The value of negative pressure wound therapy in comparison with the conventional dressing on the postoperative wound healing in diabetic foot patients

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Background
Diabetic foot ulcers (DFUs) constitute one of the most important complications of diabetes mellitus. If not treated promptly, progression of infection and sepsis may necessitate a limb amputation.
Aim
The aim of the study was to evaluate the clinical efficacy of negative-pressure wound therapy using vacuum-assisted closure (VAC) compared with the conventional dressing on the postoperative wound healing in diabetic foot patients.
Patients and methods
This was a randomized controlled trial that included two groups of postoperative diabetic foot patients, in which we had a comparison between VAC and conventional wound dressing in order to investigate which procedures had the least time of follow-up weeks for full granulation of wound.
Results
Negative-pressure wound therapy significantly reduces the time to complete wound healing by enhancing the formation granulation tissue.
Conclusion
The time to complete wound healing was significantly better in the VAC therapy group as compared to conventional dressing.

Keywords:
conventional dressing, diabetic foot ulcers, NPWT, VAC, wound healing

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Introduction

Diabetic foot ulcers (DFUs) are one of the most serious consequences of diabetes mellitus [1]. If the infection and sepsis are not treated promptly, limb amputation may be required [2].

The standard of care for DFUs involves debridement, local wound care, controlling of the infection, and off-loading of pressure. Various treatments advocated in recent years include advanced wound dressings, growth factors, hyperbaric oxygen therapy, cultured skin substitutes, and other wound therapies. Negative-pressure wound therapy (NPWT) is a newer, noninvasive adjunctive therapy system. A vacuum-assisted closure (VAC) device is used to control sub-atmospheric pressure that promote the wound healing by removing fluid from open wounds, preparing the wound bed for closure, reducing edema, and promoting the formation and perfusion of granulation tissue [3].

Aim of the work

The aim of this study was to evaluate the clinical efficacy of NPWT using VAC compared with the conventional dressing on the postoperative wound healing in diabetic foot patients.

Patients and methods

Type of study

This is a randomized control trial.

Study setting

This study included diabetic foot patients presenting to Ain Shams University and NIDE (National Institute of Diabetes and Endocrinology).

Study period

Study duration was of a period of 6 months.

Study population

Inclusion criteria

Patients presented with diabetic foot infection who underwent surgical debridement or minor amputations prior to initiation of VAC or the conventional dressing.

Exclusion criteria

(1) Patients who have coagulopathy,
(2) Patients who have active infections not resolved by initial surgical debridement,
(3) Patients with renal failure if they were undergoing dialysis,
(4) Patients receiving radiation therapy or chemotherapy,
(5) Patients with poor cardiological status (ejection fraction less than 35%), and
(6) Patients with ischemic diabetic foot.

Sampling method

Sampling method followed simple randomization.

Sample size

Our study included 40 diabetic foot patients divided into 2 groups, 20 patients in the VAC group and 20 patients in the conventional dressing group.

Ethical considerations

This study was performed according to approved standards of ethical committee of Ain Shams University.

Study procedures

This randomized controlled trial included DFUs of Wagner's Grades 2 and 3. All included diabetic foot patients were hospitalized and underwent surgical debridement or minor amputations followed by the VAC (interrupted mode around 125 mmHg) in the first group and the conventional dressing (saline and sterile gauze) in the second group.

Patients discharged from the hospital were followed up weekly and were assessed until complete wound healing (defined as 100% granulation or wound fit for split skin grafting) was achieved.

The following parameters were assessed every week:

(1) Wound depth,
(2) Wound surface area (length×width),
(3) Percent of reduction in depth and surface area,
(4) Classification and staging of the wound according to university of Texas classification,
(5) Presence of infection in the wound or not,
(6) The need for operative or bedside debridement, and
(7) The time needed for complete granulation tissue.

Statistical analysis

Data were collected, revised, coded, and entered to the Statistical Package for Social Science (IBM SPSS, Armonk, New York, USA) version 20. The qualitative data were presented as the number and percentages while quantitative data were presented as mean, standard deviations, and ranges when their distribution were to be found parametric.

The comparison between two groups with qualitative data were done by using χ^2 test and/or Fisher exact test was used instead of χ^2 test when the expected count in any cell was found to be less than 5.

The comparison between two independent groups with quantitative data and parametric distribution was done by using independent *t*-test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *P*-value was considered significant as follows:

(1) $P>0.05$=nonsignificant (NS)
(2) $P<0.05$=significant (S)
(3) $P<0.001$=highly significant (HS).

Results

Our results revealed that there was no statistically significant difference found between two groups regarding age, sex, smoking, hypertension, and renal insufficiency. In the initial laboratory investigations (hemoglobin, total leukocyte count, glycated hemoglobin, creatinine, and albumin) and initial clinical data in the first presentation postoperatively (ulcer depth, surface area, University of Texas Classification category, and presence of infection), there were also no statistically significant difference found between the two groups.

While comparing between conventional and VAC groups regarding the follow-up in 2, 4, 6, 8, and 10 weeks as represented in Tables 1–5, respectively, we found that the results in the VAC group were high statistically different from the conventional group concerning ulcer depth, percent of depth reduction (%), percentage of surface area reduction, Texas classification, and complete granulation tissue.

The results shows that there was no statistically significant difference found between the two groups regarding the number of trips to operation room and minor amputation (Table 6).

Regarding the time needed to reach full granulation tissue, it was a mean of 4.65 weeks in the VAC group and 8.40 weeks in the ordinary dressing group, which is highly significant (Fig. 1).

Table 1 Comparison between VAC (*n*=20) and conventional dressing (*n*=20) regarding follow-up data in 2 weeks of clinical data

Follow-up data in 2 weeks	VAC *N*=20, *N* (%)	Conventional dressing *N*=20, *N* (%)	Test value	*P* value	Sig.
Ulcer depth					
Mean±SD	19.40±4.45	23.00±5.67	−2.234[a]	0.031	S
Range	8 to 27	13 to 33			
Percentage of depth reduction (%)					
Mean±SD	−31.54±10.65	−13.78±6.46	−6.376[a]	0	HS
Range	−61.9 to −16.67	−35.71 to −5.88			
Ulcer surface area					
Mean±SD	5715.00±2591.74	6277.50±3564.83	−0.571[a]	0.572	NS
Range	1400 to 10 400	1100 to 11 900			
Percentage of surface area reduction					
Mean±SD	−10.86±2.38	−3.45±2.37	−9.861[a]	0	HS
Range	−16.67 to −7.14	−8.33 to −0.67			
Texas classification					
Grade1 Stage1	2 (10.0)	0	6.246[b]	0.100	NS
Grade2 Stage1	10 (50.0)	5 (25.0)			
Grade3 Stage1	6 (30.0)	13 (65.0)			
Grade3 Stage2	2 (10.0)	2 (10.0)			
Infection					
No	18 (90.0)	18 (90.0)	0[b]	1.000	NS
Yes	2 (10.0)	2 (10.0)			
Operative debridement					
No	18 (90.0)	16 (80.0)	0.784[b]	0.376	NS
Yes	2 (10.0)	4 (20.0)			
Bed-side debridement					
No	2 (10.0)	2 (10.0)	0[b]	1.000	NS
Yes	18 (90.0)	18 (90.0)			
Complete granulation					
No	20 (100.0)	20 (100.0)	NA	NA	–

NA, not applicable; SD, standard deviation; VAC, vacuum-assisted closure. *P*-value >0.05: non-significant (NS); *P*-value <0.05: significant (S); *P*-value <0.01: highly significant (HS). [a]Independent *t*-test. [b]χ^2 test.

Table 2 Comparison between VAC (*n*=20) and conventional dressing (*n*=20) regarding follow-up data in 4weeks of clinical data

Follow-up data in 4 weeks	VAC, *N*=20, *N* (%)	Conventional dressing, *N*=20, *N* (%)	Test value	*P* value	Sig.
Ulcer depth					
Mean±SD	4.20±5.89	19.80±4.75	−9.218[a]	0	HS
Range	0 to 13	11 to 28			
Percentage of depth reduction (%)					
Mean±SD	−86.29±19.31	−25.64±6.43	−13.328[a]	0	HS
Range	−100 to −53.57	−42.86 to −15.38			
Ulcer surface area					
Mean±SD	4855.00±2422.37	6057.50±3556.51	−1.250[a]	0.219	NS
Range	700 to 9100	1000 to 11 700			
Percentage of surface area reduction					
Mean±SD	−26.92±9.25	−8.84±6.70	−7.080[a]	0	HS
Range	−56.25 to −18.75	−28.57 to −2.08			
Texas classification					
Grade1 Stage1	13 (65.0)	0	22.889[b]	0	HS
Grade2 Stage1	7 (35.0)	11 (55.0)			
Grade3 Stage1	0	9 (45.0)			
Infection					
No	20 (100.0)	20 (100.0)	NA	NA	–
Operative debridement					
No	20 (100.0)	18 (90.0)	2.105[b]	0.147	NS
Yes	0	2 (10.0)			
Bed-side debridement					
No	13 (65.0)	2 (10.0)	12.907[b]	0	HS
Yes	7 (35.0)	18 (90.0%)			
Complete granulation					
No	7 (35.0)	20 (100.0)	19.259[b]	0	HS
Yes	13 (65.0)	0			

NA, not applicable; SD, standard deviation; VAC, vacuum-assisted closure. *P*-value >0.05: nonsignificant (NS); *P*-value <0.05: significant (S); *P*-value <0.01: highly significant (HS). [a]Independent *t*-test. [b]χ^2 test.

Table 3 Comparison between VAC (*n*=20) and conventional dressing (*n*=20) regarding follow-up data in 6 weeks of clinical data

Follow-up data in 6 weeks	VAC, *N*=7, *N* (%)	Conventional dressing, *N*=20, *N* (%)	Test value	*P* value	Sig.
Ulcer depth					
Mean±SD	0	12.70±5.85	−5.671[a]	0	HS
Range	0	0 to 18			
Percentage of depth reduction (%)					
Mean±SD	−100.00±0.00	−53.58±21.48	−5.646[a]	0	HS
Range	−100 to −100	−100 to −30.43			
Ulcer surface area					
Mean±SD	4042.86±1922.55	5440.00±3330.47	−1.042[a]	0.307	NS
Range	1600 to 6300	900 to 10 000			
Percentage of surface area reduction					
Mean±SD	−37.17±12.92	−19.77±10.94	−3.459[a]	0.002	HS
Range	−58.33 to −21.25	−44.44 to −6.25			
Texas classification					
Grade1 Stage1	7 (100.0)	3 (15.0)	16.065[b]	0.000	HS
Grade2 Stage1	0	17 (85.0)			
Infection					
No	7 (100.0)	20 (100.0)	NA	NA	–
Yes	0	0			
Operative debridement					
No	7 (100.0)	20 (100.0)	NA	NA	–
Yes	0	0			
Bed-side debridement					
No	7 (100.0)	15 (75.0)	2.148[b]	0.143	NS
Yes	0	5 (25.0)			
Complete granulation					
No	0	17 (85.0)	16.065[b]	0	HS
Yes	7 (100.0)	3 (15.0)			

NA, not applicable; SD, standard deviation; VAC, vacuum-assisted closure. *P*-value >0.05: nonsignificant (NS); *P*-value <0.05: significant (S); *P*-value< 0.01: highly significant (HS). [a]Independent *t*-test. [b]χ^2 test.

Table 4 Distribution of the studied cases according to follow-up data in 8 weeks of clinical data in the conventional dressing group

Follow-up data in 8 weeks	Conventional dressing, *N*=17, *N* (%)
Ulcer depth	
Mean±SD	5.18±6.44
Range	0 to15
Percentage of depth reduction (%)	
Mean±SD	−81.33±23.23
Range	−100 to −47.62
Ulcer surface area#	
Mean±SD	5694.12±3172.24
Range	800 to 9000
Percentage of surface area reduction#	
Mean±SD	−23.82±14.28
Range	−58.33 to −8.33
Texas classification	
Grade1 Stage1	10 (58.8)
Grade2 Stage1	7 (41.2)
Infection	
No	17 (100.0)
Yes	0
Operative debridement	
No	17 (100.0)
Yes	0
Bed-side debridement	
No	16 (94.1)
Yes	1 (5.9)
Complete granulation	
No	7 (41.2)
Yes	10 (58.8)

SD, standard deviation

Table 5 Distribution of the studied cases according to follow-up data in 10 weeks of clinical data in the conventional dressing group

Follow-up data in 10 weeks	Conventional dressing, *N*=7, *N* (%)
Ulcer depth	
Mean±SD	0
Range	0
Percentage of depth reduction (%)	
Mean±SD	−100.00±0
Range	−100 to −100
Ulcer surface area, *N*	
Mean±SD	6942.86±2468.20
Range	1750 to 8700
Percentage of surface area reduction	
Mean±SD	−18.66±6.77
Range	−27.5 to −9.38
Texas classification	
Grade1 Stage1	7 (100.0)
Grade2 Stage1	0
Infection	
No	7 (100.0)
Yes	0
Operative debridement	
No	7 (100.0)
Yes	0
Bed-side debridement	
No	7 (100.0)
Yes	0
Complete granulation	
No	0
Yes	7 (100.0)

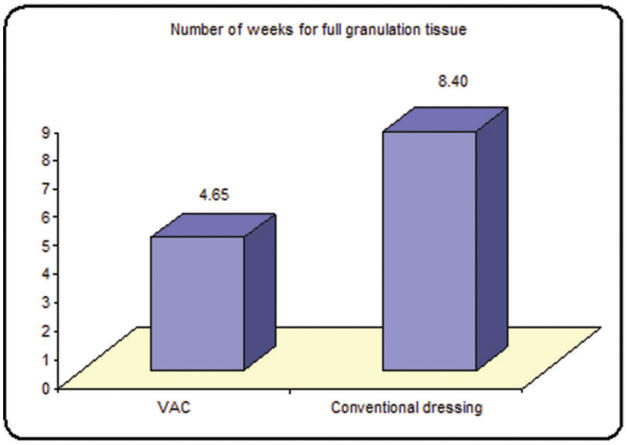
SD, standard deviation.

Table 6 Comparison between VAC (*n* =20) and conventional dressing (*n*=20) regarding the number of weeks for full granulation tissue, number of trips to the operating room, major amputation, minor amputation, limb salvage, and overall mortality

	VAC, *N*=20, *N* (%)	Conventional dressing, *N*=20, *N* (%)	Test value	*P* value	Sig.
Number of weeks for full granulation tissue					
Mean±SD	4.65±0.93	8.40±1.39	−10.008[a]	0	HS
Range	4–6	6–10			
Number of trips to the operating room					
I	18 (90.0)	16 (80.0)	2.118[b]	0.347	NS
II	2 (10.0)	2 (10.0)			
III	0	2 (10.0)			
Major amputation					
No	20 (100.0)	20 (100.0)	NA	NA	–
Minor amputation					
No	20 (100.0)	19 (95.0)	1.026[b]	0.311	NS
Yes	0	1 (5.0)			
Limb salvage					
Yes	20 (100.0)	20 (100.0)	NA	NA	–
Overall mortality					
No	20 (100.0)	20 (100.0)	NA	NA	–

NA, not applicable; SD, standard deviation; VAC, vacuum-assisted closure. *P*-value >0.05: nonsignificant (NS); *P*-value <0.05: significant (S); *P*-value <0.01: highly significant (HS). [a]Independent *t*-test. [b]χ^2 test.

Figure 1



Comparison between vacuum-assisted closure and conventional dressing regarding the number of weeks for full granulation tissue.

Discussion

One of the most serious complications of diabetes mellitus is DFUs, so proper management should be considered. because the progression of infection and sepsis may necessitate amputation of the limb. VAC therapy has been proven to have a considerable effect in many wounds, including DFUs, in studies conducted in the Western population [4].

The cost of care for diabetics with DFUs was shown to be nearly five times higher in the first year than for diabetics without foot ulcers. This is mostly due to the need for DFU patients to stay in the hospital for an extended period of time [5].

Accordingly, researchers have been encouraged to find the best modalities for DFU management. Multidisciplinary team approach can reduce the incidence of first ulcer, infection, the necessity and duration for hospitalization, as well as the frequency of major limb amputation [6].

The main approaches for management are debridement, controlling the infection, off-loading, and basic and advanced wound contact dressings [7].

Nowadays, novel modalities come with the help of conventional modalities for accelerating the process of DFU healing. NPWT has been proposed as an adjunctive treatment through several randomized clinical trials for enhanced wound healing process [8].

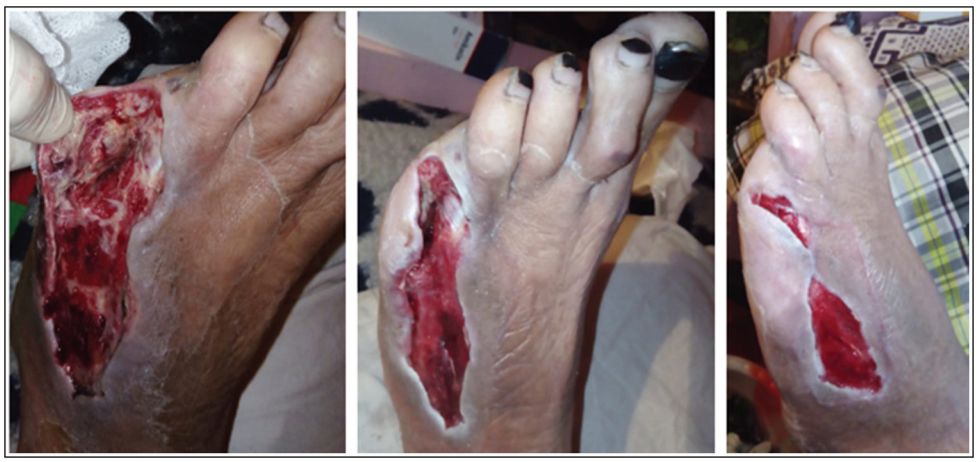
The NPWT technique is a non-invasive system by placing foam dressing in the wound and uses a negative pressure controlled by a device connected to the vacuum that promotes stimulation and wound healing [9].

The aim of this study was to evaluate the clinical efficacy of NPWT using VAC compared with the conventional dressing on the postoperative wound healing in diabetic foot patients.

This was a randomized controlled trial that included DFUs of Wagner's grades 2 and 3, in which we had a comparison between VAC and conventional wound dressing in order to investigate which procedures had the least time of follow-up weeks for full granulation of wound.

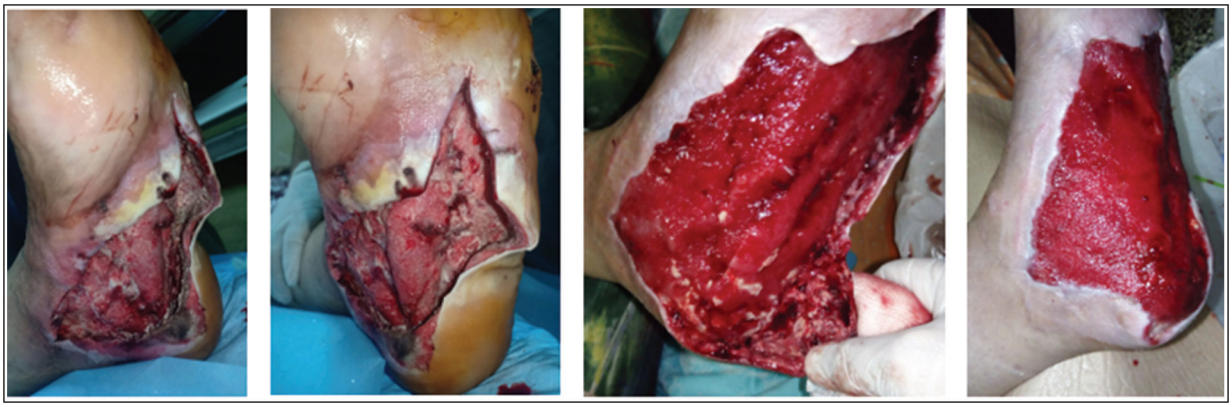
Our results revealed that time needed to reach full granulation tissue was a mean 4.65 weeks in the VAC group and 8.40 weeks in the ordinary dressing group,

Figure 2



Post fifth toe amputation and dorsum of the foot debridement (4 weeks on vacuum-assisted closure).

Figure 3



Post sole, heel, and medial aspect of the foot debridement (6 weeks on vacuum-assisted closure).

which is highly significant difference between the 2 groups. Figures 2 and 3 show the end point of this study (100% granulation tissue or wound ready for skin graft) and show the time needed to reach this stage using the VAC postoperatively.

Our results agreed with the results from the study done by Armstrong *et al.*, who showed that the median time to achieve 76–100% granulation was almost twice as faster by using NPWT than conventional dressing (median time of 42 days vs. 84 days) [10].

According to Singh *et al.*, the mean time to appearance of 100% granulation tissue in the NPWT group was 15.1 days, while it was 21.5 days in the conventional dressing group. In a Spanish research by Seplveda *et al.* [11], the mean time to achieve 90% granulation in the NPWT and traditional dressing groups was 18.8 days and 32.3 days, respectively.

In a recent systematic review and meta-analysis on the effect of NPWT on DFUs, Liu *et al.* [12] found that NPWT reduces the size of DFUs much more than regular dressing.

Also, McCallon *et al.* [13] found a reduction in the size of DFUs in those who got NPWT.

An Indian study by Nain *et al.* [14] showed similar results as the present study with mean reduction in ulcer area by 16.14 and 5.98 cm^2 in DFUs treated with NPWT and conventional dressing, respectively.

Blume *et al.* [8] demonstrated that a greater proportion of DFUs who received VAC therapy achieved complete skin closure or 100% re-epithelization.

Singh *et al.* [11] showed the mean time to complete wound closure was 41.2 days and 58.9 days in the VAC therapy and conventional groups, respectively.

In our study, the end point of the complete wound healing is 100% granulation tissue or the wound ready for skin graft but in some studies the end point of wound

healing is defined as spontaneous complete closure, that is, 100% re-epithelization. The disadvantage of having complete closure as an end point is that this may not be achieved in all wounds, as the wound size differs considerably between patients; In none of these studies did all patients reached spontaneous closure. Further waiting for a wound to fully epithelize requires prolonged follow-up or hospital stay, which adds on to the cost of treatment [15].

The faster healing in NPWT is attributed to macro-deformation, wound environment stabilization and decrease in edema, micro-deformation leading to increased cellular proliferation and angiogenesis, and decreased bacterial load, all of which lead to enhanced granulation cover [11].

NPWT causes mechanical strain at the wound–foam interface, which deforms the cytoskeleton-activating cascades bringing about cellular proliferation and angiogenesis [16].

Increased levels of fibroblast growth factor, transforming growth factor-β, fibroblast proliferation, α-smooth muscle actin, interleukin-8, and vascular endothelial growth factor are implicated in the enhancement of granulation tissue formation in NPWT [17].

Although few studies have shown NPWT to reduce the need of re-amputations, there is no explainable direct correlation of re-amputations with NPWT. Like our study, the studies by Sepúlveda *et al.* show no difference with respect to amputations [18].

Only few studies compared pain between NPWT and conventional dressing in DFUs. Pain was significantly less in the NPWT group in the present study. This could be possibly due to less number of dressings required in the VAC group. NPWT group patients required half the number of dressings as compared to those in the control group as dressing was done once in 2 days in the NPWT group. This was stated as the cause of less pain in NPWT by Nather *et al.* [19].

In some systematic reviews, researchers agree that there is a moderate-to-strong evidence for the use of NPWT in DFUs. However, results from some of them have highlighted certain negative aspects and the complications related to NPWT [20].

The FDA Safety Communication Report has warned about the potential adverse effects of NPWT, including wound maceration, wound infection, bleeding, and retention of dressings. On the other hand, available NPWT systems seem to be expensive, which may prevent their widespread usage [15].

However, faster growth of granulation tissue in the NPWT group covered the raw wound bed faster and hence also contributed to lesser pain than in the control group. The major bleeding in NPWT on DFUs is mostly due to improper hemostasis following debridement, exposed large blood vessels, and high set negative pressure, all of which are avoidable causes [11].

Conclusion

The treatment of diabetic foot requires a cross-disciplinary and systematic approach, within which NPWT is an important adjunct treatment for diabetic foot wounds.

The standardized management and application of NPWT may improve wound exudate drainage, enhance blood perfusion, and promote wound healing.

The present randomized controlled trial reports that VAC therapy is effective and safe when applied to postoperative wounds of diabetic foot patients.

It significantly reduces the time to complete wound healing by increasing the granulation tissue formation without any increase in the incidence of complication, such as bleeding and infection.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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