Economic aspects of biofilm-based wound care in diabetic foot ulcers

• **Objective:** There has been a dramatic rise in the number of chronic wounds globally, which is placing an increased demand on decreasing health-care resources. With significant cuts in health-care budgets, wound care, providers will have to achieve better outcomes quicker and with fewer resources. By using new molecular methods to fully identify wound microbiota, commercially available antimicrobials can be used more efficiently, thereby improving outcomes and decreasing cost.

• **Method:** This study is a retrospective analysis of patients treated for diabetic foot ulcers (DFU); one group healed DFUs in 2005, the other in 2013. The 2005 patients were treated with standard of care methods common today. The second cohort from 2013 included patients treated using biofilm–based wound management anchored by molecular diagnostics. DNA methods were used to identify individual wound microbiota. Then personalised gels with commercially available antibiotics were applied topically to manage the microorganisms identified.

• **Results:** For the 2013 cohort, total charges per patient for the entire course of treatment was $4,756 (total payments $3,060; £1,987). For the 2005 cohort, each patient required treatments that culminated in total charges of $14,690 (total payments $11,444; £7,429). The economic difference per patient from 2013 compared to 2005 was a reduction in total charges of 68% (reduction in total reimbursement of 73%).

• **Conclusion:** In conjunction with other cohort analysis we previously reported, we feel this economic data demonstrates the benefits not only in wounds healed faster but also more wounds healed at a greatly reduced total cost.

• **Declaration of interest:** RW has an equity position in a molecular diagnostic lab named PathoGenius.

biofilms; wound healing; health care costs; debridement; economic costs; diabetic foot ulcer

The rapid increase in chronic wounds is a global phenomenon and is emerging as a significant driver of increased health-care costs.[1] Recent responses by funding agencies to this rising cost in the USA have included dramatic reductions in funding for home health services, multiple cuts in funding (with increased regulations) for durable medical equipment companies, and recently, the introduction of CMS-1601-FC (hospital outpatient prospective payment—final rules with comment which severely limits the use of advanced wound care technologies. In addition, third–party payers are adding regulations and restrictions concerning the procedures and products wound care providers may use.

All of these changes led to fewer resources for the management of increases in, not only the number, but also the severity of chronic wounds. Wound-care providers will have to make significant changes in their practice patterns. Practitioners will have to innovate in how they manage chronic wounds, so that they can treat patients more effectively with fewer resources.

Innovations in biofilm-based wound care have improved outcomes in the management of chronic wounds and may prove to be cost-effective.

Chronic cutaneous wounds have the same clinical pattern as other chronic infections associated with biofilm-phenotype bacteria. Most bacteria in chronic wounds are organised in biofilm.[2] Many of the problems with management and the resulting higher cost of chronic wounds may be directly related to biofilm.

Biofilm is a reasonable explanation for the pathophysiology of chronic wounds, due to the way it behaves in other chronic infections. For lung infections associated with cystic fibrosis, ventilator–acquired pneumonia, chronic rhinosinusitis, and in fact, in all chronic infections, we see a different clinical pattern of infections that are persistent, they wax and wane and respond incompletely to appropriate antibiotics, only to re-emerge once the antibiotics are withdrawn. Chronic wounds, with their persistence, undulant inflammation and incomplete response to antibiotics and topical biocides seem as if they could be related to other chronic infections.[3,4]

The literature about common chronic infections associated with biofilm demonstrates that clinical

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Table 1. Information on the 2005 and 2013 cohorts

	Age	Sex M/F %	$TcP0_2$[a] <20 torr	Average number of wounds
2005	43 (27–83)	56/44	9%	2.8
2013	46 (31–81)	58/42	11%*	3.1

[a]15 patients (7%) were revascularised; $TcP0_2$ - transcutaneous oxygen pressure;

cultures are ineffective in identifying the associated bacteria.[5,6] In response, DNA diagnostic methods were developed to exploit the strengths of different molecular testing methods, which included quantitative polymerase chain reaction (PCR) and sequencing technologies. These DNA-based technologies were able to identify and quantify the microorganisms present in chronic wounds, as well as in other chronic infections.[7–9]

One consistent finding in most chronic wounds is that there are high numbers of multiple species present in a very small area on the wound surface. Since bacteria growing in planktonic phenotype compete, this finding is strong evidence that the bacteria on the surface of chronic wounds are biofilm phenotype.[10] Biofilm is known for its cooperative diversity. The diversity identified by molecular methods[11,12] along with imaging[2] has established that biofilm is present on the surface of chronic wounds.

DNA-based methods also identify–with far greater accuracy and comprehensiveness than clinical cultures, the microorganisms interfering with the healing of chronic wounds.

By using these diagnostic tools, biofilm-based wound care has been able to produce statistically significant improvements in wound outcomes.[13] The improvement in identification of the microorganisms allows for a more appropriate use of commercially available systemic antibiotics and topical antimicrobial products. The reduction in the use of first-line methicillin-resistant *Staphylococcus aureus* (MRSA) antibiotics wound care has been dramatic.[13]

Table 2. Major differences in patient wound care management

2005	2013
Aggressive debridement (several mm into good tissue)	Less aggressive debridement (to the wound bed)
Foam, alginate and hydrocolloid dressings	Self-adaptive dressing (Enluxtra) and hydration response technology dressings (Sachet S)
Dressing changes three times a week on Monday, Wednesday and Friday	Dressing changes twice a week on Monday and Thursday or Tuesday and Friday
Systemic antibiotics	Topical antibiotics
No revascularisation	Limited revascularisation (7%)
Commercial biocides	Compounded gels with antibiotics and anti-biofilm agents (mainly quorum-sensing inhibitors)

It has become clear that, if targeted treatments could be developed specifically for the microorganisms identified on the surface of chronic wounds, wound care outcomes could be improved. This led to the development of a drug delivery gel that could be used to compound personalised topical treatments for the wound biofilm identified in a specific patient.[14] A retrospective analysis of patients who were treated with molecular diagnostics followed by personalised gels showed a greater statistical significance in wound healing, with 90% of patients' first chronic wounds healed by the end of 12 weeks.[15] There was a change, not only in the type of systemic antibiotics used during this retrospective analysis, but also a tremendous decrease in the amount prescribed for healing each chronic wound.

Biofilm-based wound care has been distilled down to a very manageable rubric. The wound biofilm is sampled and diagnosed by molecular methods at the first encounter. The wound is debrided of all slough, devitalised tissue and/or foreign bodies. Next, any architecture that favours biofilm formation, such as tunnels, undermining, or surfaces that touch are altered or removed. Debridement is carried out frequently and aggressively to open a therapeutic window where biofilm has to reconstitute itself, and during that period of time, it is more susceptible to treating agents.[16] After debridement, the biofilm is suppressed by applying antimicrobial wound cleansers followed by the application of specific antibiotics, anti-biofilm agents, and selective biocides, concurrently, to suppress the microorganisms identified by DNA methods to inhabit the wound bed. Topical antibiotics and/or anti-biofilm agents are much less likely to produce antibiotic resistance of the microorganisms than systemic antibiotics.[17]

This retrospective study is an attempt to discover whether there are any economic benefits to the system of biofilm-based wound care for improving wound healing outcomes. We have anecdotal evidence that has shaped our perception that biofilm-based wound care decreases hospital admissions and complications, such as major limb amputation. The financial information on these complications is not available. However, clinic business records can be evaluated to determine the charges and reimbursement for different aspects of outpatient management of chronic wounds. We obtained this economic data from a period of time before biofilm-based wound care was introduced and compared that to our current management.

Method

Institutional review board approval for a retrospective study examining the financial records of

Table 3. The total charges and total reimbursements per patient in the 2005 and 2013 cohort groups. The largest driver for the reduction in charges (reimbursements) is the use of IV antibiotics, especially expensive first line methicillin-resistant *Staphylococcus aureus* antibiotics

Cost of healing (per patient)	Total charges	Total payments	Antibiotic charges	Antibiotic payments	Wound care charges	Wound care payments
2005 (n=189)	$14,690	$11,444	$2706	$1994	$11,984	$9,450
2013 (n=215)	$4756	$3060	$315	$155	$4,441	$2,905
Change (%)	–68%	–73%	–88%	–92%	–62%	–69%

two cohort groups was obtained from IntegReview IRB for protocol RW5656 Southwest Regional Wound Care Center on 7 July 2014.

This data has been obtained retrospectively through data mining of a clinical electronic medical record. The electronic medical record, held on the Centricity Version 12 (General Electric) system, contains all the charges and collections for the outpatient services provided through Southwest Regional Wound Care Center. The patient populations evaluated were those with diabetic foot ulcers (DFU) that healed in 2005 and in 2013. The subjects were patients who were identified as having DFUs and who had four or more visits for the DFU(s) in question. The patients' charts recorded that practitioners had certified that the DFU(s) had completely healed, and billing records showed that at least one debridement the wound was full-thickness.

In 2005, 189 patients were identified as meeting these inclusion criteria; in 2013, 215 patients met the criteria. With the patients identified, the economic data for evaluation was obtained. The information obtained included the: number of visits to the Wound Care Center to be managed by a wound care provider; number of total wounds; and the total amount billed and collected for management of the patient for the entire course of therapy. The codes for debridement were detailed individually. Finally, we also collected data on the billing and collection of systemic antibiotics (intravenous (IV)/ intramuscular (IM)) administered in the clinic.

Table 4. The most common debridement codes used in 2005 and 2013 are analysed. Codes 97597 and 97598 were introduced in 2007 and took the place of code 11041.

	2005	2005	2013	2013
Codes	**Charges**	**Payments**	**Charges**	**Payments**
97597, 97598	N/A	N/A	$191	$132
11041	$13	$10	N/A	N/A
11042, 11045	$264	$211	$1216	$865
11043, 11046	$3529	$2696	$252	$172
11044, 11047	$2340	$1947	$130	$91
15000-15342	$1067	$873	$501	$423
TOTALS	$7213	$5737	$2290	$1260
Change (%)			**–68%**	**–78%**

Results

The findings of this retrospective analysis of charges and reimbursements incurred for the healing of DFUs in a freestanding comprehensive wound care centre are interesting. Table 1 shows the two cohorts were fairly evenly matched for age, sex, critical limb ischaemia and average number of wounds. Table 2 shows very few (7%) of the 2013 cohort were revascularised compared to none in 2005. There did not appear to be any significant differences between the cohort from 2005 consisting of 189 patients and the 2013 cohort of 215 patients with healed DFUs.

All charges recorded in the patient's electronic medical record from the time of initial admission for a DFU until the time the patient was discharged after healing is included in the analysis (Table 3). We also included total reimbursements of the charges to give a better idea of what third–party payers actually reimburse. Since many wound care centres do not provide IV antibiotics infusion services and because these antibiotic charges were quite high, antibiotic charges were reported separately. This left all other charges directly related to the management of the DFUs. The major cost in each group when only direct wound care charges were considered was debridement (Table 4).

When considering the total costs of a patient from the time of admission to the time of healing of all diabetic foot wounds, the 2005 cohort group was found to have total charges of $14,690 (£9,536) ,the total reimbursed was $11,444 (£7,429). When comparing the total charges, there was a 68% decrease in charges and a 73% decrease in reimbursement for the 2013 cohort (Table 3).

Much of this decrease in charges between 2005 and 2013 was due to a significant reduction in debridement charges. The per-patient total debridement charge for all DFUs healed was $7,213 (£4,683) in 2005, but only $2,290 in 2013. This is a 68% reduction in debridement charges from 2005 to 2013

(Table 4). In addition, there is no question that there were economic benefits from fewer visits, because healing rates were faster in 2013 than in 2005.

However, the major reductions in charges and therefore decreased costs to third-party payers were down to significant decreases in antibiotic use, along with the impressive decrease in total debridement charges in 2013. We consider these findings to be economically significant.

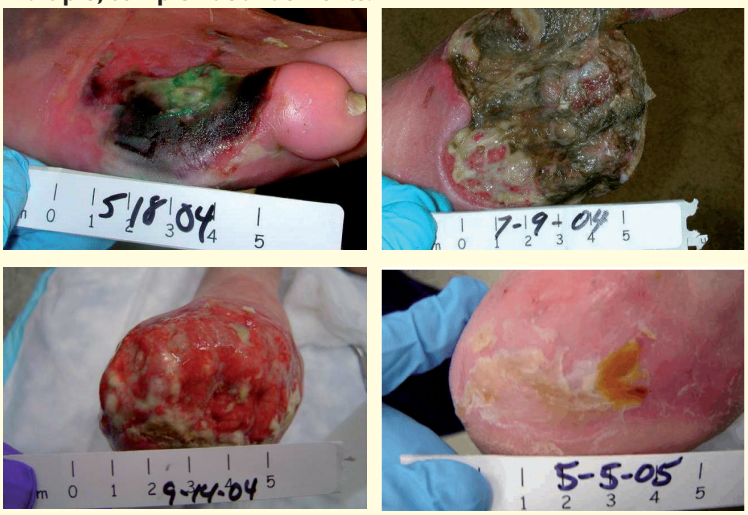
Discussion

The wound healing pattern for DFUs in 2005 was quite different from what is seen now. In the past, many DFUs would present with black, devitalised tissue. Despite aggressive debridement and heavy use of systemic antibiotics, the wound would erode and extensive tissue loss would result (Fig 1). The consequence was high-level debridements, (bone, muscle or tendon) that occurred for long durations, to slow progressive necrosis was controlled.

With the advent of molecular diagnostics and personalised management of the wound bioburden, the pattern of loss of extensive tissue into the forefoot has greatly diminished (Fig 2). This cannot be credited entirely to suppression of wound biofilm in that there has been some use of revascularisation, newer dressings and offloading have been introduced. The medical management of diabetes mellitus had also improved over the eight-year interval. That said, the major change in the practice pattern between 2005 and 2013 was the introduction of the ability to diagnose and treat wound biofilm. Biofilm-based wound care is reasonably the main driver for the underlying improvement in wound outcomes and the dramatic economic improvement demonstrated.

Our data shows that there was a 73% decrease in total cost (payment) to obtain complete healing in the 2013 cohort in comparison to the 2005 cohort. One major reason for this was the dramatic decrease in the use of systemic antibiotics, especially expensive antibiotics, such as daptomycin, linezolid and tygecycline. There was also a significant decrease in the use of systemic antipseudomonal antibiotics.

Fig 1. Traditional wound care. Gangrenous changes quickly spread to envelop the forefoot. Microcirculatory impairment contributes to this process but the main cause is a chronic infection (biofilm phenotype microbes) overwhelming host defences. Without biofilm suppression, the wound required multiple, complex debridements.

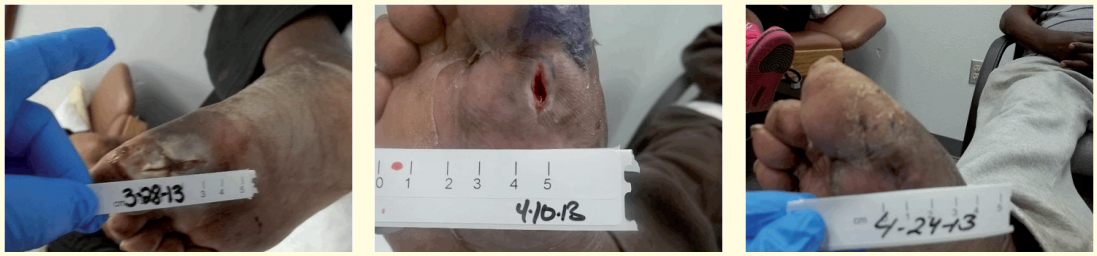


Also of note is that debridements in 2013 are at a much lower level, which has resulted in a significantly lower costs for debridement services under biofilm-based wound care. It seems counterintuitive that a treatment strategy predicated on frequent debridement would result in fewer total procedures and lower-complexity procedures with less overall cost. However, it should not be surprising in the context of biofilm causing impaired healing.

Limitations

It is interesting to note that previous detailed analyses of wound-care outcomes from a group of all wounds in 2005 compared to a group of all wounds in 2009 showed more than a 50% decrease in visits[16]. Data in the current study indicates only a 33% (18.9 versus

Fig 2. Biofilm-based wound care, with wound biofilm suppressed, this wound behaves much more like an acute wound despite microcirculatory impairment (TCpO2 26 torr dorsum of foot). This wound to the metatarsal-phalangeal joint healed in four weeks



12.5) decrease in visits for this subgroup of DFUs. However, the two studies are different. The 2005 group contained all wounds, not just DFUs. In addition, 50% of all wounds healed in four weeks, and wounds healing in the first four weeks were excluded from this analysis. Also, in the previous investigation, patients were followed only until the first wound healed, while all wounds had to be healed in this analysis. Still, biofilm-based wound care reduces the number of visits by 33%, which is an important finding.

Conclusion

Biofilm-based wound care is predicated on using multiple different treatment strategies simultaneously including antibiotics, anti-biofilm agents, selective biocides and frequent debridement. For over a decade, debridement has been economically discouraged. An Office of the Inspector General report demonstrated between 2001–2005 Medicare-allowed payments grew by 44% from $140 million to $202 million for surgical debridement services for chronic wounds in outpatient settings;[18] this has led to onerous regulations. Debridement is an easily learned and effective clinical technique that can be used to manage wound biofilm on all chronic wounds. Frequent debridement is a pivotal tool in biofilm-based wound care in that it opens a time-dependent window that makes treating agents much more effective, thus improving wound healing outcomes[17]. In one randomised control trial, more frequent debridement decreased the time to healing, with more patients healed.[19]

By adding accurate DNA diagnostics of the microbial bioburden and allowing for specific treatment of those microorganisms, wound healing is improved. The basic tenet of Oslerian medicine is to base all diagnosis and treatment on firm science. The corollary is that we must first diagnose then treat, yet, the majority of times, treatments for chronic wounds are chosen by a trial and error. It is interesting to point out that Koch's culturing methods (1860s) that are still used for clinical cultures today were developed before Sir William Osler was just out of his training.

There was a 73% decrease in total cost for obtaining complete healing in all the wounds of patients with DFUs with biofilm-based wound care. While visits and less complex debridements were the main drivers for the decreased cost, the sharp decrease in the need for expensive IV/IM antibiotics also contributed. Reimbursement for antibiotics in 2005 did not cover the cost of the antibiotics administered, which significantly hurt clinics' bottom line. So the decrease in antibiotic use, while decreasing top-line revenue, has helped our centre significantly.

The question is: how can a wound care centre continue using biofilm-based wound care given the draconian reduction in revenue? First, supplies used per patient came down significantly but not proportionately. Second, the number of new patients per month increased because of faster healing rates. Third, with increased success of rapidly healing wounds more patients will seek biofilm based wound care. This will increase the number of new patients to a wound care center. Fourth, it is far more satisfying professionally when you are part of a team that is exceeding expectations. Finally, the real benefit comes with patients healed and healed more quickly at a lower total cost. This will set a wound care centre apart if medicine transitions to a pay-for-performance paradigm. ■

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