* 2004)]

Results

Patients and demographics

The demographic analysis of the enrolled patients indicated an even distribution of baseline characteristics. Over a period of nine days 52 patients were enrolled and 202 vaculitres observed (2387 drip hours).

Primary endpoint

The primary study endpoint of reduction in AEs was based on the roller clamp groups (38 patients with 146 main line IV-bags).

A chi-square analysis assesses the relationship between device type and the occurrence of AEs. The number of AEs generates frequency data and therefore a Chi-square analysis is indicated. The 55% reduction in AEs was an improvement on the 50% anticipated reduction. In the IVF/RC group, the frequency of AEs was 15.4% compared with the 33.8% in the STD/RC group. Fig. 2 shows the various AE manifestations noted for the Roller Clamp arms (Table 1).

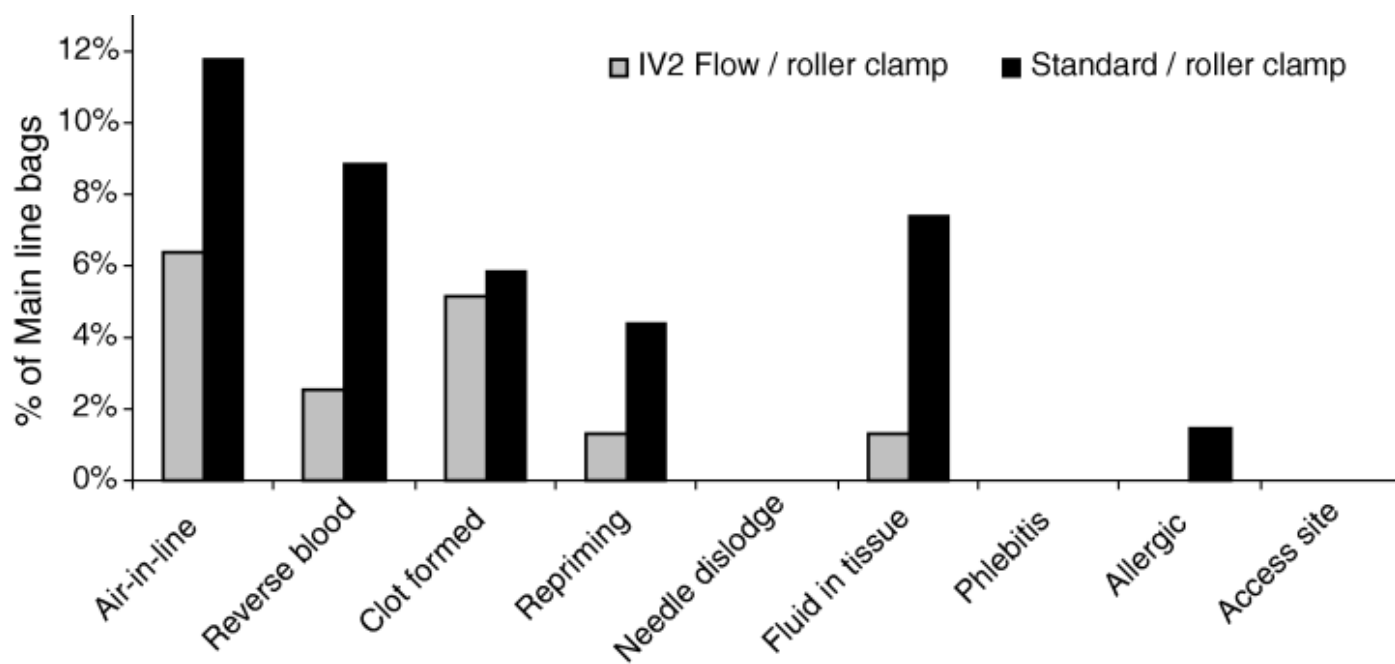


Figure 2 AE manifestations as a percentage of main line bags (roller clamp groups).

	Main line bags observed	Main line bags with AEs	Number of AEs	Frequency of AEs
Standard/roller clamp	68	20	23	33.8%
IV ² flow/roller clamp	78	9	12	15.4%*

*Significantly different from standard/roller clamp: $p = 0.00693$.

Table 1 Frequency of adverse events (AEs)

	<i>n</i>	Deviation (ml per hour)	SD	SE
Standard/roller clamp	68	-29.7	50.9	6.2*
IVF/Roller clamp	78	-5	60.6	6.9
Standard/dial-a-flow	38	-36	35.5	5.8
IVF/dial-a-flow	14	-7.2	75.9	20.3

*Significant difference for IVF/RC vs. STD/RC $p = 0.032$.

Table 2 Mean flow rate accuracy (vs. prescribed flow rate)

Secondary endpoint

The deviation in flow rate as calculated by the difference between prescribed and observed flow rates, was analysed by means of analyses of variance (ANOVA) and *t*-tests. There was a significant difference between IVF lines and STD lines as far as deviation in flow rate was concerned ($p = 0.00818$). Results of a *t*-test of flow rate deviations strengthened this observation ($p = 0.000699$).

As is evident from Table 2, the magnitude of mean deviations in ml per hour was -5 (IVF/RC) and -7.2 (IVF/DF) to -36.0 (STD/DF) and -29.7 (STD/RC).

These mean deviations are point estimates (based on deviation from prescribed flow rate). It is therefore clear that the mean deviations associated with IVF-arms are significantly lower than that for the standard IV line.

	AE rate	Frequency of AE's	Ave cost per AE	Total wastage per 1000 IV-bags
Standard/roller clamp	34%	338	*R47.12	*R15 939
IV-flow (IVF)/roller clamp	15%	154	*R24.65	*R3792
Difference	-18%	-184	*R -22.47	*R -12 147
Variance	-55%	-55%	-48%	-76%

Table 3 Cost of adverse event (AE) related wastage with infusion of 1000 main line bags

Days infused	Number of bags	Break-even
0-3	1	*R12.15
1	3	*R36.44
2	6	*R72.88
3	9	*R109.32
4	12	*R145.76

Table 4 Rank-order stability analysis

Pharmacoeconomic evaluation

The resource use associated with management of each AE manifestation (such as air-in-line) is reflected in Appendix 1. Type and frequency of AEs has been identified as major cost drivers. Appendixes 2 and 3 reflects the full cost modelling which incorporate cost and frequency of occurrence.

Table 3 reflects the cost to manage a hypothetical 1000 IV-bags infused. The IVF/RC group achieves a significant wastage reduction of 76%.

To determine cost-effectiveness of the IVF-device the Cost to Patient or Third party should be known. Therefore, a ROSA (rank-order stability analysis) (Einarson *et al.* 1995) was employed to project a break-even point (Table 4).

The ROSA indicates that if the addition of the IVF-device to STD IV-sets cost less than R12·15 a cost saving would be achieved from the first IV-bag infused. This cost-effectiveness would escalate with every additional bag infused (as reflected by increased break-even point).

Discussion

Providers must evaluate the associated costs as well as the system characteristics when deciding on a method for administration of intravenous medications. Complications associated with gravitational infusion sets impact negatively on patient care and resource utilization.

The parent study (Stargait) aimed to quantify possible superiority with regards to clinical administration and economic outcomes, of standard gravitational sets equipped with the IVF to those without IVF. This study clearly demonstrates the reduction in incidence of AEs (e.g. air in line, reverse flow, clotting, etc.) as well as the significant impact on costs. The absolute 18% reduction ($p \leq 0\cdot0069$) is remarkable over the short duration of the study (55% relative reduction), which translates into a 76% cost saving per 1000 IV-bags infused. A vaculitre in the control arm (standard/roller clamp) had a 2·2 times greater chance of an adverse event than a vaculitre in the IVF/roller clamp arm.

The superiority of the IVF group over the standard IV line in achieving an accurate flow rate has been demonstrated. The mean deviation associated with IVF (just more than 5 ml/hour) is significantly lower than that for the standard IV-line (30 ml/hour).

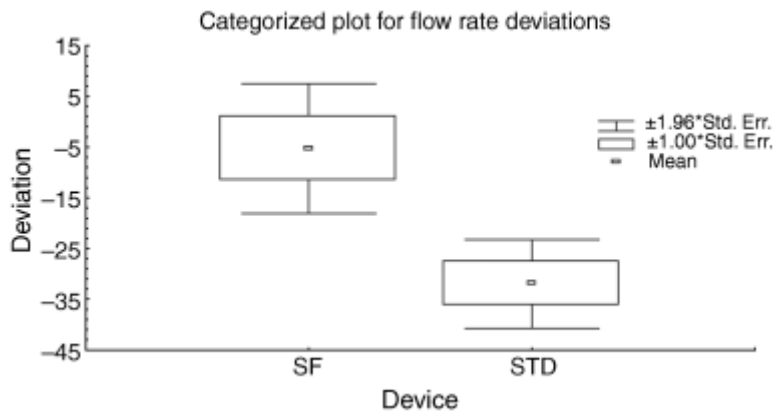


Figure 3 Box and whisker plot: the significance of the difference between the two groups of observations and the superiority of the IV^{2TM} flow group over the standard IV line group – as indicated by smaller mean deviations (Note: SF = IV^{2TM}flow).

The Stargait trial evaluated hard endpoints with regards to equipment (i.e. IVF vs. standard IV infusion sets) and management thereof and did not measure patient disease outcomes directly. Patient specific parameters such as volume overload, dehydration, AEs and the impact thereof on disease and length of hospital stay were not measured and forms part of a future study. It is, however, clear that a simple but effective change in how we administer intravenous fluids already makes a significant difference when we calculate nursing care costs, patient specific impact (AEs) and accuracy of fluid administration.

The impact of a flow variation of 30 ml/hour may seem small on a hourly basis but calculated over 24 hours makes a big difference to the total volume administered. This can clearly lead to inadequate volume replacement in patients with compromised organ functions or with extensive disease such as burns where input and output measurement and administration is critical to the clinical outcome of the patient (Shafiee *et al.* 2004).

In environments where accurate medicine administration is mandatory, a more reliable and simple device may benefit patients, especially in more resource constrained settings.

Conclusion

The intervention in this trial, the IVF, as an add-on device in standard gravitational sets, was proven to be care- and cost-effective. The investigators support the routine implementation of the IVF-device in everyday clinical practise.

Contributions

Study design: NF, JRS, GN, FW; data collection: NF, SV, PN, DW, AV, AH, SCM, CR; analysis: NF, GN, FW and manuscript preparation: NF, GN, JRS, FW.

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Appendix

Appendix 1: Cost dictionary per manifestation

				Air-In-line	Rev blood flow	Clot formed	Repriming	Needle dislodge	Fluid in tissue	Phlebitis	Allergic reaction	Access site related
Labour costs (IV-Event)												
Nursing staff (cost per min)			R0-70	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38
Nursing staff time (min) per AE*			7-7									
Consumable costs												
		CODE	SEP (incl VAT)									
Ave cost per IV-bag (1000 ml)			R43-89				R2-98	R2-98	R2-98	R2-98	R2-98	R2-98
Wastage* (%)			6-8%									
Syringes	5 ml	232	R6-88	R6-88	R6-88	R6-88						
Needles		249	R1-75	R1-75	R1-75	R1-75						
Webcol		252	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49
Gloves examination		712	R1-80				R1-80	R1-80	R1-80	R1-80	R1-80	R1-80
Linen saver		889	R1-43				R1-43	R1-43	R1-43	R1-43	R1-43	R1-43
IV-tray		631	R15-00				R15-00	R15-00	R15-00	R15-00	R15-00	R15-00
Jelco		283	R60-77				R60-77	R60-77	R60-77	R60-77	R60-77	R60-77
Tegaderm	1626	463	R29-43				R29-43	R29-43	R29-43	R29-43	R29-43	R29-43
Water	5 ml	28	R5-24			R5-24						
			Cost per manifestation	R14-50	R14-50	R19-74	R117-28	R117-28	R117-28	R117-28	R117-28	R117-28
*As per IV-Event Study												

Appendix 2: AE and manifestation schedule – STD/RC

	Air-In-line	Rev blood flow	Clot formed	Repriming	Needle dislodge	Access site related	Fluid in tissue	Reverse blood + clot	Reverse + fluid	Reprime + fluid + allergic reaction	Number of manifest	Number of 1000
Number of bags in study arm											68	34%
Number of patients with AE											11	
Number of bags with AE											20	
Number of AE's											23	338
Number of manifestations	8	4	3	2			3	1	1	1	27	R15 939
Labour costs												
Nursing staff (cost per min)	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38	R5-38		
Consumable costs												
Wastage (%)	7-8%			R3-41	R3-41	R3-41	R3-41	R3-41	R3-41	R3-41		
Syringes	R6-88	R6-88	R6-88					R6-88	R6-88			
Needles	R1-75	R1-75	R1-75					R1-75	R1-75			
Webcol	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49	R0-49		
Gloves examination				R1-80	R1-80	R1-80	R1-80		R1-80	R1-80		
Linen saver				R1-43	R1-43	R1-43	R1-43		R1-43	R1-43		
IV-tray				R15-00	R15-00	R15-00	R15-00		R15-00	R15-00		
Jelco				R60-77	R60-77	R60-77	R60-77		R60-77	R60-77		
Tegaderm				R29-43	R29-43	R29-43	R29-43		R29-43	R29-43		
Water			R5-24					R5-24				
Cost per manifestation	R14-50	R14-50	R19-74	R117-28	R117-71	R117-71	R117-71	R17-91	R127-34	R117-71		
Total cost of manifestations	R115-98	R57-99	R59-21	R234-56	R0-00	R0-00	R353-14	R17-91	R127-34	R117-71	R1084	
Ave cost per AE											R47-12	
	R43-02	R21-51	R16-13	R10-75	-	-	R16-13	R5-38	R5-38	R5-38	R123-67	11-4%
											R5-38	

Appendix 3: AE and manifestation schedule – IVF/RC

	Air-In-line	Rev blood flow	Clot formed	Repriming	Needle dislodge	Access site related	Reprime + fluid	Number of manifest	Number of 1000
Number of Bags in study arm								78	
Number of Patients with AE								8	
Number of Bags with AE								9	15.4%
Number of AE's								12	154
Number of Manifestations	5	2	4				1	13	R3 792.01
Labour costs									
Nursing staff (cost per min)	R5.38	R5.38	R5.38	R5.38	R5.38	R5.38	R5.38		
Consumable costs									
Fluid wastage (%) (1000 ml)	2.4%			R2.98	R2.98	R2.98	R1.05		
Syringes	R6.88	R6.88	R6.88						
Needles	R1.75	R1.75	R1.75						
Webcol	R0.49	R0.49	R0.49	R0.49	R0.49	R0.49	R0.49		
Gloves examination				R1.80	R1.80	R1.80	R1.80		
Linen saver				R1.43	R1.43	R1.43	R1.43		
IV-tray				R15.00	R15.00	R15.00	R15.00		
Jelco				R60.77	R60.77	R60.77	R60.77		
Tegaderm				R29.43	R29.43	R29.43	R29.43		
Water			R5.24						
Cost per manifestation	R14.50	R14.50	R19.74	R117.28	R117.28	R117.28	R115.35		
Total cost of manifestations	R72.49	R28.99	R78.95	R0.00	R0.00	R0.00	R115.35	R296	
Ave cost per AE								R24.65	
	R26.89	R10.75	R21.51	–	–	–	R5.38	R64.53	21.8%
								R5.38	