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Hiding in plain sight: using routine data to identify opportunities to increase value and reduce waste in health systems

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Abstract

Objectives: In resource constrained health care systems opportunities to de-implement contradicted and unproven practices in order to increase value and reduce waste must be explored. Using the management of complex wounds as an exemplar, this study investigates temporal trends in the use of antimicrobials dressings, places this in the context of available evidence and discusses the potential impacts on the UK National Health Service (NHS).

Design: Secondary analysis of NHS prescription data

Setting: NHS Prescribing Cost Analysis (PCA) details all NHS prescriptions dispensed in the community in England on an annual basis

Interventions: An interrupted time series (ITS) design was used to compare annual changes in the expenditure and usage of anti-microbial and non-antimicrobial wound dressings before and after the publication of the 'intervention' of key evidence-based guidance in 2010

Primary and secondary outcome measures: Trends in use and expenditure of antimicrobial dressings in relation to published clinical guidance.

Results: There was a large increase in the prescribing of, and expenditure on, antimicrobial wound dressings between 1997 and 2016. In 1997 the total number of dressings prescribed was 5,792,700; by 2009 this had increased to 11,447,102 with expenditure increasing from £1,960,386 to £32,841,263 over the same period. Antimicrobial dressings have taken an increasing market share of dressings used and account for a disproportionate amount of expenditure despite no compelling evidence to support their routine use.

Conclusions: Routinely available prescribing data can be used to identify products of unproven benefit and which also impose a significant financial burden on health systems. This study quantifies the huge increase in the use of antimicrobial wound dressings over a 20-year period despite the lack of compelling research evidence to support their routine use. Routine data can be used to as part of more systematic efforts to increase value and reduce waste in health systems.

Strengths and limitations of the study

- The first research study identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years.
- Methods using these data show how new products can be adopted in relation to the published evidence of clinical or cost-effectiveness.
- Interrupted Time Series analysis has been used to explore the possible impact of a national clinical guidelines on the use of antimicrobial dressings
- The prescribing data are not wound-specific and limited to English community prescriptions; however, the community is where most complex wounds are treated
- A summary of the general status of evidence helps provides important contextual information in which to interpret the data.

Introduction

Resource constrained health care systems face increasing demands due to ageing populations, emerging medical conditions, modern lifestyles and advances in technology (1). It is imperative we increase the value of health care and improve outcomes for patients relative to costs (2). Clinical practice should, where possible, be informed by research evidence to ensure that limited funds are spent on resources and treatments with proven beneficial outcomes; in some cases the de-implementation of contradicted and unproven practices is required in order to increase value and reduce waste (3-5).

The management of complex wounds such as leg, foot and pressure ulcers, places a huge burden on healthcare resources. Although these wounds are managed in a variety of healthcare settings, in the UK the majority of care is delivered by community nurses (6). These open wounds are usually covered with a wound dressing and there are many options available ranging from simple gauzes to advanced dressings that have different absorptive properties such as foam, hydrocolloid and alginates(7). The availability of such a wide range of dressings can cause decision uncertainty amongst practitioners which in turn is reflected wide variation in terms of antimicrobial dressing use within and across different health care providers (6;8)

Wound dressings are classed as external medical devices and, as such, require a lower level of evidence to support marketing authorisation. The European regulatory framework for evaluating and regulating medical devices only requires manufacturers to demonstrate that new devices are safe and fit for purpose (9). A new Medical Device Regulation (MDR) is due to be fully applied in 2020 and will replace the European Union's current Medical Device Directive (MDD) and aims to ensure greater confidence in the effective protection of public health and patient safety (10). However, to-date, new dressing products come to market relatively rapidly and are not always supported by evidence of effectiveness (11).

The mid-1990s saw an increase in the availability of dressings claiming to have valuable antimicrobial properties due to the inclusion of ingredients such as silver, honey and iodine. Such dressings were developed and promoted for the prevention and treatment of wound infection and to ultimately improve wound healing (12). Generally antimicrobial dressings are more expensive to buy than their non-antimicrobial counter-parts. This study aimed to investigate temporal trends in the use of antimicrobials dressings, and place use in the context of available evidence. Specifically, we aimed to address:

- How many antimicrobial dressings are used by NHS community services in England and how much does this cost?
- How has use of antimicrobial dressings changed over time?
- What impact has the publication of evidence based guidance had on trends in antimicrobial dressing?

In addition to these analyses, we also qualitatively present this antimicrobial use and cost data in the context of contemporaneously available systematic review findings and other clinical guideline recommendations.

Methods

Extraction of data on antimicrobial dressing use and cost

UK National Health Service (NHS) Prescribing Cost Analysis (PCA) details all NHS prescriptions dispensed in the community in England on an annual basis (13). This includes all prescriptions dispensed by pharmacists, doctors and appliance contractors (e.g. suppliers of stoma and continence care equipment). PCA data give detail of the quantity (measured in units depending on the formulation of the product (e.g. one tablet, pack or dressing)) and also the Net Ingredient Cost (NIC) (expenditure on the product before discounts, not including any dispensing costs or fees). The drugs/dressings/devices are listed by British National Formulary (BNF) therapeutic class (14). PCA data are produced per annum and an Excel file for each year is available for download on the NHS Digital website (13). We extracted annual expenditure and quantity data from BNF Chapter 20 (Dressings), Section 3 (Wound management and other dressings) and Section 4 (Gauzes and gauze tissue) for a 20 year period (1997 to 2016). We searched for terms and brand names in four antimicrobial dressings categories; silver, honey, iodine and other antimicrobial dressings (14). 'Other' antimicrobial dressings include those containing agents other than those specified above, such as Polyhexamethylene Biguanide Hydrochloride (PHMB) and chlorohexidine. To ensure accuracy this identification and categorisation process was carried out independently by two authors and any discrepancies resolved through discussion. The quantity and expenditure (NIC) for 1997 to 2016 were plotted and presented as totals per annum. We chose this period of data analysis in part due to rounding to provide analyses for complete decades, but also to include the point in time when honey and silver dressings first appeared in the data. Data for the years 1992 to 1996 were checked to ensure there were no records of honey- or silver-containing wound dressings prior to 1997.

Identification of relevant guidelines and systematic reviews

Firstly we located key national guidelines relevant to the use of wound dressings in the community; these were clinical practice guidelines for complex wounds such as leg ulcers, foot ulcers and pressure ulcers (venous leg ulcers are the most prevalent complex wounds in the community setting) (15). We restricted our search to recognised UK-based producers of high quality, evidence-based guidelines who follow a transparent, rigorous process of guideline production – i.e. The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and relevant professional bodies such as the Royal Colleges. Secondly we searched for relevant Cochrane systematic reviews. We focused on Cochrane reviews as their production follows a rigorous and transparent process and they are freely available and highly accessed in the UK (in 2017 Cochrane reviews collectively had 2,136,922 full-text downloads in the UK alone) (16). Recommendations regarding the use of antimicrobial dressings were detailed in the published clinical guidance.

Interrupted Time Series (ITS) analysis

An interrupted time series (ITS) design was used to compare annual changes in the expenditure and usage of anti-microbial and non-antimicrobial wound dressings; focusing first on all antimicrobial dressings and then just those containing silver. The time periods to be compared were selected *a priori* and covered 2005 to 2009, with 2010 as the intervention point and the following five years as the post-intervention period (2011 to 2015). We chose 2010 as the intervention point since this was when the SIGN Guidelines for the treatment of venous leg ulcers were published, which itself was shortly after publication of a major trial of silver-dressings for the treatment of venous leg ulcers (17). In 2010 the SIGN Guidelines were the first new, national (UK) complex wound-related guidelines to be published for a number of years and subsequent to the introduction of silver dressings. The selected 5 year time periods were kept close to the intervention point (i.e. the guideline publication date) to reduce potential confounding by events occurring at a more distant time, whilst still giving sufficient data points for analysis. Ordinary least squares regression was used to estimate the temporal trends before, during and after the interventions with presentation of Newey–West standard errors to handle autocorrelation. The Cumby-Huizinga test was used to investigate autocorrelation. The analysis was undertaken in Stata 14 using the *itsa* command (18).

Patient and Public Involvement

There is no patient and public involvement in this study

Results

Trends in dressing use and expenditure

From 1997 to 2016 there was an increase in the use of (Figure 1) and expenditure on (Figure 2) antimicrobial dressings. In terms of quantity prescribed 5,792,700 antimicrobial dressings were prescribed in 1997 compared with 11,029,304 in 2006 and 11,344,471 in 2016.

In 1997 the only antimicrobial dressings included in the prescription data were those containing iodine or chlorhexidine (classed here as an 'other antimicrobial dressing'). Silver-containing dressings first appeared in the prescription data in 1998 and honey dressings in 2004. Whilst iodine dressings have been prescribed relevantly consistently between 1998 and 2006, during the same period the quantity of silver dressings prescribed increased from 143,600 to 5,485,684 (a 38-fold increase).

The increase in quantity of antimicrobial dressing use is matched by changes in expenditure over time (Figure 2). In 1997 the total expenditure on antimicrobial dressings was £1,960,386, increasing to a high of £32,841,263 in 2009 (an almost 17-fold increase). The most notable increase in annual expenditure was for silver dressings where annual spend increased year on year from 1998 onwards reaching a peak in 2009 with annual expenditure of over £26.5 million.

Figure 3 plots antimicrobial dressing prescriptions (quantity and expenditure) as a proportion of all wound dressings prescribed in the community in England. Over time antimicrobial dressings have comprised a greater proportion of all dressings used and an even greater share of expenditure.

Summary of relevant evidence synthesis and guidelines on antimicrobial dressing use for complex wounds

Table 1 outlines the key publications summarising evidence and giving guidance on the use of antimicrobial dressings in the treatment of complex wounds. The first UK guidance we found was published 1998 (19) and suggested little or no good research evidence that using antimicrobial dressings influenced wound outcomes. Guidance universally recommends using simple, non-adherent wound dressings for complex wounds and agrees that there is little research evidence to suggest that antimicrobial dressings are clinically or cost effective.

Table 1. Published evidence giving recommendations on the use of antimicrobial dressings for treatment of complex wounds

CODE	PUBLISHED GUIDANCE	MONTH	YEAR	EVIDENCE FOR USE OF ANTIMICROBIAL DRESSINGS	RECOMMENDATION or CONCLUSIONS
A	Clinical Practice Guidelines: The nursing management of patients with venous leg ulcers (20)	First published 1998, updated 2005 and 2006		The evidence in the guidance for 'Antimicrobial agents versus placebo or standard care' is based on a systematic review by O'Meara published in 2000 reviewing 14 RCTs. The RCTs were small and of poor quality, therefore no firm conclusions could be drawn.	Dressings must be simple, low adherent and acceptable to the patient. Cost effectiveness of leg ulcer dressings should be determined by their ability to stay in place for up to a week
B	Cochrane review: Topical silver for treating wound infection(21)	January	2007	This assessed topical silver products (creams or dressings) for the prevention of wound infection through the evaluation of 26 RCTs. The majority of studies found no statistical difference in infection rates between silver and non-silver dressings. Most of the trials were small and of poor quality.	There is insufficient evidence to support the use of silver dressings as they did not promote wound healing or promote information
C	Cochrane review: Honey as a topical treatment for wounds(22)	First published 2008, updated 2015		26 trials were identified. Two of high quality found that honey dressings heal partial thickness burns more quickly than conventional dressings. Other trials either showed no difference between treatments or were based on low quality evidence	The evidence for the effect of honey compared with other dressings is low quality, and therefore not robust enough basis for decision making
D	SIGN guidance: Management of venous leg ulcers(23)	August	2010	The recommendations for silver dressings are based on a Cochrane review in 2007 by Vermeulen *et al* and the Vulcan Trial in 2009. These found insufficient evidence to show improved healing rates for wounds treated with silver dressings compared to other types of dressings.	Guidance concludes that simple non-adherent dressings are recommended for VLU management. Silver dressings are not.
E	NICE guidance: Pressure ulcers: prevention and management(24)	April	2014	Alginate versus silver alginate. No statistical difference, very low quality evidence	The evidence did not allow for a recommendation of any specific type of dressing. Recommends a dressing that promotes an optimal healing environment rather than a specific type
F	NICE guidance: Diabetic foot problems: prevention and management(25)	August	2015	Included one RCT comparing iodine impregnated dressings with others; found no difference in healing rates.	Take into account clinical assessment of the wound and patient preference. Use dressing of lowest acquisition cost appropriate
G	Chronic wounds: advanced wound dressings and antimicrobial dressings(11)	March	2016	Gives an overview of previously published evidence and summarises research findings	There is little good quality evidence to support the use of antimicrobial dressings. Healthcare professionals should choose the least costly option which will provide the optimal environment for the type of wound and stage of healing

Interrupted time series (ITS) before and after publication of the SIGN guidance in 2010

Data from 2005 to the intervention year - 2010

The results of the ITS analysis for expenditure on antimicrobial dressings from 2005 to 2015 are shown in Table 2 and Appendix 1. £25.9 million (95% confidence intervals, £24.4 to £27.5) was spent on antimicrobial dressings in 2005, followed by an increase in spending of, on average, £1.6 million per year (£1.0 to £2.1) until 2009. In 2010 (the year of the SIGN guidance publication and one year after publication of the VULCAN study), there was a reduction in the expected spending on antimicrobial dressings (based on the pre-intervention trend) of -£5.2 million (-£8.6 to -£1.7, see Appendix 1 panel C); this reduction was largely driven by a reduction in silver dressing spend (see Table 2 and Appendix 1 panel E). There was no corresponding significant reduction in expenditure on non-antimicrobial dressings in 2010 (£0.9 million; -£4.8 to £3.0, Table 2 and Appendix 1 panel A).

Trends in quantity and expenditure of dressing use across the pre and post intervention period

Prior to the SIGN intervention during 2005 to 2009 the usage of anti-microbial dressings (by quantity) was significantly increasing by 170,000 dressings per year (110,000 to 230,000) assuming a linear trend but following the SIGN intervention during 2011 to 2015 the increasing trend slowed and was no longer significant (increasing by 70, 000 dressings per year; -180, 000 to 310,000). This change in the trend after the SIGN intervention compared with before the SIGN intervention was not significant (a reduction in average annual usage 100,000 dressings per year relative to the pre-SIGN trend; -370,000 to 160,000). For a graphical illustration see Appendix 1 panel D.

This pattern was significantly different from the annual decrease in usage of non-antimicrobial dressings, which continuously declined from 2005 to 2015 (Table 2 and comparing panels B and D in Appendix 1). The reasons for this reduction in non-anti-microbial dressing use are not obvious from these data and are considered further in the discussion. Taking the pre-intervention trend as the counterfactual the mean annual reduction in expenditure post-intervention was £1.6 million (-£2.9 to -£0.2) for antimicrobial dressings and £2.1 million (-£3.0 to -£1.2) for non-antimicrobial dressings (not a statistically significant difference i.e. the higher cost of anti-microbial dressings meant that they contributed more or less equally to the cost reductions when compared with non-antimicrobial dressings even though the quantities used were lower, see Table 2).

Differences between dressing use and expenditure in the post-intervention period

Comparing usage of antimicrobial and non-antimicrobial dressings in the post-intervention period (from 2011 to 2015) we observe increasing expenditure on non-antimicrobials dressings with

decreased usage (by quantity). Again reasons for this increased cost with reducing use are not obvious from these data and are considered further in the discussion. Data show that the increasing trend for expenditure on non-antimicrobial dressings is significantly different to the flat trend for antimicrobial dressings (Table 2).

Table 2. Interrupted time series analysis of annual costs and usage of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

	Units (Cost or quantity of dressings)	A. Annual cost or usage of dressings in 2005 (95% confidence intervals, CI)	B. Annual increase in cost or usage from 2005 to 2009 **Pre-intervention trend (95% CI)**	C. Decrease in cost or usage in 2010 **Change in intervention year (95% CI)**	D. Annual change in cost or usage from 2011- 2015 relative to 2005-2009 **(95% CI)**	E. Annual change in cost or usage from 2011- 2015 **Post-intervention trend (95% CI)**
1. All antimicrobial dressings	£ million	25.9 (24.4 to 27.5)	1.6 (1.0 to 2.1)	-5.2 (-8.6 to -1.7)	-1.6 (-2.9 to -0.2)	0.01 (-1.0 to 1.0)
	P values for comparison with non-antimicrobial dressings[1]			Significantly different P<0.1	Not significantly different	Significantly different P<0.05
	Quantity millions	10.8 (10.6 to 10.9)	0.17 (0.11 to 0.23)	-0.93 (-1.79 to - 0.07)	-0.10 (-0.37 to 0.16)	0.07 (-0.18 to 0.31)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Significantly different P<0.05	Significantly different P<0.001
2. Silver containing antimicrobial dressings	£ million	23.7 (22.3 to 25.1)	0.6 (0.0 to 1.1)	-5.1 (-8.6 to -1.5)	-1.0 (-2.3 to 0.4)	-0.4 (-1.5 to 0.7)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Not significantly different	Significantly different P<0.05
	Quantity millions	5.5 (5.3 to 5.5)	-0.02 (-0.07 to 0.03)	-0.99 (-1.68 to -0.30)	-0.07 (-0.30 to 0.14)	-0.1 (-0.03 to -0.1)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Significantly different P<0.05	Significantly different P<0.001
3. Non-antimicrobial dressings (reference group)	£ million	91.7 (90.0 to 93.4)	3.5 (2.7 to 4.3)	-0.9 (-4.8 to 3.0)	-2.1 (-3.0 to -1.2)	1.4 (0.7 to 2.0)
	Quantity millions	126.6 (122.4 to 130.8)	-4.5 (-6.0 to -3.0)	-0.57 (-11.4 to -0.01)	1.41 (-0.09 to 2.93)	-3.1 (-3.8 to -2. 4)

[1] the P values compare each cell in the row with non-antimicrobial dressings, *i.e.* the reference group is the corresponding cell in row 3

Discussion

Summary of main findings

Prescription of antimicrobial wound dressings in the UK has increased since 1997. This increase is particularly notable for silver-containing dressings. The Clinical guidance and Cochrane reviews presented in Table 1 show there is no research evidence to support the routine use of antimicrobial dressings for complex wounds. Thus, there has been a large increase in use of silver-containing wound dressings that cannot be explained by the contemporaneous research evidence. Historic use of silver, iodine and honey in wound healing is well documented (26-28). It has been suggested that resurgence in the use of these topical agents may be partly due to concerns about antibiotic-resistant bacteria and the need to reduce antibiotic prescribing (29). It is not clear if there has been any impact of increased antimicrobial dressing use on antibiotic use as there are no data on use of antibiotics specifically for wound treatment.

Our analysis shows that, following a period of rapid increase in antimicrobial dressing prescribing and expenditure, the publication of SIGN guidelines for venous leg ulcer management (2010) was followed by a significant reduction (both in cost and number of items). There was no commensurate change in the prescribing of other dressings. It is not clear why the reduction in antimicrobial use was not matched by an increase in use of other dressings to compensate for this differential usage. A possible explanation may be that other dressings were being taken from stock resources and so are not counted in the prescribing data. Being in stock means that the products are obtained directly via procurement in bulk – this would be most common for standard dressings. We note that whilst prescribing of silver-containing dressings reduced, there appears to have been an increase in prescribing of honey, iodine and 'other' antimicrobial dressings. If these trends are to be considered, in some part, to be an impact of the publication of the SIGN guideline, the guideline had more of an impact on the use of silver dressings than of other antimicrobial dressings. A potential explanation for this differential effect on antimicrobial dressing prescribing lies in the strength of the recommendations. The SIGN guidelines graded recommendations A to D based on the quality of the evidence and these differed for different dressings. The recommendation for silver dressings was graded A, that for honey was graded B and the recommendation for iodine dressings was unclassified (23). It may be that the strength of the recommendation for not using silver dressings was considered more compelling or that this recommendation had a greater effect because of the higher cost of silver dressings and the potential savings.

When looking across the entire study period, our analysis suggests that the total number of dressings used per annum may be decreasing. Conversely total expenditure on dressings appear to be increasing (13). The reasons for this pattern requires further exploration – potential areas to explore include the use of other medical devices or advanced dressings which are relatively expensive but may require less frequent changes (12) and/or the potential for increased unit prices for non-antimicrobial dressings. Finally dressings can be both prescribed and also kept as stock: increases in this type of activity may mean that using prescription data in the way we have, under-estimates the use of these dressings.

Treatment-related decision making in wound care

It is widely acknowledged that the process of decision-making is highly contingent and context dependent (30), particularly so in community and primary care (31). Reliable sources of evidence-based information including clinical guidelines and systematic reviews can influence decision making especially where a single clear message is conveyed to professional audiences who themselves are aware that a change in practice is required (32). A national evaluation of the implementation of NICE guidance found that recommendations are more likely to be adopted when there is strong professional support, clear guidance and no increased or unfunded costs (33). We know that the clinical decisions of community nurses are often based on experiential rather than research knowledge (34) and that 'human sources' are often preferred to written guidance (35). It seems clear from the temporal trends that the increases in dressing use are not driven by knowledge of the research evidence (36). This may suggest that strategies seeking to influence community nurses may need to be more focused on the type of change necessary to generate reduction in specific prescribing practices (37). A change involving substitution with related replacement may necessitate a multi-level approach that goes beyond knowledge dissemination to promote learning and unlearning to one that encompasses other interventions such as restriction of formulary options and routine monitoring and feedback of individuals prescribing practice to ensure adherence to organisational policies.

The widespread availability of wound care products of apparent low or no clinical value is in part reflective of the threshold for evidence necessary for marketing authorisation of devices (9). Because the threshold of evidence is low, there is little or no incentive for manufacturers to demonstrate that their devices are clinically effective. The emphasis is therefore on incremental product development and innovation. Adopting a medical device when there is little or no evidence to support its use may then in turn lead to a reduction in the likelihood of further relevant research as the innovation becomes standard and integrated into care (4).

Rothery *et al*, suggest that rather than binary choice of adopt or select, policy decisions on innovation introduction may be helped by guidance recommending either options of 'only in research' or 'approval with research' (38). The former allowing further research to establish the value of an innovation before wider access and the latter granting the possibility of product withdrawal should further research prove clinical and cost ineffectiveness (4). NICE has the ability to issue guidance to recommend 'only in research' but this is not routinely used and rarely if ever for medical devices (39).

Strengths and weaknesses

This is the first research study we have identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years. These simple data show powerfully how new products can be adopted rapidly despite a lack of robust evidence for clinical or cost-effectiveness. This reinforces the complex nature of decision making in wound care and importance of other spheres of information and knowledge including expert opinion and peer-to-peer advice (36). The role of marketing and company activity in successfully promoting product use is also an area that may have had impact here although this would need to be explored in further work (40).

Our analysis of wound care prescribing is limited by the available data. The prescribing data are not wound-specific and limited to English community prescriptions; however, we note that the community is where most complex wounds are treated (41). We also note that prescribing data will not include data on those standard dressings which are kept as stock. ITS analysis has been used to explore the possible impact of the first significant national clinical guideline, the SIGN guideline, on the management of venous leg ulcers. There is a suggestion of some impact of this 'intervention' however it has to be noted (as above) that this guidance is specific to venous leg ulcers whereas the PCA data cover dressing use for any wound type. These analyses did not include multiple 'interventions' incorporating the publication of other guidelines as it was decided to use the single intervention point of 2010 for reasons stated in the methods. However, presenting a summary of the general status of evidence (Table 1) which is so consistent in its message helps provides important contextual information in which to interpret the data.

A limitation of the ITS design is that any hypothesised relationship between the implementation of guidelines and changes in dressing usage is based purely on a temporal association. We have no direct evidence of causation. Furthermore the ordinary least squares model forecasts linear trends yet the post-SIGN trends for anti-microbial dressings do not appear to be linear and show a reversal

of the initial decreasing trend from 2012. This is partly explained by the differences in usage of silver and other antimicrobial dressings (see Appendix 2 panel F). As future data becomes available it will be important to monitor the usage of antimicrobial dressings in case further intervention is needed to reduce usage. However these changes are temporarily distant from the SIGN guidance and the primary aim of the ITS analysis was to examine changes occurring around the time of the SIGN guidance.

Conclusions

This paper suggests that in the last 20 years there has been a large increase in the use of antimicrobial wound dressings despite a lack of research evidence to support their routine use. Expenditure on antimicrobial wound dressings has risen by over £28 million between and 2016.

Our analysis shows that routinely available PCA data can be used to identify unproven products with significant net financial burden to the NHS may offer a transparent and systematic route to 'only in research' and ultimately to de-implementation. If using routine data in this way is to have an impact on prescribing at scale, then it needs to be linked to a multi-level response that targets procurement processes alongside individual practices to ensure increased value and reduced waste.

Figure Legends

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

Appendix 1. Interrupted time series analysis of annual costs and usage of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

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Competing interests

The authors declare they have no competing interests

Authors' contributions

Louise Hussey: First author of manuscript and data analysis

Jill Stocks: Interrupted time series analysis and interpretation

Paul Wilson: Interpretation of data and manuscript revision

Jo Dumville: Study concept and design, interpretation of data and manuscript revision

Nicky Cullum: Interpretation of data and manuscript revision

All authors reviewed and approved the final manuscript before submission

Data sharing

Prescription data is freely available from NHS digital (13)

Research Checklist

There is no research checklist relevant to this study

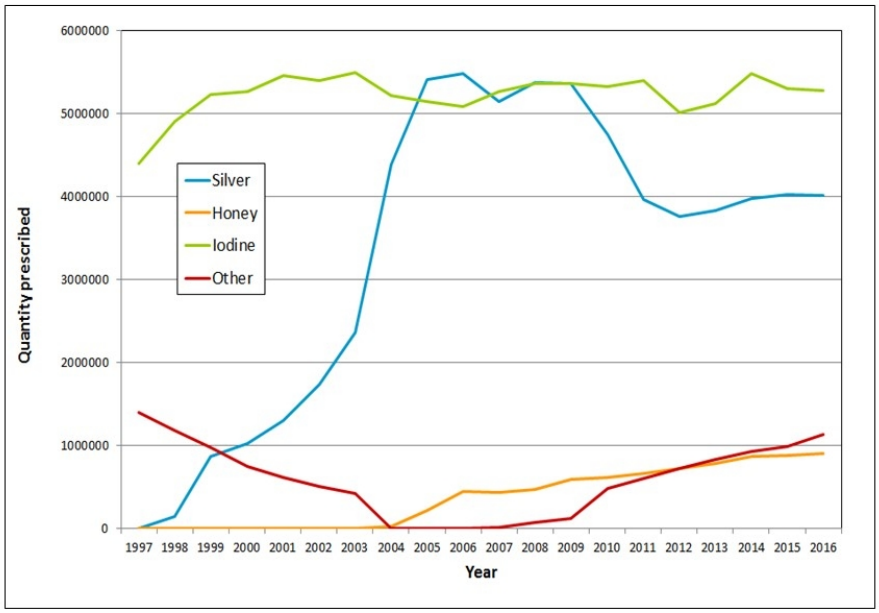


Figure 1. The quantity per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

254x190mm (96 x 96 DPI)

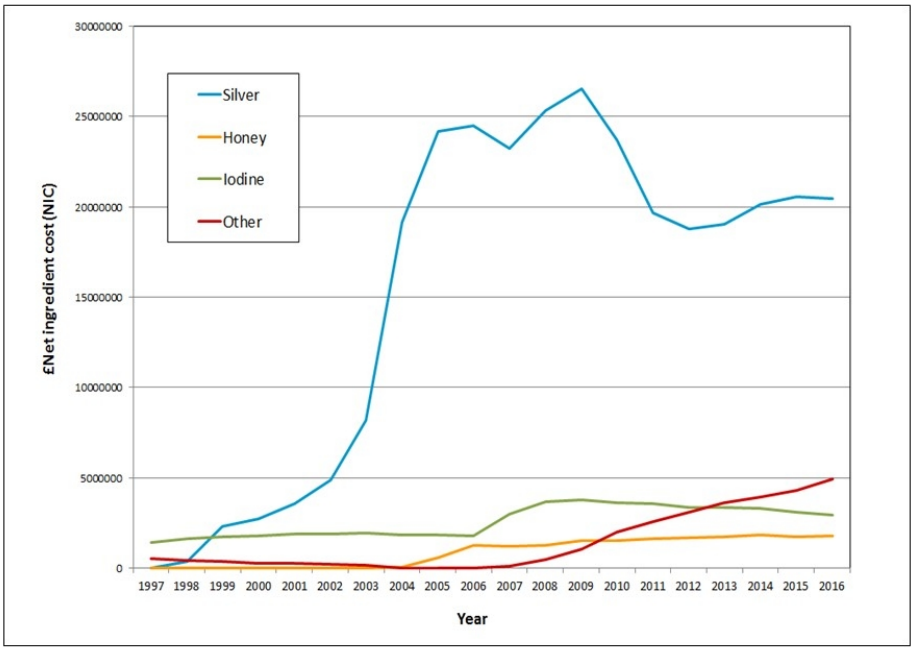


Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

254x190mm (96 x 96 DPI)

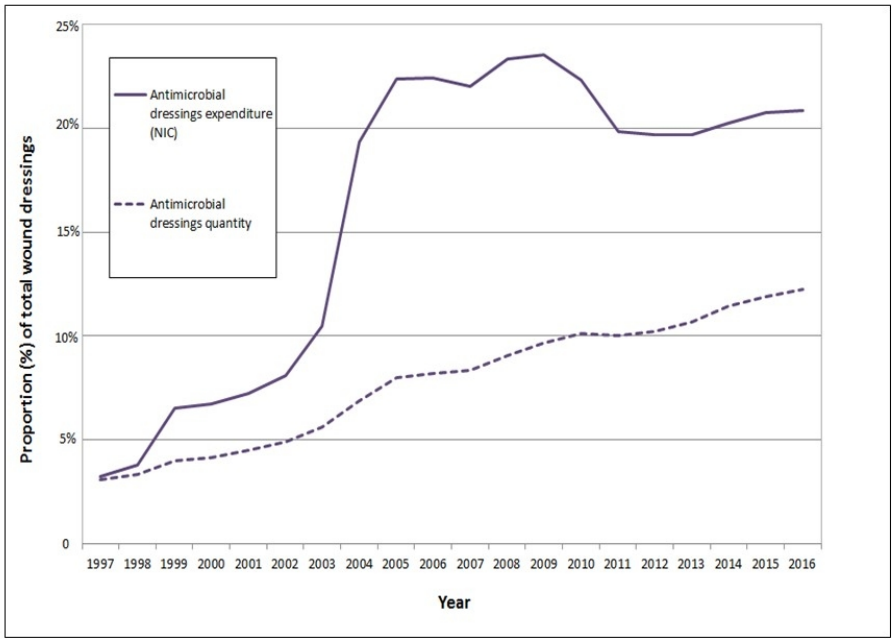
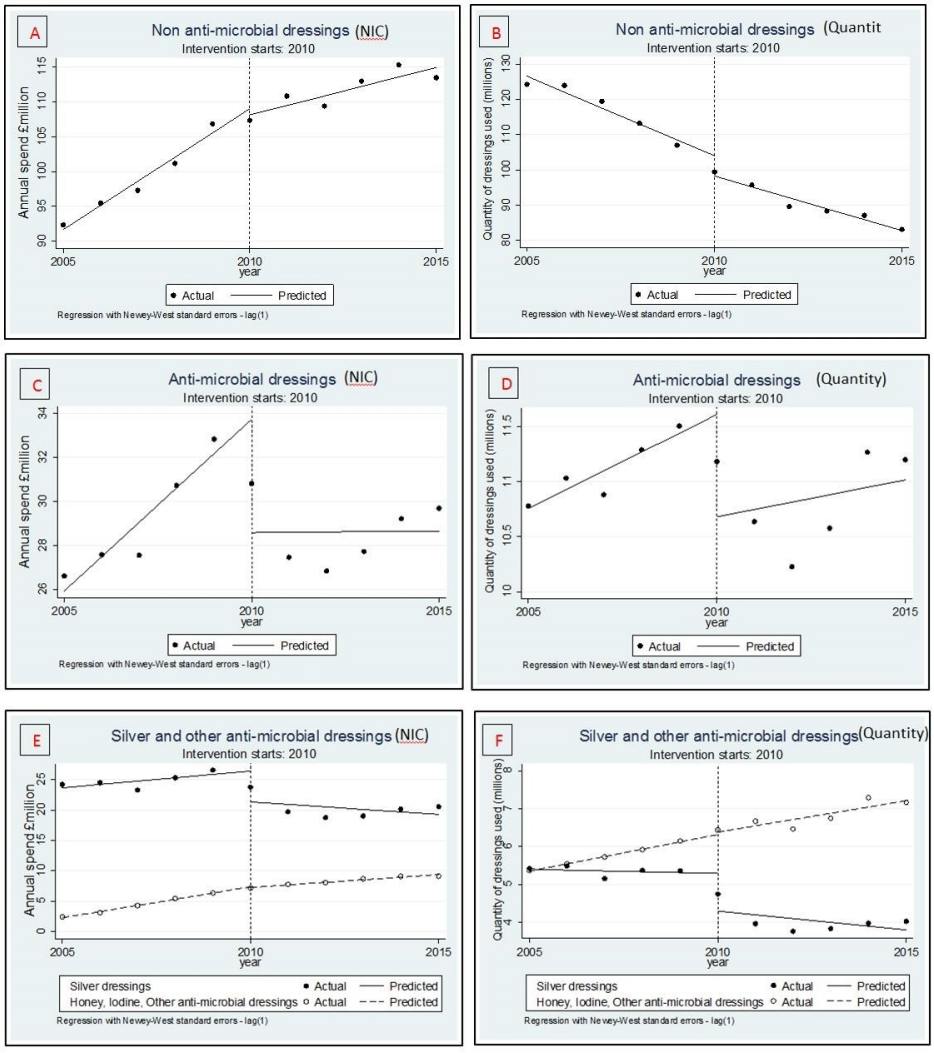


Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

254x190mm (96 x 96 DPI)



Appendix 1. Interrupted time series analysis of annual costs and usage of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

317x355mm (96 x 96 DPI)

BMJ Open

The use of antimicrobial dressings and the association with published clinical guidance: interrupted time series analysis

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The use of antimicrobial dressings and the association with published clinical guidance: interrupted time series analysis

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Abstract

Objectives: In health care systems practices and products of unproven value and cost-effectiveness can decrease value and increase waste. Using the management of complex wounds, this study investigates temporal trends in the use of antimicrobials dressings, places this in the context of available evidence and discusses the potential impacts on the UK National Health Service (NHS).

Design: Secondary descriptive and interrupted time series (ITS) analysis of NHS prescription data

Setting: Prescribing Cost Analysis (PCA) details all NHS prescriptions dispensed in the community in England.

Interventions: An ITS design was used to compare annual changes in the expenditure and use of antimicrobial and non-antimicrobial dressings before and after the publication of the 'intervention' of key evidence-based SIGN (Scottish Intercollegiate Guidelines Network) guidance in 2010.

Primary and secondary outcome measures: Trends in use and expenditure of antimicrobial dressings in relation to published clinical guidance.

Results: There was a large increase in the prescribing of, and expenditure on, antimicrobial wound dressings between 1997 and 2016. In 1997 the total number of dressings prescribed was 5,792,700; increasing to 11,447,102 in 2009 with expenditure increasing from £1,960,386 to £32,841,263. During the year of the SIGN intervention (2010) there was a significant drop in the use of silver but there was no consistent ongoing reduction from 2011 to 2015.

Conclusions: Prescribing data can be used to identify products of unproven benefit which also impose a significant financial burden. This study quantifies the huge increase in the use of antimicrobial wound dressings over a 20-year period despite the lack of compelling evidence to support their routine use, there is some suggestion, however that the use and expenditure decreased after the publication of key guidance. Routine data can be used to as part of more systematic efforts to increase value and reduce waste in health systems.

Strengths and limitations of the study

- The first research study identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years.
- Techniques such as interrupted time series analysis of prescribing data can be used to explore and illustrate the relationship between treatment choice and the contemporaneous availability of evidence about clinical and cost effectiveness.
- Interrupted Time Series analysis has been used to explore the possible impact of a national clinical guidelines on the use of antimicrobial dressings
- The prescribing data are not wound-specific and limited to English community prescriptions; however, the community is where most complex wounds are treated
- A summary of the general status of evidence helps provides important contextual information in which to interpret the data.

Introduction

Resource constrained health care systems face increasing demands due to ageing populations, emerging medical conditions, modern lifestyles and advances in technology (1). It is imperative we increase the value of health care and improve outcomes for patients relative to costs (2). Clinical practice should, where possible, be informed by research evidence to ensure that limited funds are spent on resources and treatments with proven beneficial outcomes; in some cases the de-implementation of contradicted and unproven practices is required in order to increase value and reduce waste (3-5).

The management of complex wounds such as leg, foot and pressure ulcers, places a huge burden on healthcare resources. Although these wounds are managed in a variety of healthcare settings, in the UK the majority of care is delivered by community nurses (6). These open wounds are usually covered with a wound dressing and there are many options available ranging from simple gauzes to advanced dressings that have different absorptive properties such as foam, hydrocolloid and alginates (7). The availability of such a wide range of dressings can cause decision uncertainty amongst practitioners which in turn is reflected in a wide variation in terms of antimicrobial dressing use within and across different health care providers (6;8)

Wound dressings are classed as external medical devices and, as such, require a lower level of evidence to support marketing authorisation. The European regulatory framework for evaluating and regulating medical devices only requires manufacturers to demonstrate that new devices are safe and fit for purpose (9). A new Medical Device Regulation (MDR) is due to be fully applied in 2020 and will replace the European Union's current Medical Device Directive (MDD) and aims to ensure greater confidence in the effective protection of public health and patient safety (10). However, to-date, new dressing products come to market relatively rapidly and are not always supported by evidence of effectiveness (11;12).

The mid-1990s saw an increase in the availability of dressings claiming to have valuable antimicrobial properties due to the inclusion of ingredients such as silver, honey and iodine. Such dressings were developed and promoted for the prevention and treatment of wound infection and to ultimately improve wound healing (13). Generally antimicrobial dressings are more expensive to buy than their non-antimicrobial counter-parts. This study aimed to investigate temporal trends in the use of antimicrobials dressings, and place use in the context of available evidence. Specifically, we aimed to address:

- How many antimicrobial dressings are used by NHS community services in England and how much does this cost?
- How has use of antimicrobial dressings changed over time?
- What impact has the publication of evidence based guidance had on trends in antimicrobial dressing?

In addition to these analyses, we also present this antimicrobial use and cost data in the context of contemporaneously available systematic review findings and other clinical guideline recommendations to examine whether trends may reflect any resulting change in practice.

Methods

Extraction of data on antimicrobial dressing use and cost

UK National Health Service (NHS) Prescribing Cost Analysis (PCA) is freely available information accessed from 'NHS Digital' and details all NHS prescriptions dispensed in the community in England on an annual basis (14). This includes all prescriptions dispensed by pharmacists, doctors and appliance contractors (e.g. suppliers of stoma and continence care equipment). PCA data give detail of the quantity (measured in units depending on the formulation of the product (e.g. one tablet, pack or dressing)) and also the Net Ingredient Cost (NIC) (expenditure on the product before discounts, not including any dispensing costs or fees). The drugs/dressings/devices are listed by British National Formulary (BNF) therapeutic class (15). PCA data are produced per annum and an Excel file for each year is available for download on the NHS Digital website (14). We extracted annual expenditure and quantity data from BNF Chapter 20 (Dressings), Section 3 (Wound management and other dressings) and Section 4 (Gauzes and gauze tissue) for a 20 year period (1997 to 2016). We searched for terms and brand names in four antimicrobial dressings categories; silver, honey, iodine and other antimicrobial dressings (15). 'Other' antimicrobial dressings include those containing agents other than those specified above, such as Polyhexamethylene Biguanide Hydrochloride (PHMB) and chlorohexidine. To ensure accuracy this identification and categorisation process was carried out independently by two authors and any discrepancies resolved through discussion. The quantity and expenditure (NIC) for 1997 to 2016 were plotted and presented as totals per annum. We chose this period of data analysis in part due to rounding to provide analyses for complete decades, but also to include the point in time when honey and silver dressings first appeared in the data. Data for the years 1992 to 1996 were checked to ensure there were no records of honey- or silver-containing wound dressings prior to 1997.

Identification of relevant guidelines and systematic reviews

Firstly we located key national guidelines relevant to the use of wound dressings in the community. We restricted our search to recognised UK-based producers of high quality, evidence-based guidelines who follow a transparent, rigorous process of guideline production – i.e. The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and relevant professional bodies such as the Royal Colleges. Secondly we searched for relevant Cochrane systematic reviews which follow a rigorous and transparent process and they are freely available and highly accessed in the UK. Recommendations regarding the use of antimicrobial dressings were detailed in the published clinical guidance.

Interrupted Time Series (ITS) analysis

An interrupted time series (ITS) design was used to compare annual changes in the expenditure and use of anti-microbial and non-antimicrobial wound dressings; focusing first on all antimicrobial dressings and then just those containing silver. The time periods to be compared were selected *a priori* and covered 2005 to 2009, with 2010 as the intervention point and the following five years as the post-intervention period (2011 to 2015). We chose 2010 as the intervention point since this was when the SIGN Guidelines (16) for the treatment of venous leg ulcers were published, which itself was shortly after publication of a major trial of silver-dressings for the treatment of venous leg ulcers (17). In 2010 the SIGN Guidelines were the first new, national (UK) complex wound-related guidelines to be published for a number of years and subsequent to the introduction of silver dressings. The selected five year time periods were kept close to the intervention point (i.e. the guideline publication date) to reduce potential confounding by events occurring at a more distant time, whilst still giving sufficient data points for analysis. Ordinary least squares regression was used to estimate the temporal trends before, during and after the interventions with presentation of Newey–West standard errors to handle autocorrelation. The Cumby-Huizinga test was used to investigate autocorrelation. The analysis was undertaken in Stata 14 using the *itsa* command (18). We used 3 categories just to make it easier to read so if labelled:

$p<0.001$ then is as it reads

$p<0.05$ is less than 0.05 but greater than 0>0.001

$p<0.1$ is less than 0.1 but greater than 0.05

Patient and Public Involvement

There is no patient and public involvement in this study

Ethical approval

Ethical approval was not required as this study is based on secondary analysis of freely available PCA information

Results

Trends in dressing use and expenditure

From 1997 to 2016 there was an increase in the use of (Figure 1) and expenditure on (Figure 2) antimicrobial dressings. In terms of quantity prescribed 5,792,700 antimicrobial dressings were prescribed in 1997 compared with 11,029,304 in 2006 and 11,344,471 in 2016.

In 1997 the only antimicrobial dressings included in the prescription data were those containing iodine or chlorhexidine (classed here as an 'other antimicrobial dressing'). Silver-containing dressings first appeared in the prescription data in 1998 and honey dressings in 2004. Whilst iodine dressings have been prescribed relatively consistently between 1998 and 2006, during the same period the quantity of silver dressings prescribed increased from 143,600 to 5,485,684.

The increase in quantity of antimicrobial dressing use is matched by changes in expenditure over time (Figure 2). In 1997 the total expenditure on antimicrobial dressings was £1,960,386, increasing to a high of £32,841,263 in 2009 (an almost 17-fold increase). The most notable increase in annual expenditure was for silver dressings where annual spend increased year on year from 1998 onwards reaching a peak in 2009 with annual expenditure of over £26.5 million.

Figure 3 plots antimicrobial dressing prescriptions (quantity and expenditure) as a proportion of all wound dressings prescribed in the community in England. Over time antimicrobial dressings have comprised a greater proportion of all dressings used and an even greater share of expenditure.

Summary of relevant evidence synthesis and guidelines on antimicrobial dressing use for complex wounds

Table 1 outlines the key publications summarising evidence and giving guidance on the use of antimicrobial dressings in the treatment of complex wounds. The first UK guidance we found was published 1998 (19) and suggested little or no good research evidence that using antimicrobial

dressings influenced wound outcomes. Guidance universally recommends using simple, non-adherent wound dressings for complex wounds and agrees that there is little research evidence to suggest that antimicrobial dressings are clinically or cost effective.

Table 1. Published evidence giving recommendations on the use of antimicrobial dressings for treatment of complex wounds

CODE	PUBLISHED GUIDANCE	MONTH	YEAR	EVIDENCE FOR USE OF ANTIMICROBIAL DRESSINGS	RECOMMENDATION or CONCLUSIONS
A	Clinical Practice Guidelines: The nursing management of patients with venous leg ulcers (19)	First published 1998, updated 2005 and 2006		The evidence in the guidance for 'Antimicrobial agents versus placebo or standard care' is based on a systematic review by O'Meara published in 2000 reviewing 14 RCTs. The RCTs were small and of poor quality, therefore no firm conclusions could be drawn.	Dressings must be simple, low adherent and acceptable to the patient. Cost effectiveness of leg ulcer dressings should be determined by their ability to stay in place for up to a week
B	Cochrane review: Topical silver for treating wound infection (20)	January	2007	This assessed topical silver products (creams or dressings) for the prevention of wound infection through the evaluation of 26 RCTs. The majority of studies found no statistical difference in infection rates between silver and non-silver dressings. Most of the trials were small and of poor quality.	There is insufficient evidence to support the use of silver dressings as they did not reduce infection or promote wound healing
C	Cochrane review: Honey as a topical treatment for wounds (21)	First published 2008, updated 2015		26 trials were identified. Two of high quality found that honey dressings heal partial thickness burns more quickly than conventional dressings. Other trials either showed no difference between treatments or were based on low quality evidence	The evidence for the effect of honey compared with other dressings is low quality, and therefore not robust enough basis for decision making
D	SIGN guidance: Management of venous leg ulcers (16)	August	2010	The recommendations for silver dressings are based on a Cochrane review in 2007 by Vermeulen *et al* and the Vulcan Trial in 2009. These found insufficient evidence to show improved healing rates for wounds treated with silver dressings compared to other types of dressings.	Guidance concludes that simple non-adherent dressings are recommended for VLU management. Silver dressings are not.
E	NICE guidance: Pressure ulcers: prevention and management (22)	April	2014	Alginate versus silver alginate. No statistical difference, very low quality evidence	The evidence did not allow for a recommendation of any specific type of dressing. Recommends a dressing that promotes an optimal healing environment rather than a specific type
F	NICE guidance: Diabetic foot problems: prevention and management (23)	August	2015	Included one RCT comparing iodine impregnated dressings with others; found no difference in healing rates.	Take into account clinical assessment of the wound and patient preference. Use dressing of lowest acquisition cost appropriate
G	Chronic wounds: advanced wound dressings and antimicrobial dressings (11)	March	2016	Gives an overview of previously published evidence and summarises research findings	There is little good quality evidence to support the use of antimicrobial dressings. Healthcare professionals should choose the least costly option which will provide the optimal environment for the type of wound and stage of healing

Interrupted time series (ITS) before and after publication of the SIGN guidance in 2010

Data from 2005 to the intervention year - 2010

The results of the ITS analysis for expenditure on antimicrobial dressings from 2005 to 2015 are shown in Table 2 and Appendix 1. £25.9 million (95% confidence intervals, £24.4 to £27.5) was spent on antimicrobial dressings in 2005, followed by an increase in spending of, on average, £1.6 million per year (£1.0 to £2.1) until 2009. In 2010 (the year of the SIGN guidance publication and one year after publication of the VULCAN study), there was a reduction in the expected spending on antimicrobial dressings (based on the pre-intervention trend) of -£5.2 million (-£8.6 to -£1.7, see Appendix 1 panel A); this reduction was largely driven by a reduction in silver dressing spend (see Table 2 and Appendix 1 panel B (expenditure) and C (use)). There was no corresponding significant reduction in expenditure on non-antimicrobial dressings in 2010 (£0.9 million; -£4.8 to £3.0, Table 2 and Appendix 1 panel D).

Trends in quantity and expenditure of dressing use across the pre and post intervention period

Prior to the SIGN intervention during 2005 to 2009 the use of anti-microbial dressings (by quantity) was significantly increasing by 170,000 dressings per year (110,000 to 230,000) assuming a linear trend but following the SIGN intervention during 2011 to 2015 the increasing trend slowed and was no longer significant (increasing by 70, 000 dressings per year; -180, 000 to 310,000). This change in the trend after the SIGN intervention compared with before the SIGN intervention was not significant (a reduction in average annual use 100,000 dressings per year relative to the pre-SIGN trend; -370,000 to 160,000). For a graphical illustration see Appendix 1 panel E.

This pattern was significantly different from the annual decrease in use of non-antimicrobial dressings, which continuously declined from 2005 to 2015 (Table 2 and comparing panels E and F in Appendix 1). Taking the pre-intervention trend as the counterfactual the mean annual reduction in expenditure post-intervention was £1.6 million (-£2.9 to -£0.2) for antimicrobial dressings and £2.1 million (-£3.0 to -£1.2) for non-antimicrobial dressings (not a statistically significant difference i.e. the higher cost of anti-microbial dressings meant that they contributed more or less equally to the cost reductions when compared with non-antimicrobial dressings even though the quantities used were lower, see Table 2).

Differences between dressing use and expenditure in the post-intervention period

Comparing use of antimicrobial and non-antimicrobial dressings in the post-intervention period (from 2011 to 2015) we observe increasing expenditure on non-antimicrobials dressings with decreased use (by quantity). Data show that the increasing trend for expenditure on non-antimicrobial dressings is significantly different to the flat trend for antimicrobial dressings (Table 2).

1

Table 2. Interrupted time series analysis of annual costs and use of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

	Units (Cost or quantity of dressings)	A. Annual cost or use of dressings in 2005 (95% confidence intervals, CI)	B. Annual increase in cost or use from 2005 to 2009 Pre-intervention trend (95% CI)	C. Decrease in cost or use in 2010 Change in intervention year (95% CI)	D. Annual change in cost or use from 2011- 2015 relative to 2005-2009 (95% CI)	E. Annual change in cost or use from 2011- 2015 Post-intervention trend (95% CI)
1. All antimicrobial dressings	£ million	25.9 (24.4 to 27.5)	1.6 (1.0 to 2.1)	-5.2 (-8.6 to -1.7)	-1.6 (-2.9 to -0.2)	0.01 (-1.0 to 1.0)
	P values for comparison with non-antimicrobial dressings[1]			Significantly different P<0.1	Not significantly different	Significantly different P<0.05
	Quantity millions	10.8 (10.6 to 10.9)	0.17 (0.11 to 0.23)	-0.93 (-1.79 to - 0.07)	-0.10 (-0.37 to 0.16)	0.07 (-0.18 to 0.31)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Significantly different P<0.05	Significantly different P<0.001
2. Silver containing antimicrobial dressings	£ million	23.7 (22.3 to 25.1)	0.6 (0.0 to 1.1)	-5.1 (-8.6 to -1.5)	-1.0 (-2.3 to 0.4)	-0.4 (-1.5 to 0.7)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Not significantly different	Significantly different P<0.05
	Quantity millions	5.5 (5.3 to 5.5)	-0.02 (-0.07 to 0.03)	-0.99 (-1.68 to -0.30)	-0.07 (-0.30 to 0.14)	-0.1 (-0.03 to -0.1)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Significantly different P<0.05	Significantly different P<0.001
3. Non-antimicrobial dressings (reference group)	£ million	91.7 (90.0 to 93.4)	3.5 (2.7 to 4.3)	-0.9 (-4.8 to 3.0)	-2.1 (-3.0 to -1.2)	1.4 (0.7 to 2.0)
	Quantity millions	126.6 (122.4 to 130.8)	-4.5 (-6.0 to -3.0)	-0.57 (-11.4 to -0.01)	1.41 (-0.09 to 2.93)	-3.1 (-3.8 to -2. 4)

[1] the P values compare each cell in the row with non-antimicrobial dressings, *i.e.* the reference group is the corresponding cell in row 3

Discussion

Summary of main findings

Prescription of antimicrobial wound dressings in the UK has increased since 1997. This increase is particularly notable for silver-containing dressings. The Clinical guidance and Cochrane reviews presented in Table 1 show there is no research evidence to support the routine use of antimicrobial dressings for complex wounds. Thus, there has been a large increase in use of silver-containing wound dressings that cannot be explained by the contemporaneous research evidence. Historic use of silver, iodine and honey in wound healing is well documented (24-26). It has been suggested that resurgence in the use of these topical agents may be partly due to concerns about antibiotic-resistant bacteria and the need to reduce antibiotic prescribing (27).

Our analysis shows that, following a period of rapid increase in antimicrobial dressing prescribing and expenditure, the publication of SIGN guidelines for venous leg ulcer management (2010) was followed by a significant reduction (both in cost and number of items). There was no commensurate change in the prescribing of other dressings. It is not clear why the reduction in antimicrobial use was not matched by an increase in use of other dressings to compensate for this differential use. A possible explanation may be that other dressings were being taken from stock resources and so are not counted in the prescribing data. Being in stock means that the products are obtained directly via procurement in bulk – this would be most common for standard dressings. We note that whilst prescribing of silver-containing dressings reduced, there appears to have been an increase in prescribing of honey, iodine and 'other' antimicrobial dressings. If these trends are to be considered, in some part, to be an impact of the publication of the SIGN guideline, the guideline had more of an impact on the use of silver dressings than of other antimicrobial dressings. A potential explanation for this differential effect on antimicrobial dressing prescribing lies in the strength of the recommendations. The SIGN guidelines graded recommendations A to D based on the quality of the evidence and these differed for different dressings. The recommendation for silver dressings was graded A, that for honey was graded B and the recommendation for iodine dressings was unclassified (16). It may be that the strength of the recommendation for not using silver dressings was considered more compelling or that this recommendation had a greater effect because of the higher cost of silver dressings and the potential savings.

When looking across the entire study period, our analysis suggests that the total number of dressings used per annum may be decreasing. Conversely total expenditure on dressings appear to be increasing (14). The reasons for this pattern requires further exploration – potential areas to explore include the

use of other medical devices or advanced dressings which are relatively expensive but may require less frequent changes (13) and/or the potential for increased unit prices for non-antimicrobial dressings.

Treatment-related decision making in wound care

It is widely acknowledged that the process of decision-making is highly contingent and context dependent (30), particularly so in community and primary care (28). Reliable sources of evidence-based information including clinical guidelines and systematic reviews can influence decision making especially where a single clear message is conveyed to professional audiences who themselves are aware that a change in practice is required (29). A national evaluation of the implementation of NICE guidance found that recommendations are more likely to be adopted when there is strong professional support, clear guidance and no increased or unfunded costs (30). We know that the clinical decisions of community nurses are often based on experiential rather than research knowledge (31) and that 'human sources' are often preferred to written guidance (32). It seems clear from the temporal trends that the increases in dressing use are not driven by knowledge of the research evidence (33). This may suggest that any action aimed at implementing evidence-based guidance within community nursing may benefit from being more focused on the type of change necessary to generate a reduction in specific prescribing practices such as restriction of formulary options and routine monitoring and feedback of individuals prescribing practice to ensure adherence to organisational policies (34).

Patient preference may also play a part in dressing section. Research has shown that healing time was ranked by patients as the most important factor (compared to other factors such as dressing change frequency and pain) (35). Choosing Wisely is a global initiative to address issues such as patient and clinician preferences and making better decisions about care with the aim that this will help avoid tests, treatments or procedures that are unlikely to be of benefit. Choosing Wisely UK is led by the Academy of Medical Royal Colleges and as yet does not encompass nursing as a profession or have any guidance focused on the management of complex wounds (36;37).

The widespread availability of wound care products of apparent low or no clinical value is in part reflective of the threshold for evidence necessary for marketing authorisation of devices (9). Because the threshold of evidence is low, there is little or no incentive for manufacturers to demonstrate that their devices are clinically effective. Research showing how evidence is used to support claims made in product advertisements within two wound care journals found just 35% of claims about the benefits of a product cited supporting evidence. When these sources of evidence were investigated the cited

evidence did not support the claim being made in 56% of cases (12). The emphasis is therefore on incremental product development and innovation. Adopting a medical device when there is little or no evidence to support its use may then in turn lead to a reduction in the likelihood of further relevant research as the innovation becomes standard and integrated into care (4).

Rothery *et al*, suggest that rather than binary choice of adopt or select, policy decisions on innovation introduction may be helped by guidance recommending either options of 'only in research' or 'approval with research' (38). The former allowing further research to establish the value of an innovation before wider access and the latter granting the possibility of product withdrawal should further research prove clinical and cost ineffectiveness (4). NICE has the ability to issue guidance to recommend 'only in research' but this is not routinely used and rarely if ever for medical devices (39).

Strengths and weaknesses

This is the first research study we have identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years. These simple data show powerfully how new products can be adopted rapidly despite a lack of robust evidence for clinical or cost-effectiveness. This reinforces the complex nature of decision making in wound care and importance of other spheres of information and knowledge including expert opinion and peer-to-peer advice (33). The role of marketing and company activity in successfully promoting product use is also an area that may have had impact here although this would need to be explored in further work (40).

Our analysis of wound care prescribing is limited by the available data. Temporal changes in dressing use and expenditure may also be influenced by demographic and epidemiological factors (e.g. an ageing population and the rise in chronic diseases such as diabetes) (41). The prescribing data are not wound-specific and limited to English community prescriptions; however, we note that the community is where most complex wounds are treated (42). We also note that prescribing data will not include data on those standard dressings which are kept as stock. ITS analysis has been used to explore the possible impact of the first significant national clinical guideline, the SIGN guideline, on the management of venous leg ulcers. There is a suggestion of some impact of this 'intervention' however it has to be noted (as above) that this guidance is specific to venous leg ulcers whereas the PCA data cover dressing use for any wound type. These analyses did not include multiple 'interventions' incorporating the publication of other guidelines as it was decided to use the single intervention point of 2010 for reasons stated in the methods. However, presenting a summary of the general status of evidence (Table 1) which is so consistent in its message helps provides important contextual information in which to interpret the data.

A limitation of the ITS design is that any hypothesised relationship between the implementation of guidelines and changes in dressing use is based purely on a temporal association. We have no direct evidence of causation. Furthermore the ordinary least squares model forecasts linear trends yet the post-SIGN trends for anti-microbial dressings do not appear to be linear and show a reversal of the initial decreasing trend from 2012. This is partly explained by the differences in use of silver and other antimicrobial dressings (see Appendix 2 panel F). As future data becomes available it will be important to monitor the use of antimicrobial dressings in case further intervention is needed to reduce use. However these changes are temporarily distant from the SIGN guidance and the primary aim of the ITS analysis was to examine changes occurring around the time of the SIGN guidance.

Conclusions

This paper suggests that in the last 20 years there has been a large increase in the use of antimicrobial wound dressings despite a lack of research evidence to support their routine use. Expenditure on antimicrobial wound dressings has risen by over £28 million between and 2016.

Our analysis shows that routinely available PCA data can be used to identify unproven products with significant net financial burden to the NHS may offer a transparent and systematic route to 'only in research' and ultimately to de-implementation. If using routine data in this way is to have an impact on prescribing at scale, then it needs to be linked to a multi-level response that targets procurement processes alongside individual practices to ensure increased value and reduced waste.

Figure Legends

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

Appendix 1. Interrupted time series analysis of annual costs and use of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

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Competing interests

The authors declare they have no competing interests

Authors' contributions

Louise Hussey: First author of manuscript and data analysis

Jill Stocks: Interrupted time series analysis and interpretation

Paul Wilson: Interpretation of data and manuscript revision

Jo Dumville: Study concept and design, interpretation of data and manuscript revision

Nicky Cullum: Interpretation of data and manuscript revision

All authors reviewed and approved the final manuscript before submission

Data sharing

Prescription data is freely available from NHS digital (14)

Research Checklist

There is no research checklist relevant to this study

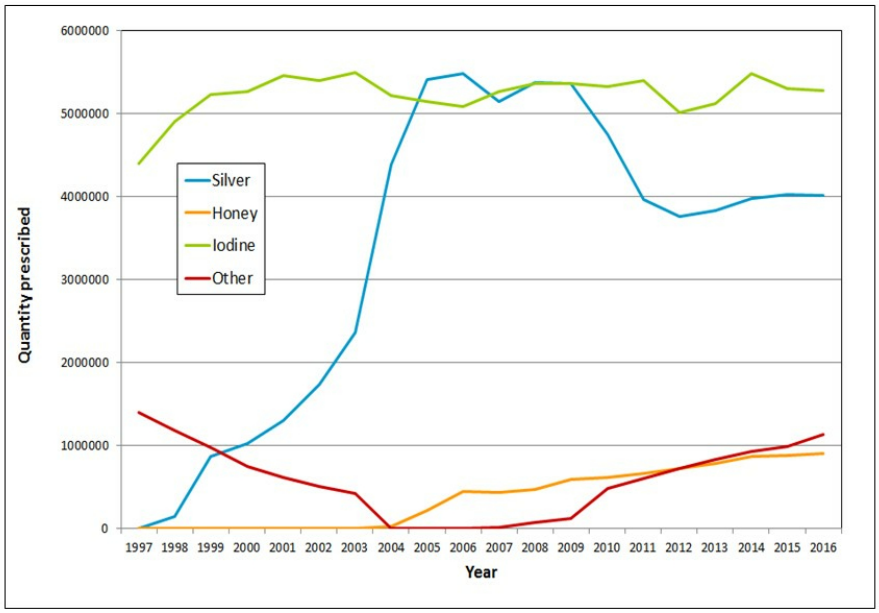

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

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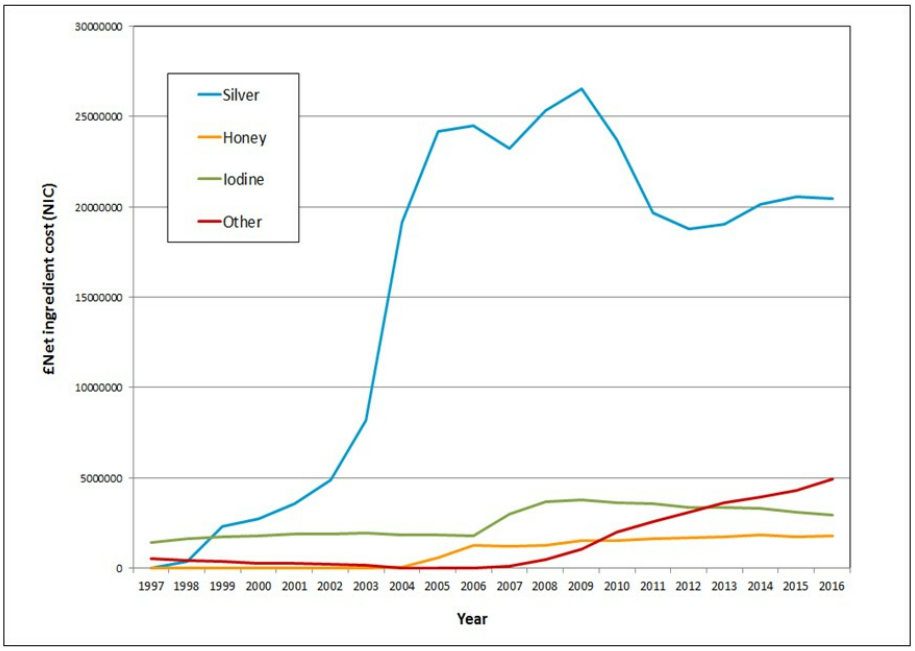


Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

81x60mm (300 x 300 DPI)

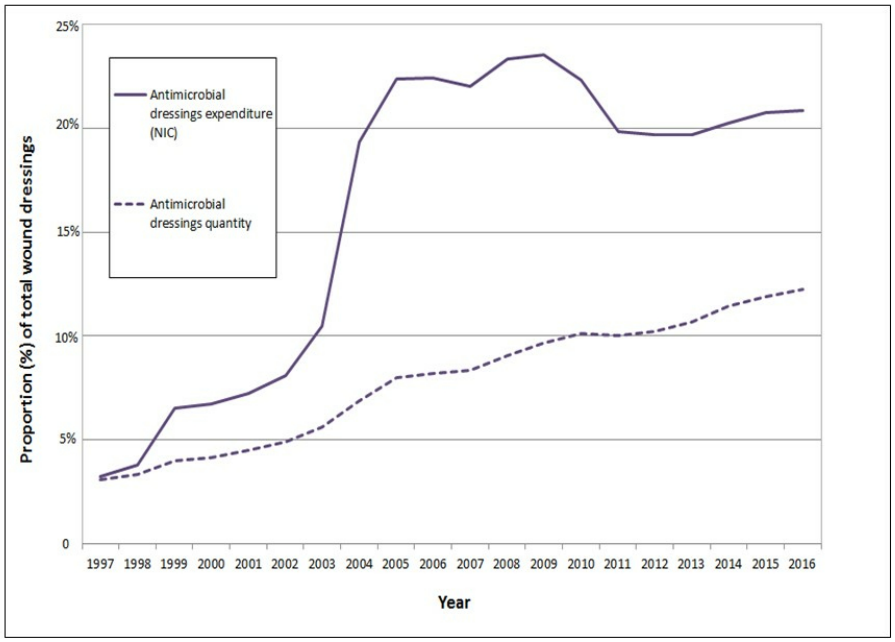
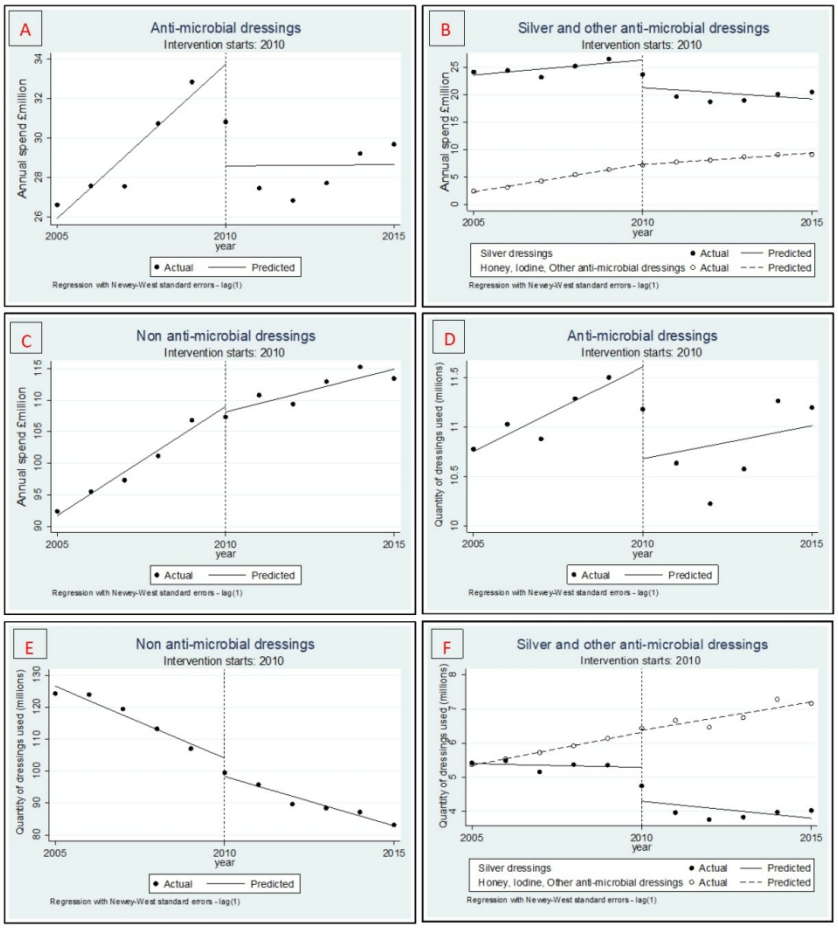


Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

81x60mm (300 x 300 DPI)



Appendix 1. Interrupted time series analysis of annual costs and usage of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

104x148mm (300 x 300 DPI)

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The use of antimicrobial dressings and the association with published clinical guidance: interrupted time series analysis

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The use of antimicrobial dressings and the association with published clinical guidance: interrupted time series analysis

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Abstract

Objectives: In health care systems practices and products of unproven value and cost-effectiveness can decrease value and increase waste. Using the management of complex wounds, this study investigates temporal trends in the use of antimicrobials dressings, places this in the context of available evidence and discusses the potential impacts on the UK National Health Service (NHS).

Design: Secondary descriptive and interrupted time series (ITS) analysis of NHS prescription data

Setting: Prescribing Cost Analysis (PCA) details all NHS prescriptions dispensed in the community in England.

Interventions: An ITS design was used to compare annual changes in the expenditure and use of antimicrobial and non-antimicrobial dressings before and after the publication of the 'intervention' of key evidence-based SIGN (Scottish Intercollegiate Guidelines Network) guidance in 2010.

Primary and secondary outcome measures: Trends in use and expenditure of antimicrobial dressings in relation to published clinical guidance.

Results: There was a large increase in the prescribing of, and expenditure on, antimicrobial wound dressings between 1997 and 2016. In 1997 the total number of dressings prescribed was 5,792,700; increasing to 11,447,102 in 2009 with expenditure increasing from £1,960,386 to £32,841,263. During the year of the SIGN intervention (2010) there was a significant drop in the use of silver but there was no consistent ongoing reduction from 2011 to 2015.

Conclusions: Prescribing data can be used to identify products of unproven benefit which also impose a significant financial burden. This study quantifies the huge increase in the use of antimicrobial wound dressings over a 20-year period despite the lack of compelling evidence to support their routine use, there is some suggestion, however that the use and expenditure decreased after the publication of key guidance. Routine data can be used to as part of more systematic efforts to increase value and reduce waste in health systems.

Strengths and limitations of the study

- The first research study identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years.
- Techniques such as interrupted time series analysis of prescribing data can be used to explore and illustrate the relationship between treatment choice and the contemporaneous availability of evidence about clinical and cost effectiveness.
- Interrupted Time Series analysis has been used to explore the possible impact of a national clinical guidelines on the use of antimicrobial dressings
- The prescribing data are not wound-specific and limited to English community prescriptions; however, the community is where most complex wounds are treated
- A summary of the general status of evidence helps provides important contextual information in which to interpret the data.

Introduction

Resource constrained health care systems face increasing demands due to ageing populations, emerging medical conditions, modern lifestyles and advances in technology (1). It is imperative we increase the value of health care and improve outcomes for patients relative to costs (2). Clinical practice should, where possible, be informed by research evidence to ensure that limited funds are spent on resources and treatments with proven beneficial outcomes; in some cases the de-implementation of contradicted and unproven practices is required in order to increase value and reduce waste (3-5).

The management of complex wounds such as leg, foot and pressure ulcers, places a huge burden on healthcare resources. Although these wounds are managed in a variety of healthcare settings, in the UK the majority of care is delivered by community nurses (6). These open wounds are usually covered with a wound dressing and there are many options available ranging from simple gauzes to advanced dressings that have different absorptive properties such as foam, hydrocolloid and alginates (7). The availability of such a wide range of dressings can cause decision uncertainty amongst practitioners which in turn is reflected in a wide variation in terms of antimicrobial dressing use within and across different health care providers (6;8)

Wound dressings are classed as external medical devices and, as such, require a lower level of evidence to support marketing authorisation. The European regulatory framework for evaluating and regulating medical devices only requires manufacturers to demonstrate that new devices are safe and fit for purpose (9). A new Medical Device Regulation (MDR) is due to be fully applied in 2020 and will replace the European Union's current Medical Device Directive (MDD) and aims to ensure greater confidence in the effective protection of public health and patient safety (10). However, to-date, new dressing products come to market relatively rapidly and are not always supported by evidence of effectiveness (11;12).

The mid-1990s saw an increase in the availability of dressings claiming to have valuable antimicrobial properties due to the inclusion of ingredients such as silver, honey and iodine. Such dressings were developed and promoted for the prevention and treatment of wound infection and to ultimately improve wound healing (13). Generally antimicrobial dressings are more expensive to buy than their non-antimicrobial counter-parts. This study aimed to investigate temporal trends in the use of antimicrobials dressings, and place use in the context of available evidence. Specifically, we aimed to address:

- How many antimicrobial dressings are used by NHS community services in England and how much does this cost?
- How has use of antimicrobial dressings changed over time?
- What impact has the publication of evidence based guidance had on trends in antimicrobial dressing?

In addition to these analyses, we also present this antimicrobial use and cost data in the context of contemporaneously available systematic review findings and other clinical guideline recommendations to examine whether trends may reflect any resulting change in practice.

Methods

Extraction of data on antimicrobial dressing use and cost

UK National Health Service (NHS) Prescribing Cost Analysis (PCA) is freely available information accessed from 'NHS Digital' and details all NHS prescriptions dispensed in the community in England on an annual basis (14). This includes all prescriptions dispensed by pharmacists, doctors and appliance contractors (e.g. suppliers of stoma and continence care equipment). PCA data give detail of the quantity (measured in units depending on the formulation of the product (e.g. one tablet, pack or dressing)) and also the Net Ingredient Cost (NIC) (expenditure on the product before discounts, not including any dispensing costs or fees). The drugs/dressings/devices are listed by British National Formulary (BNF) therapeutic class (15). PCA data are produced per annum and an Excel file for each year is available for download on the NHS Digital website (14). We extracted annual expenditure and quantity data from BNF Chapter 20 (Dressings), Section 3 (Wound management and other dressings) and Section 4 (Gauzes and gauze tissue) for a 20 year period (1997 to 2016). We searched for terms and brand names in four antimicrobial dressings categories; silver, honey, iodine and other antimicrobial dressings (15). 'Other' antimicrobial dressings include those containing agents other than those specified above, such as Polyhexamethylene Biguanide Hydrochloride (PHMB) and chlorohexidine. To ensure accuracy this identification and categorisation process was carried out independently by two authors and any discrepancies resolved through discussion. The quantity and expenditure (NIC) for 1997 to 2016 were plotted and presented as totals per annum. We chose this period of data analysis in part due to rounding to provide analyses for complete decades, but also to include the point in time when honey and silver dressings first appeared in the data. Data for the years 1992 to 1996 were checked to ensure there were no records of honey- or silver-containing wound dressings prior to 1997.

Identification of relevant guidelines and systematic reviews

Firstly we located key national guidelines relevant to the use of wound dressings in the community. We restricted our search to recognised UK-based producers of high quality, evidence-based guidelines who follow a transparent, rigorous process of guideline production – i.e. The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and relevant professional bodies such as the Royal Colleges. Secondly we searched for relevant Cochrane systematic reviews which follow a rigorous and transparent process and they are freely available and highly accessed in the UK. Recommendations regarding the use of antimicrobial dressings were detailed in the published clinical guidance.

Interrupted Time Series (ITS) analysis

An interrupted time series (ITS) design was used to compare annual changes in the expenditure and use of anti-microbial and non-antimicrobial wound dressings; focusing first on all antimicrobial dressings and then just those containing silver. The time periods to be compared were selected *a priori* and covered 2005 to 2009, with 2010 as the intervention point and the following five years as the post-intervention period (2011 to 2015). We chose 2010 as the intervention point since this was when the SIGN Guidelines (16) for the treatment of venous leg ulcers were published, which itself was shortly after publication of a major trial of silver-dressings for the treatment of venous leg ulcers (17). In 2010 the SIGN Guidelines were the first new, national (UK) complex wound-related guidelines to be published for a number of years and subsequent to the introduction of silver dressings. The selected five year time periods were kept close to the intervention point (i.e. the guideline publication date) to reduce potential confounding by events occurring at a more distant time, whilst still giving sufficient data points for analysis. Ordinary least squares regression was used to estimate the temporal trends before, during and after the interventions with presentation of Newey–West standard errors to handle autocorrelation. The Cumby-Huizinga test was used to investigate autocorrelation. The analysis was undertaken in Stata 14 using the *itsa* command (18). We used 3 categories just to make it easier to read so if labelled:

$p<0.001$ then is as it reads

$p<0.05$ is less than 0.05 but greater than 0>0.001

$p<0.1$ is less than 0.1 but greater than 0.05

Patient and Public Involvement

There is no patient and public involvement in this study

Ethical approval

Ethical approval was not required as this study is based on secondary analysis of freely available PCA information

Results

Trends in dressing use and expenditure

From 1997 to 2016 there was an increase in the use of (Figure 1) and expenditure on (Figure 2) antimicrobial dressings. In terms of quantity prescribed 5,792,700 antimicrobial dressings were prescribed in 1997 compared with 11,029,304 in 2006 and 11,344,471 in 2016.

In 1997 the only antimicrobial dressings included in the prescription data were those containing iodine or chlorhexidine (classed here as an 'other antimicrobial dressing'). Silver-containing dressings first appeared in the prescription data in 1998 and honey dressings in 2004. Whilst iodine dressings have been prescribed relatively consistently between 1998 and 2006, during the same period the quantity of silver dressings prescribed increased from 143,600 to 5,485,684.

The increase in quantity of antimicrobial dressing use is matched by changes in expenditure over time (Figure 2). In 1997 the total expenditure on antimicrobial dressings was £1,960,386, increasing to a high of £32,841,263 in 2009 (an almost 17-fold increase). The most notable increase in annual expenditure was for silver dressings where annual spend increased year on year from 1998 onwards reaching a peak in 2009 with annual expenditure of over £26.5 million.

Figure 3 plots antimicrobial dressing prescriptions (quantity and expenditure) as a proportion of all wound dressings prescribed in the community in England. Over time antimicrobial dressings have comprised a greater proportion of all dressings used and an even greater share of expenditure.

Summary of relevant evidence synthesis and guidelines on antimicrobial dressing use for complex wounds

Table 1 outlines the key publications summarising evidence and giving guidance on the use of antimicrobial dressings in the treatment of complex wounds. The first UK guidance we found was published 1998 (19) and suggested little or no good research evidence that using antimicrobial

dressings influenced wound outcomes. Guidance universally recommends using simple, non-adherent wound dressings for complex wounds and agrees that there is little research evidence to suggest that antimicrobial dressings are clinically or cost effective.

Table 1. Published evidence giving recommendations on the use of antimicrobial dressings for treatment of complex wounds

CODE	PUBLISHED GUIDANCE	MONTH	YEAR	EVIDENCE FOR USE OF ANTIMICROBIAL DRESSINGS	RECOMMENDATION or CONCLUSIONS
A	Clinical Practice Guidelines: The nursing management of patients with venous leg ulcers (19)	First published 1998, updated 2005 and 2006		The evidence in the guidance for 'Antimicrobial agents versus placebo or standard care' is based on a systematic review by O'Meara published in 2000 reviewing 14 RCTs. The RCTs were small and of poor quality, therefore no firm conclusions could be drawn.	Dressings must be simple, low adherent and acceptable to the patient. Cost effectiveness of leg ulcer dressings should be determined by their ability to stay in place for up to a week
B	Cochrane review: Topical silver for treating wound infection (20)	January	2007	This assessed topical silver products (creams or dressings) for the prevention of wound infection through the evaluation of 26 RCTs. The majority of studies found no statistical difference in infection rates between silver and non-silver dressings. Most of the trials were small and of poor quality.	There is insufficient evidence to support the use of silver dressings as they did not reduce infection or promote wound healing
C	Cochrane review: Honey as a topical treatment for wounds (21)	First published 2008, updated 2015		26 trials were identified. Two of high quality found that honey dressings heal partial thickness burns more quickly than conventional dressings. Other trials either showed no difference between treatments or were based on low quality evidence	The evidence for the effect of honey compared with other dressings is low quality, and therefore not robust enough basis for decision making
D	SIGN guidance: Management of venous leg ulcers (16)	August	2010	The recommendations for silver dressings are based on a Cochrane review in 2007 by Vermeulen *et al* and the Vulcan Trial in 2009. These found insufficient evidence to show improved healing rates for wounds treated with silver dressings compared to other types of dressings.	Guidance concludes that simple non-adherent dressings are recommended for VLU management. Silver dressings are not.
E	NICE guidance: Pressure ulcers: prevention and management (22)	April	2014	Alginate versus silver alginate. No statistical difference, very low quality evidence	The evidence did not allow for a recommendation of any specific type of dressing. Recommends a dressing that promotes an optimal healing environment rather than a specific type
F	NICE guidance: Diabetic foot problems: prevention and management (23)	August	2015	Included one RCT comparing iodine impregnated dressings with others; found no difference in healing rates.	Take into account clinical assessment of the wound and patient preference. Use dressing of lowest acquisition cost appropriate
G	Chronic wounds: advanced wound dressings and antimicrobial dressings (11)	March	2016	Gives an overview of previously published evidence and summarises research findings	There is little good quality evidence to support the use of antimicrobial dressings. Healthcare professionals should choose the least costly option which will provide the optimal environment for the type of wound and stage of healing

Interrupted time series (ITS) before and after publication of the SIGN guidance in 2010

Data from 2005 to the intervention year - 2010

The results of the ITS analysis for expenditure on antimicrobial dressings from 2005 to 2015 are shown in Table 2 and Appendix 1. £25.9 million (95% confidence intervals, £24.4 to £27.5) was spent on antimicrobial dressings in 2005, followed by an increase in spending of, on average, £1.6 million per year (£1.0 to £2.1) until 2009. In 2010 (the year of the SIGN guidance publication and one year after publication of the VULCAN study), there was a reduction in the expected spending on antimicrobial dressings (based on the pre-intervention trend) of -£5.2 million (-£8.6 to -£1.7, see Appendix 1 panel A); this reduction was largely driven by a reduction in silver dressing spend (see Table 2 and Appendix 1 panel B (expenditure) and C (use)). There was no corresponding significant reduction in expenditure on non-antimicrobial dressings in 2010 (£0.9 million; -£4.8 to £3.0, Table 2 and Appendix 1 panel D).

Trends in quantity and expenditure of dressing use across the pre and post intervention period

Prior to the SIGN intervention during 2005 to 2009 the use of anti-microbial dressings (by quantity) was significantly increasing by 170,000 dressings per year (110,000 to 230,000) assuming a linear trend but following the SIGN intervention during 2011 to 2015 the increasing trend slowed and was no longer significant (increasing by 70, 000 dressings per year; -180, 000 to 310,000). This change in the trend after the SIGN intervention compared with before the SIGN intervention was not significant (a reduction in average annual use 100,000 dressings per year relative to the pre-SIGN trend; -370,000 to 160,000). For a graphical illustration see Appendix 1 panel E.

This pattern was significantly different from the annual decrease in use of non-antimicrobial dressings, which continuously declined from 2005 to 2015 (Table 2 and comparing panels E and F in Appendix 1). Taking the pre-intervention trend as the counterfactual the mean annual reduction in expenditure post-intervention was £1.6 million (-£2.9 to -£0.2) for antimicrobial dressings and £2.1 million (-£3.0 to -£1.2) for non-antimicrobial dressings (not a statistically significant difference i.e. the higher cost of anti-microbial dressings meant that they contributed more or less equally to the cost reductions when compared with non-antimicrobial dressings even though the quantities used were lower, see Table 2).

Differences between dressing use and expenditure in the post-intervention period

Comparing use of antimicrobial and non-antimicrobial dressings in the post-intervention period (from 2011 to 2015) we observe increasing expenditure on non-antimicrobials dressings with decreased use (by quantity). Data show that the increasing trend for expenditure on non-antimicrobial dressings is significantly different to the flat trend for antimicrobial dressings (Table 2).

1

Table 2. Interrupted time series analysis of annual costs and use of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

	Units (Cost or quantity of dressings)	A. Annual cost or use of dressings in 2005 (95% confidence intervals, CI)	B. Annual increase in cost or use from 2005 to 2009 Pre-intervention trend (95% CI)	C. Decrease in cost or use in 2010 Change in intervention year (95% CI)	D. Annual change in cost or use from 2011- 2015 relative to 2005-2009 (95% CI)	E. Annual change in cost or use from 2011- 2015 Post-intervention trend (95% CI)
1. All antimicrobial dressings	£ million	25.9 (24.4 to 27.5)	1.6 (1.0 to 2.1)	-5.2 (-8.6 to -1.7)	-1.6 (-2.9 to -0.2)	0.01 (-1.0 to 1.0)
	P values for comparison with non-antimicrobial dressings[1]			Significantly different P<0.1	Not significantly different	Significantly different P<0.05
	Quantity millions	10.8 (10.6 to 10.9)	0.17 (0.11 to 0.23)	-0.93 (-1.79 to - 0.07)	-0.10 (-0.37 to 0.16)	0.07 (-0.18 to 0.31)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Significantly different P<0.05	Significantly different P<0.001
2. Silver containing antimicrobial dressings	£ million	23.7 (22.3 to 25.1)	0.6 (0.0 to 1.1)	-5.1 (-8.6 to -1.5)	-1.0 (-2.3 to 0.4)	-0.4 (-1.5 to 0.7)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Not significantly different	Significantly different P<0.05
	Quantity millions	5.5 (5.3 to 5.5)	-0.02 (-0.07 to 0.03)	-0.99 (-1.68 to -0.30)	-0.07 (-0.30 to 0.14)	-0.1 (-0.03 to -0.1)
	P values for comparison with non-antimicrobial dressings			Significantly different P<0.1	Significantly different P<0.05	Significantly different P<0.001
3. Non-antimicrobial dressings (reference group)	£ million	91.7 (90.0 to 93.4)	3.5 (2.7 to 4.3)	-0.9 (-4.8 to 3.0)	-2.1 (-3.0 to -1.2)	1.4 (0.7 to 2.0)
	Quantity millions	126.6 (122.4 to 130.8)	-4.5 (-6.0 to -3.0)	-0.57 (-11.4 to -0.01)	1.41 (-0.09 to 2.93)	-3.1 (-3.8 to -2. 4)

[1] the P values compare each cell in the row with non-antimicrobial dressings, *i.e.* the reference group is the corresponding cell in row 3

Discussion

Summary of main findings

Prescription of antimicrobial wound dressings in the UK has increased since 1997. This increase is particularly notable for silver-containing dressings. The Clinical guidance and Cochrane reviews presented in Table 1 show there is no research evidence to support the routine use of antimicrobial dressings for complex wounds. Thus, there has been a large increase in use of silver-containing wound dressings that cannot be explained by the contemporaneous research evidence. Historic use of silver, iodine and honey in wound healing is well documented (24-26). It has been suggested that resurgence in the use of these topical agents may be partly due to concerns about antibiotic-resistant bacteria and the need to reduce antibiotic prescribing (27).

Our analysis shows that, following a period of rapid increase in antimicrobial dressing prescribing and expenditure, the publication of SIGN guidelines for venous leg ulcer management (2010) was followed by a significant reduction (both in cost and number of items). There was no commensurate change in the prescribing of other dressings. It is not clear why the reduction in antimicrobial use was not matched by an increase in use of other dressings to compensate for this differential use. A possible explanation may be that other dressings were being taken from stock resources and so are not counted in the prescribing data. Being in stock means that the products are obtained directly via procurement in bulk – this would be most common for standard dressings. We note that whilst prescribing of silver-containing dressings reduced, there appears to have been an increase in prescribing of honey, iodine and 'other' antimicrobial dressings. If these trends are to be considered, in some part, to be an impact of the publication of the SIGN guideline, the guideline had more of an impact on the use of silver dressings than of other antimicrobial dressings. A potential explanation for this differential effect on antimicrobial dressing prescribing lies in the strength of the recommendations. The SIGN guidelines graded recommendations A to D based on the quality of the evidence and these differed for different dressings. The recommendation for silver dressings was graded A, that for honey was graded B and the recommendation for iodine dressings was unclassified (16). It may be that the strength of the recommendation for not using silver dressings was considered more compelling or that this recommendation had a greater effect because of the higher cost of silver dressings and the potential savings.

When looking across the entire study period, our analysis suggests that the total number of dressings used per annum may be decreasing. Conversely total expenditure on dressings appear to be increasing (14). The reasons for this pattern requires further exploration – potential areas to explore include the

use of other medical devices or advanced dressings which are relatively expensive but may require less frequent changes (13) and/or the potential for increased unit prices for non-antimicrobial dressings.

Treatment-related decision making in wound care

It is widely acknowledged that the process of decision-making is highly contingent and context dependent (28), particularly so in community and primary care (29). Reliable sources of evidence-based information including clinical guidelines and systematic reviews can influence decision making especially where a single clear message is conveyed to professional audiences who themselves are aware that a change in practice is required (30). A national evaluation of the implementation of NICE guidance found that recommendations are more likely to be adopted when there is strong professional support, clear guidance and no increased or unfunded costs (30). We know that the clinical decisions of community nurses are often based on experiential rather than research knowledge (31) and that 'human sources' are often preferred to written guidance (32). It seems clear from the temporal trends that the increases in dressing use are not driven by knowledge of the research evidence (33). This may suggest that any action aimed at implementing evidence-based guidance within community nursing may benefit from being more focused on the type of change necessary to generate a reduction in specific prescribing practices such as restriction of formulary options and routine monitoring and feedback of individuals prescribing practice to ensure adherence to organisational policies (34).

Patient preference may also play a part in dressing section. Research has shown that healing time was ranked by patients as the most important factor (compared to other factors such as dressing change frequency and pain) (35). Choosing Wisely is a global initiative to address issues such as patient and clinician preferences and making better decisions about care with the aim that this will help avoid tests, treatments or procedures that are unlikely to be of benefit. Choosing Wisely UK is led by the Academy of Medical Royal Colleges and as yet does not encompass nursing as a profession or have any guidance focused on the management of complex wounds (36;37).

The widespread availability of wound care products of apparent low or no clinical value is in part reflective of the threshold for evidence necessary for marketing authorisation of devices (9). Because the threshold of evidence is low, there is little or no incentive for manufacturers to demonstrate that their devices are clinically effective. Research showing how evidence is used to support claims made in product advertisements within two wound care journals found just 35% of claims about the benefits of a product cited supporting evidence. When these sources of evidence were investigated the cited

evidence did not support the claim being made in 56% of cases (12). The emphasis is therefore on incremental product development and innovation. Adopting a medical device when there is little or no evidence to support its use may then in turn lead to a reduction in the likelihood of further relevant research as the innovation becomes standard and integrated into care (4).

Rothery *et al*, suggest that rather than binary choice of adopt or select, policy decisions on innovation introduction may be helped by guidance recommending either options of 'only in research' or 'approval with research' (38). The former allowing further research to establish the value of an innovation before wider access and the latter granting the possibility of product withdrawal should further research prove clinical and cost ineffectiveness (4). NICE has the ability to issue guidance to recommend 'only in research' but this is not routinely used and rarely if ever for medical devices (39).

Strengths and weaknesses

This is the first research study we have identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years. These simple data show powerfully how new products can be adopted rapidly despite a lack of robust evidence for clinical or cost-effectiveness. This reinforces the complex nature of decision making in wound care and importance of other spheres of information and knowledge including expert opinion and peer-to-peer advice (33). The role of marketing and company activity in successfully promoting product use is also an area that may have had impact here although this would need to be explored in further work (40).

Our analysis of wound care prescribing is limited by the available data. Temporal changes in dressing use and expenditure may also be influenced by demographic and epidemiological factors (e.g. an ageing population and the rise in chronic diseases such as diabetes) (41). The prescribing data are not wound-specific and limited to English community prescriptions; however, we note that the community is where most complex wounds are treated (42). We also note that prescribing data will not include data on those standard dressings which are kept as stock. ITS analysis has been used to explore the possible impact of the first significant national clinical guideline, the SIGN guideline, on the management of venous leg ulcers. There is a suggestion of some impact of this 'intervention' however it has to be noted (as above) that this guidance is specific to venous leg ulcers whereas the PCA data cover dressing use for any wound type. These analyses did not include multiple 'interventions' incorporating the publication of other guidelines as it was decided to use the single intervention point of 2010 for reasons stated in the methods. However, presenting a summary of the general status of evidence (Table 1) which is so consistent in its message helps provides important contextual information in which to interpret the data.

A limitation of the ITS design is that any hypothesised relationship between the implementation of guidelines and changes in dressing use is based purely on a temporal association. We have no direct evidence of causation. Furthermore the ordinary least squares model forecasts linear trends yet the post-SIGN trends for anti-microbial dressings do not appear to be linear and show a reversal of the initial decreasing trend from 2012. This is partly explained by the differences in use of silver and other antimicrobial dressings (see Appendix 1 panel F). As future data becomes available it will be important to monitor the use of antimicrobial dressings in case further intervention is needed to reduce use. However these changes are temporarily distant from the SIGN guidance and the primary aim of the ITS analysis was to examine changes occurring around the time of the SIGN guidance.

Conclusions

This paper suggests that in the last 20 years there has been a large increase in the use of antimicrobial wound dressings despite a lack of research evidence to support their routine use. Expenditure on antimicrobial wound dressings has risen by over £28 million between and 2016.

Our analysis shows that routinely available PCA data can be used to identify unproven products with significant net financial burden to the NHS may offer a transparent and systematic route to 'only in research' and ultimately to de-implementation. If using routine data in this way is to have an impact on prescribing at scale, then it needs to be linked to a multi-level response that targets procurement processes alongside individual practices to ensure increased value and reduced waste.

Figure Legends

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

Appendix 1. Interrupted time series analysis of annual costs and use of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

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Competing interests

The authors declare they have no competing interests

Authors' contributions

Louise Hussey: First author of manuscript and data analysis

Jill Stocks: Interrupted time series analysis and interpretation

Paul Wilson: Interpretation of data and manuscript revision

Jo Dumville: Study concept and design, interpretation of data and manuscript revision

Nicky Cullum: Interpretation of data and manuscript revision

All authors reviewed and approved the final manuscript before submission

Data availability

Prescription data is freely available from NHS digital

https://digital.nhs.uk/data-and-information/publications/statistical/prescription-cost-analysis

Research Checklist

There is no research checklist relevant to this study

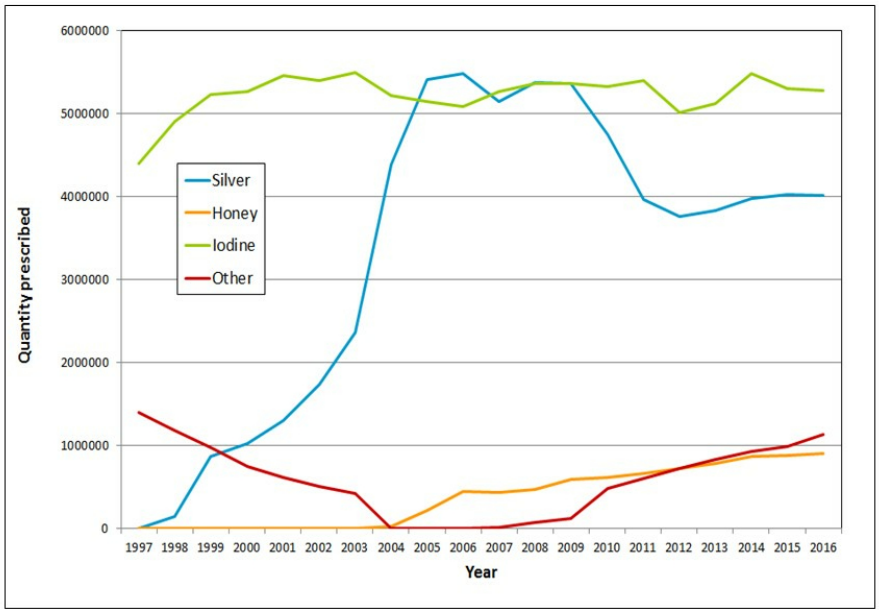

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

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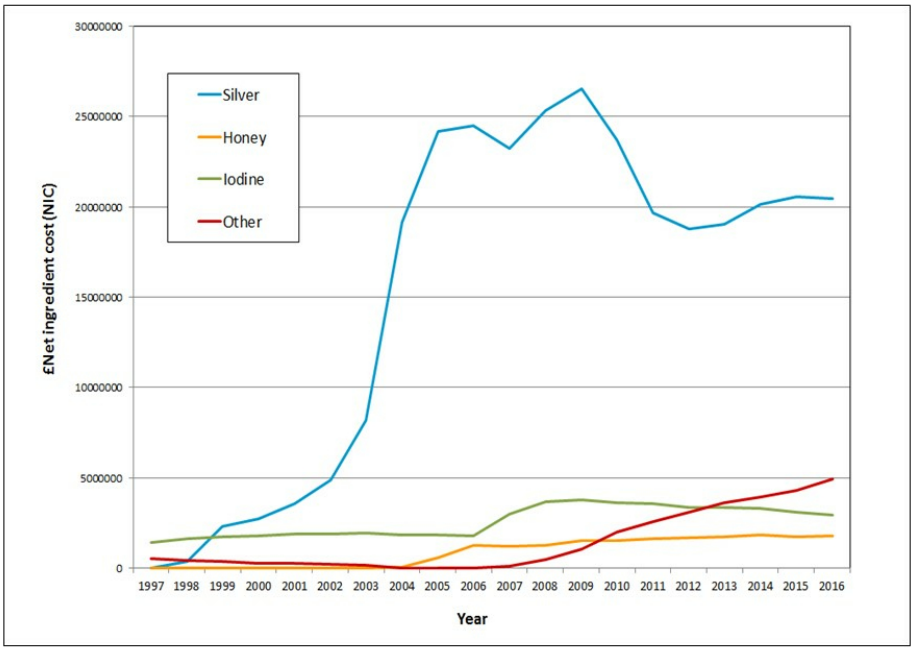
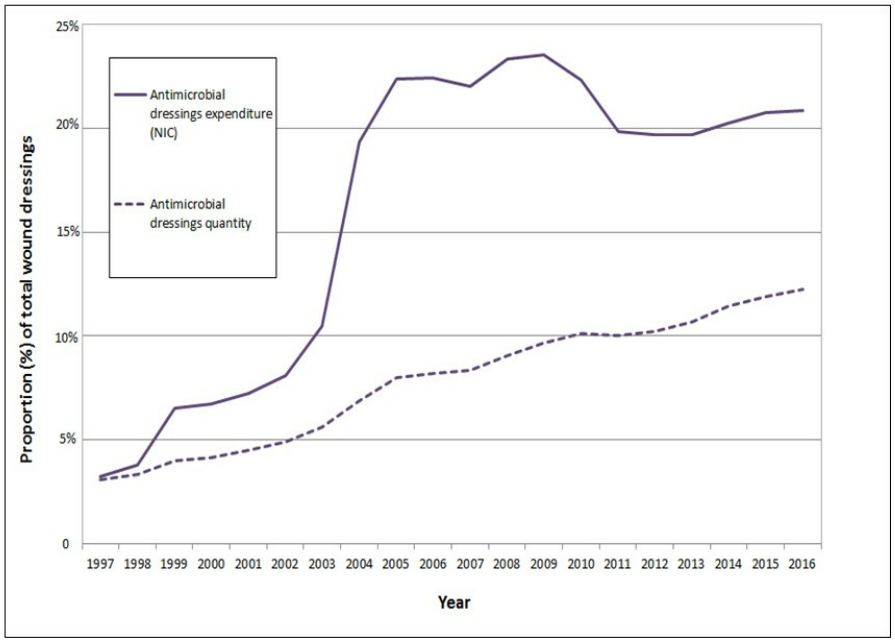


Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

81x60mm (300 x 300 DPI)



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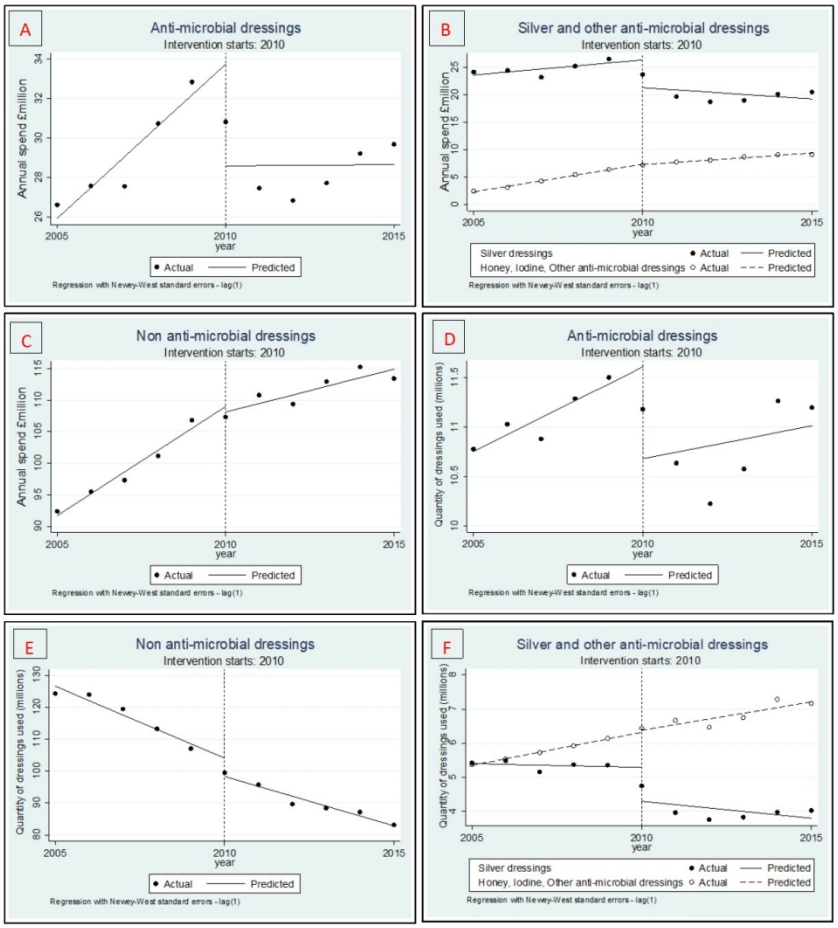

Appendix 1. Interrupted time series analysis of annual costs and usage of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

104x148mm (300 x 300 DPI)

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The use of antimicrobial dressings in England and the association with published clinical guidance: interrupted time series analysis

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The use of antimicrobial dressings in England and the association with published clinical guidance: interrupted time series analysis

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Abstract

Objectives: In health care systems practices and products of unproven value and cost-effectiveness can decrease value and increase waste. Using the management of complex wounds, this study investigates temporal trends in the use of antimicrobials dressings, places this in the context of available evidence and discusses the potential impacts on the UK National Health Service (NHS).

Design: Secondary descriptive and interrupted time series (ITS) analysis of NHS prescription data

Setting: Prescribing Cost Analysis (PCA) details all NHS prescriptions dispensed in the community in England.

Interventions: An ITS design was used to compare annual changes in the expenditure and use of antimicrobial and non-antimicrobial dressings before and after the publication of the 'intervention' of key evidence-based SIGN (Scottish Intercollegiate Guidelines Network) guidance in 2010.

Primary and secondary outcome measures: Trends in use and expenditure of antimicrobial dressings in relation to published clinical guidance.

Results: There was a large increase in the prescribing of, and expenditure on, antimicrobial wound dressings between 1997 and 2016. In 1997 the total number of dressings prescribed was 5,792,700; increasing to 11,447,102 in 2009 with expenditure increasing from £1,960,386 to £32,841,263. During the year of the SIGN intervention (2010) there was a significant drop in the use of silver but there was no consistent ongoing reduction from 2011 to 2015.

Conclusions: Prescribing data can be used to identify products of unproven benefit which also impose a significant financial burden. This study quantifies the huge increase in the use of antimicrobial wound dressings over a 20-year period despite the lack of compelling evidence to support their routine use, there is some suggestion, however that the use and expenditure decreased after the publication of key guidance. Routine data can be used to as part of more systematic efforts to increase value and reduce waste in health systems.

Strengths and limitations of the study

- The first research study identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years.
- Techniques such as interrupted time series analysis of prescribing data can be used to explore and illustrate the relationship between treatment choice and the contemporaneous availability of evidence about clinical and cost effectiveness.
- Interrupted Time Series analysis has been used to explore the possible impact of a national clinical guidelines on the use of antimicrobial dressings
- The prescribing data are not wound-specific and limited to English community prescriptions; however, the community is where most complex wounds are treated
- A summary of the general status of evidence helps provides important contextual information in which to interpret the data.

Introduction

Resource constrained health care systems face increasing demands due to ageing populations, emerging medical conditions, modern lifestyles and advances in technology (1). It is imperative we increase the value of health care and improve outcomes for patients relative to costs (2). Clinical practice should, where possible, be informed by research evidence to ensure that limited funds are spent on resources and treatments with proven beneficial outcomes; in some cases the de-implementation of contradicted and unproven practices is required in order to increase value and reduce waste (3-5).

The management of complex wounds such as leg, foot and pressure ulcers, places a huge burden on healthcare resources. Although these wounds are managed in a variety of healthcare settings, in the UK the majority of care is delivered by community nurses (6). These open wounds are usually covered with a wound dressing and there are many options available ranging from simple gauzes to advanced dressings that have different absorptive properties such as foam, hydrocolloid and alginates (7). The availability of such a wide range of dressings can cause decision uncertainty amongst practitioners which in turn is reflected in a wide variation in terms of antimicrobial dressing use within and across different health care providers (6;8)

Wound dressings are classed as external medical devices and, as such, require a lower level of evidence to support marketing authorisation. The European regulatory framework for evaluating and regulating medical devices only requires manufacturers to demonstrate that new devices are safe and fit for purpose (9). A new Medical Device Regulation (MDR) is due to be fully applied in 2020 and will replace the European Union's current Medical Device Directive (MDD) and aims to ensure greater confidence in the effective protection of public health and patient safety (10). However, to-date, new dressing products come to market relatively rapidly and are not always supported by evidence of effectiveness (11;12).

The mid-1990s saw an increase in the availability of dressings claiming to have valuable antimicrobial properties due to the inclusion of ingredients such as silver, honey and iodine. Such dressings were developed and promoted for the prevention and treatment of wound infection and to ultimately improve wound healing (13). Generally antimicrobial dressings are more expensive to buy than their non-antimicrobial counter-parts. This study aimed to investigate temporal trends in the use of antimicrobials dressings, and place use in the context of available evidence. Specifically, we aimed to address:

- How many antimicrobial dressings are used by NHS community services in England and how much does this cost?
- How has use of antimicrobial dressings changed over time?
- What impact has the publication of evidence based guidance had on trends in antimicrobial dressing?

In addition to these analyses, we also present this antimicrobial use and cost data in the context of contemporaneously available systematic review findings and other clinical guideline recommendations to examine whether trends may reflect any resulting change in practice.

Methods

Extraction of data on antimicrobial dressing use and cost

UK National Health Service (NHS) Prescribing Cost Analysis (PCA) is freely available information accessed from 'NHS Digital' and details all NHS prescriptions dispensed in the community in England on an annual basis (14). This includes all prescriptions dispensed by pharmacists, doctors and appliance contractors (e.g. suppliers of stoma and continence care equipment). PCA data give detail of the quantity (measured in units depending on the formulation of the product (e.g. one tablet, pack or dressing)) and also the Net Ingredient Cost (NIC) (expenditure on the product before discounts, not including any dispensing costs or fees). The drugs/dressings/devices are listed by British National Formulary (BNF) therapeutic class (15). PCA data are produced per annum and an Excel file for each year is available for download on the NHS Digital website (14). We extracted annual expenditure and quantity data from BNF Chapter 20 (Dressings), Section 3 (Wound management and other dressings) and Section 4 (Gauzes and gauze tissue) for a 20 year period (1997 to 2016). We searched for terms and brand names in four antimicrobial dressings categories; silver, honey, iodine and other antimicrobial dressings (15). 'Other' antimicrobial dressings include those containing agents other than those specified above, such as Polyhexamethylene Biguanide Hydrochloride (PHMB) and chlorohexidine. To ensure accuracy this identification and categorisation process was carried out independently by two authors and any discrepancies resolved through discussion. The quantity and expenditure (NIC) for 1997 to 2016 were plotted and presented as totals per annum. We chose this period of data analysis in part due to rounding to provide analyses for complete decades, but also to include the point in time when honey and silver dressings first appeared in the data. Data for the years 1992 to 1996 were checked to ensure there were no records of honey- or silver-containing wound dressings prior to 1997.

Identification of relevant guidelines and systematic reviews

Firstly we located key national guidelines relevant to the use of wound dressings in the community. We restricted our search to recognised UK-based producers of high quality, evidence-based guidelines who follow a transparent, rigorous process of guideline production – i.e. The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and relevant professional bodies such as the Royal Colleges. Secondly we searched for relevant Cochrane systematic reviews which follow a rigorous and transparent process and they are freely available and highly accessed in the UK. Recommendations regarding the use of antimicrobial dressings were detailed in the published clinical guidance.

Interrupted Time Series (ITS) analysis

An interrupted time series (ITS) design was used to compare annual changes in the expenditure and use of anti-microbial and non-antimicrobial wound dressings; focusing first on all antimicrobial dressings and then just those containing silver. The time periods to be compared were selected *a priori* and covered 2005 to 2009, with 2010 as the intervention point and the following five years as the post-intervention period (2011 to 2015). We chose 2010 as the intervention point since this was when the SIGN Guidelines (16) for the treatment of venous leg ulcers were published, which itself was shortly after publication of a major trial of silver-dressings for the treatment of venous leg ulcers (17). In 2010 the SIGN Guidelines were the first new, national (UK) complex wound-related guidelines to be published for a number of years and subsequent to the introduction of silver dressings. The selected five year time periods were kept close to the intervention point (i.e. the guideline publication date) to reduce potential confounding by events occurring at a more distant time, whilst still giving sufficient data points for analysis. Ordinary least squares regression was used to estimate the temporal trends before, during and after the interventions with presentation of Newey–West standard errors to handle autocorrelation. The Cumby-Huizinga test was used to investigate autocorrelation. The analysis was undertaken in Stata 14 using the *itsa* command (18). We used 3 categories just to make it easier to read so if labelled:

$p<0.001$ then is as it reads

$p<0.05$ is less than 0.05 but greater than 0>0.001

$p<0.1$ is less than 0.1 but greater than 0.05

Patient and Public Involvement

Patients and the public were not involved in the design or planning of the study

Ethical approval

Ethical approval was not required as this study is based on secondary analysis of freely available PCA information

Results

Trends in dressing use and expenditure

From 1997 to 2016 there was an increase in the use of (Figure 1) and expenditure on (Figure 2) antimicrobial dressings. In terms of quantity prescribed 5,792,700 antimicrobial dressings were prescribed in 1997 compared with 11,029,304 in 2006 and 11,344,471 in 2016.

In 1997 the only antimicrobial dressings included in the prescription data were those containing iodine or chlorhexidine (classed here as an 'other antimicrobial dressing'). Silver-containing dressings first appeared in the prescription data in 1998 and honey dressings in 2004. Whilst iodine dressings have been prescribed relatively consistently between 1998 and 2006, during the same period the quantity of silver dressings prescribed increased from 143,600 to 5,485,684.

The increase in quantity of antimicrobial dressing use is matched by changes in expenditure over time (Figure 2). In 1997 the total expenditure on antimicrobial dressings was £1,960,386, increasing to a high of £32,841,263 in 2009 (an almost 17-fold increase). The most notable increase in annual expenditure was for silver dressings where annual spend increased year on year from 1998 onwards reaching a peak in 2009 with annual expenditure of over £26.5 million.

Figure 3 plots antimicrobial dressing prescriptions (quantity and expenditure) as a proportion of all wound dressings prescribed in the community in England. Over time antimicrobial dressings have comprised a greater proportion of all dressings used and an even greater share of expenditure.

Summary of relevant evidence synthesis and guidelines on antimicrobial dressing use for complex wounds

Table 1 outlines the key publications summarising evidence and giving guidance on the use of antimicrobial dressings in the treatment of complex wounds. The first UK guidance we found was published 1998 (19) and suggested little or no good research evidence that using antimicrobial

dressings influenced wound outcomes. Guidance universally recommends using simple, non-adherent wound dressings for complex wounds and agrees that there is little research evidence to suggest that antimicrobial dressings are clinically or cost effective.

Table 1. Published evidence giving recommendations on the use of antimicrobial dressings for treatment of complex wounds

CODE	PUBLISHED GUIDANCE	MONTH	YEAR	EVIDENCE FOR USE OF ANTIMICROBIAL DRESSINGS	RECOMMENDATION or CONCLUSIONS
A	Clinical Practice Guidelines: The nursing management of patients with venous leg ulcers (19)	First published 1998, updated 2005 and 2006		The evidence in the guidance for 'Antimicrobial agents versus placebo or standard care' is based on a systematic review by O'Meara published in 2000 reviewing 14 RCTs. The RCTs were small and of poor quality, therefore no firm conclusions could be drawn.	Dressings must be simple, low adherent and acceptable to the patient. Cost effectiveness of leg ulcer dressings should be determined by their ability to stay in place for up to a week
B	Cochrane review: Topical silver for treating wound infection (20)	January	2007	This assessed topical silver products (creams or dressings) for the prevention of wound infection through the evaluation of 26 RCTs. The majority of studies found no statistical difference in infection rates between silver and non-silver dressings. Most of the trials were small and of poor quality.	There is insufficient evidence to support the use of silver dressings as they did not reduce infection or promote wound healing
C	Cochrane review: Honey as a topical treatment for wounds (21)	First published 2008, updated 2015		26 trials were identified. Two of high quality found that honey dressings heal partial thickness burns more quickly than conventional dressings. Other trials either showed no difference between treatments or were based on low quality evidence	The evidence for the effect of honey compared with other dressings is low quality, and therefore not robust enough basis for decision making
D	SIGN guidance: Management of venous leg ulcers (16)	August	2010	The recommendations for silver dressings are based on a Cochrane review in 2007 by Vermeulen *et al* and the Vulcan Trial in 2009. These found insufficient evidence to show improved healing rates for wounds treated with silver dressings compared to other types of dressings.	Guidance concludes that simple non-adherent dressings are recommended for VLU management. Silver dressings are not.
E	NICE guidance: Pressure ulcers: prevention and management (22)	April	2014	Alginate versus silver alginate. No statistical difference, very low quality evidence	The evidence did not allow for a recommendation of any specific type of dressing. Recommends a dressing that promotes an optimal healing environment rather than a specific type
F	NICE guidance: Diabetic foot problems: prevention and management (23)	August	2015	Included one RCT comparing iodine impregnated dressings with others; found no difference in healing rates.	Take into account clinical assessment of the wound and patient preference. Use dressing of lowest acquisition cost appropriate
G	Chronic wounds: advanced wound dressings and antimicrobial dressings (11)	March	2016	Gives an overview of previously published evidence and summarises research findings	There is little good quality evidence to support the use of antimicrobial dressings. Healthcare professionals should choose the least costly option which will provide the optimal environment for the type of wound and stage of healing

Interrupted time series (ITS) before and after publication of the SIGN guidance in 2010

Data from 2005 to the intervention year - 2010

The results of the ITS analysis for expenditure on antimicrobial dressings from 2005 to 2015 are shown in Table 2 and Appendix 1. £25.9 million (95% confidence intervals, £24.4 to £27.5) was spent on antimicrobial dressings in 2005, followed by an increase in spending of, on average, £1.6 million per year (£1.0 to £2.1) until 2009. In 2010 (the year of the SIGN guidance publication and one year after publication of the VULCAN study), there was a reduction in the expected spending on antimicrobial dressings (based on the pre-intervention trend) of -£5.2 million (-£8.6 to -£1.7, see Appendix 1 panel A); this reduction was largely driven by a reduction in silver dressing spend (see Table 2 and Appendix 1 panel B (expenditure) and C (use)). There was no corresponding significant reduction in expenditure on non-antimicrobial dressings in 2010 (£0.9 million; -£4.8 to £3.0, Table 2 and Appendix 1 panel D).

Trends in quantity and expenditure of dressing use across the pre and post intervention period

Prior to the SIGN intervention during 2005 to 2009 the use of anti-microbial dressings (by quantity) was significantly increasing by 170,000 dressings per year (110,000 to 230,000) assuming a linear trend but following the SIGN intervention during 2011 to 2015 the increasing trend slowed and was no longer significant (increasing by 70, 000 dressings per year; -180, 000 to 310,000). This change in the trend after the SIGN intervention compared with before the SIGN intervention was not significant (a reduction in average annual use 100,000 dressings per year relative to the pre-SIGN trend; -370,000 to 160,000). For a graphical illustration see Appendix 1 panel E.

This pattern was significantly different from the annual decrease in use of non-antimicrobial dressings, which continuously declined from 2005 to 2015 (Table 2 and comparing panels E and F in Appendix 1). Taking the pre-intervention trend as the counterfactual the mean annual reduction in expenditure post-intervention was £1.6 million (-£2.9 to -£0.2) for antimicrobial dressings and £2.1 million (-£3.0 to -£1.2) for non-antimicrobial dressings (not a statistically significant difference i.e. the higher cost of anti-microbial dressings meant that they contributed more or less equally to the cost reductions when compared with non-antimicrobial dressings even though the quantities used were lower, see Table 2).

Differences between dressing use and expenditure in the post-intervention period

Comparing use of antimicrobial and non-antimicrobial dressings in the post-intervention period (from 2011 to 2015) we observe increasing expenditure on non-antimicrobials dressings with decreased use (by quantity). Data show that the increasing trend for expenditure on non-antimicrobial dressings is significantly different to the flat trend for antimicrobial dressings (Table 2).

Table 2. Interrupted time series analysis of annual costs and use of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

	Units (Cost or quantity of dressings)	A. Annual cost or use of dressings in 2005 (95% confidence intervals, CI)	B. Annual increase in cost or use from 2005 to 2009 Pre-intervention trend (95% CI)	C. Decrease in cost or use in 2010 Change in intervention year (95% CI)	D. Annual change in cost or use from 2011- 2015 relative to 2005-2009 (95% CI)	E. Annual change in cost or use from 2011- 2015 Post-intervention trend (95% CI)
1. All antimicrobial dressings	£ million	25.9 (24.4 to 27.5)	1.6 (1.0 to 2.1)	-5.2 (-8.6 to -1.7)	-1.6 (-2.9 to -0.2)	0.01 (-1.0 to 1.0)
	P values for comparison with non-antimicrobial dressings[1]			P=0.07	P=0.4	P=0.02
	Quantity millions	10.8 (10.6 to 10.9)	0.17 (0.11 to 0.23)	-0.93 (-1.79 to - 0.07)	-0.10 (-0.37 to 0.16)	0.07 (-0.18 to 0.31)
	P values for comparison with non-antimicrobial dressings			P=0.07	P=0.03	P<0.001
2. Silver containing antimicrobial dressings	£ million	23.7 (22.3 to 25.1)	0.6 (0.0 to 1.1)	-5.1 (-8.6 to -1.5)	-1.0 (-2.3 to 0.4)	-0.4 (-1.5 to 0.7)
	P values for comparison with non-antimicrobial dressings			P=0.08	P=0.12	P=0.006
	Quantity millions	5.5 (5.3 to 5.5)	-0.02 (-0.07 to 0.03)	-0.99 (-1.68 to -0.30)	-0.07 (-0.30 to 0.14)	-0.1 (-0.03 to -0.1)
	P values for comparison with non-antimicrobial dressings			P=0.07	P=0.04	P<0.001
3. Non-antimicrobial dressings (reference group)	£ million	91.7 (90.0 to 93.4)	3.5 (2.7 to 4.3)	-0.9 (-4.8 to 3.0)	-2.1 (-3.0 to -1.2)	1.4 (0.7 to 2.0)
	Quantity millions	126.6 (122.4 to 130.8)	-4.5 (-6.0 to -3.0)	-0.57 (-11.4 to -0.01)	1.41 (-0.09 to 2.93)	-3.1 (-3.8 to -2. 4)

[1] the P values compare each cell in the row with non-antimicrobial dressings, *i.e.* the reference group is the corresponding cell in row 3

Discussion

Summary of main findings

Prescription of antimicrobial wound dressings in the UK has increased since 1997. This increase is particularly notable for silver-containing dressings. The Clinical guidance and Cochrane reviews presented in Table 1 show there is no research evidence to support the routine use of antimicrobial dressings for complex wounds. Thus, there has been a large increase in use of silver-containing wound dressings that cannot be explained by the contemporaneous research evidence. Historic use of silver, iodine and honey in wound healing is well documented (24-26). It has been suggested that resurgence in the use of these topical agents may be partly due to concerns about antibiotic-resistant bacteria and the need to reduce antibiotic prescribing (27).

Our analysis shows that, following a period of rapid increase in antimicrobial dressing prescribing and expenditure, the publication of SIGN guidelines for venous leg ulcer management (2010) was followed by a significant reduction (both in cost and number of items). There was no commensurate change in the prescribing of other dressings. It is not clear why the reduction in antimicrobial use was not matched by an increase in use of other dressings to compensate for this differential use. A possible explanation may be that other dressings were being taken from stock resources and so are not counted in the prescribing data. Being in stock means that the products are obtained directly via procurement in bulk – this would be most common for standard dressings. We note that whilst prescribing of silver-containing dressings reduced, there appears to have been an increase in prescribing of honey, iodine and 'other' antimicrobial dressings. If these trends are to be considered, in some part, to be an impact of the publication of the SIGN guideline, the guideline had more of an impact on the use of silver dressings than of other antimicrobial dressings. A potential explanation for this differential effect on antimicrobial dressing prescribing lies in the strength of the recommendations. The SIGN guidelines graded recommendations A to D based on the quality of the evidence and these differed for different dressings. The recommendation for silver dressings was graded A, that for honey was graded B and the recommendation for iodine dressings was unclassified (16). It may be that the strength of the recommendation for not using silver dressings was considered more compelling or that this recommendation had a greater effect because of the higher cost of silver dressings and the potential savings.

When looking across the entire study period, our analysis suggests that the total number of dressings used per annum may be decreasing. Conversely total expenditure on dressings appear to be increasing (14). The reasons for this pattern requires further exploration – potential areas to explore include the

use of other medical devices or advanced dressings which are relatively expensive but may require less frequent changes (13) and/or the potential for increased unit prices for non-antimicrobial dressings.

Treatment-related decision making in wound care

It is widely acknowledged that the process of decision-making is highly contingent and context dependent (28), particularly so in community and primary care (29). Reliable sources of evidence-based information including clinical guidelines and systematic reviews can influence decision making especially where a single clear message is conveyed to professional audiences who themselves are aware that a change in practice is required (30). A national evaluation of the implementation of NICE guidance found that recommendations are more likely to be adopted when there is strong professional support, clear guidance and no increased or unfunded costs (30). We know that the clinical decisions of community nurses are often based on experiential rather than research knowledge (31) and that 'human sources' are often preferred to written guidance (32). It seems clear from the temporal trends that the increases in dressing use are not driven by knowledge of the research evidence (33). This may suggest that any action aimed at implementing evidence-based guidance within community nursing may benefit from being more focused on the type of change necessary to generate a reduction in specific prescribing practices such as restriction of formulary options and routine monitoring and feedback of individuals prescribing practice to ensure adherence to organisational policies (34).

Patient preference may also play a part in dressing section. Research has shown that healing time was ranked by patients as the most important factor (compared to other factors such as dressing change frequency and pain) (35). Choosing Wisely is a global initiative to address issues such as patient and clinician preferences and making better decisions about care with the aim that this will help avoid tests, treatments or procedures that are unlikely to be of benefit. Choosing Wisely UK is led by the Academy of Medical Royal Colleges and as yet does not encompass nursing as a profession or have any guidance focused on the management of complex wounds (36;37).

The widespread availability of wound care products of apparent low or no clinical value is in part reflective of the threshold for evidence necessary for marketing authorisation of devices (9). Because the threshold of evidence is low, there is little or no incentive for manufacturers to demonstrate that their devices are clinically effective. Research showing how evidence is used to support claims made in product advertisements within two wound care journals found just 35% of claims about the benefits of a product cited supporting evidence. When these sources of evidence were investigated the cited

evidence did not support the claim being made in 56% of cases (12). The emphasis is therefore on incremental product development and innovation. Adopting a medical device when there is little or no evidence to support its use may then in turn lead to a reduction in the likelihood of further relevant research as the innovation becomes standard and integrated into care (4).

Rothery *et al*, suggest that rather than binary choice of adopt or select, policy decisions on innovation introduction may be helped by guidance recommending either options of 'only in research' or 'approval with research' (38). The former allowing further research to establish the value of an innovation before wider access and the latter granting the possibility of product withdrawal should further research prove clinical and cost ineffectiveness (4). NICE has the ability to issue guidance to recommend 'only in research' but this is not routinely used and rarely if ever for medical devices (39).

Strengths and weaknesses

This is the first research study we have identified that clearly reports the temporal changes in the use of relatively costly wound care products in the UK community over several years. These simple data show powerfully how new products can be adopted rapidly despite a lack of robust evidence for clinical or cost-effectiveness. This reinforces the complex nature of decision making in wound care and importance of other spheres of information and knowledge including expert opinion and peer-to-peer advice (33). The role of marketing and company activity in successfully promoting product use is also an area that may have had impact here although this would need to be explored in further work (40).

Our analysis of wound care prescribing is limited by the available data. Temporal changes in dressing use and expenditure may also be influenced by demographic and epidemiological factors (e.g. an ageing population and the rise in chronic diseases such as diabetes) (41). The prescribing data are not wound-specific and limited to English community prescriptions; however, we note that the community is where most complex wounds are treated (42). We also note that prescribing data will not include data on those standard dressings which are kept as stock. ITS analysis has been used to explore the possible impact of the first significant national clinical guideline, the SIGN guideline, on the management of venous leg ulcers. There is a suggestion of some impact of this 'intervention' however it has to be noted (as above) that this guidance is specific to venous leg ulcers whereas the PCA data cover dressing use for any wound type. These analyses did not include multiple 'interventions' incorporating the publication of other guidelines as it was decided to use the single intervention point of 2010 for reasons stated in the methods. However, presenting a summary of the general status of evidence (Table 1) which is so consistent in its message helps provides important contextual information in which to interpret the data.

A limitation of the ITS design is that any hypothesised relationship between the implementation of guidelines and changes in dressing use is based purely on a temporal association. We have no direct evidence of causation. Furthermore the ordinary least squares model forecasts linear trends yet the post-SIGN trends for anti-microbial dressings do not appear to be linear and show a reversal of the initial decreasing trend from 2012. This is partly explained by the differences in use of silver and other antimicrobial dressings (see Appendix 1 panel F). As future data becomes available it will be important to monitor the use of antimicrobial dressings in case further intervention is needed to reduce use. However these changes are temporarily distant from the SIGN guidance and the primary aim of the ITS analysis was to examine changes occurring around the time of the SIGN guidance.

Conclusions

This paper suggests that in the last 20 years there has been a large increase in the use of antimicrobial wound dressings despite a lack of research evidence to support their routine use. Expenditure on antimicrobial wound dressings has risen by over £28 million between and 2016.

Our analysis shows that routinely available PCA data can be used to identify unproven products with significant net financial burden to the NHS may offer a transparent and systematic route to 'only in research' and ultimately to de-implementation. If using routine data in this way is to have an impact on prescribing at scale, then it needs to be linked to a multi-level response that targets procurement processes alongside individual practices to ensure increased value and reduced waste.

Figure Legends

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

Appendix 1. Interrupted time series analysis of annual costs and use of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

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Competing interests

The authors declare they have no competing interests

Authors' contributions

Louise Hussey: First author of manuscript and data analysis

Jill Stocks: Interrupted time series analysis and interpretation

Paul Wilson: Interpretation of data and manuscript revision

Jo Dumville: Study concept and design, interpretation of data and manuscript revision

Nicky Cullum: Interpretation of data and manuscript revision

All authors reviewed and approved the final manuscript before submission

Data availability

Prescription data is freely available from NHS digital

https://digital.nhs.uk/data-and-information/publications/statistical/prescription-cost-analysis

Research Checklist

There is no research checklist relevant to this study

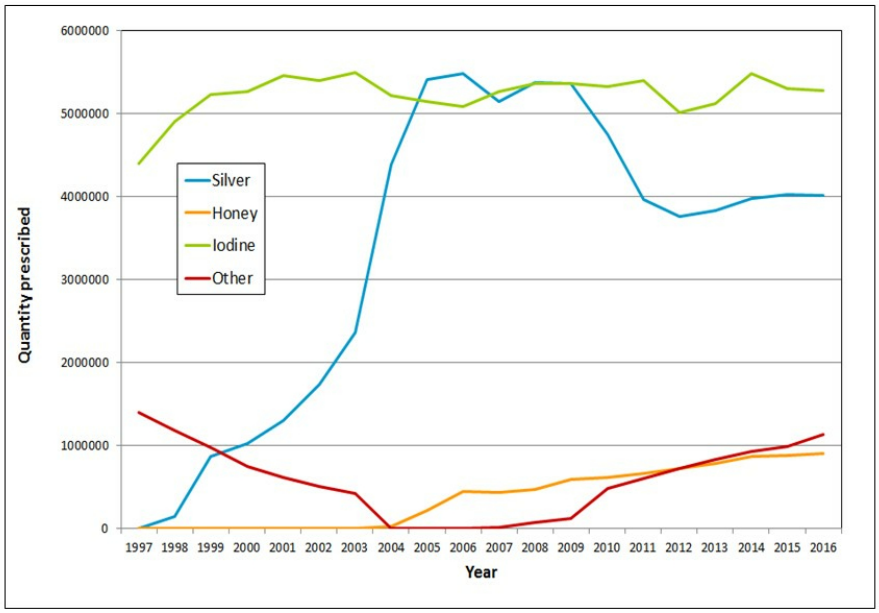

Figure 1. The quantity prescribed per annum of silver, honey, iodine and other antimicrobial dressings prescribed in the community in England (1997 to 2016)

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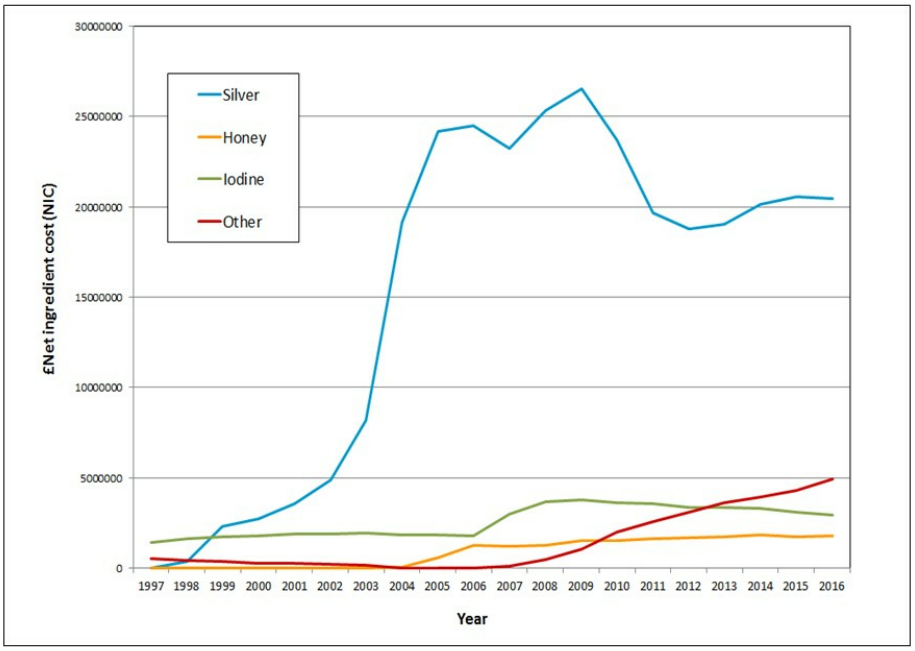

Figure 2. The Net Ingredient Cost (NIC) (total expenditure) per annum of silver, honey, iodine and other antimicrobial wound dressings prescribed in the community in England (1997 to 2016)

81x60mm (300 x 300 DPI)

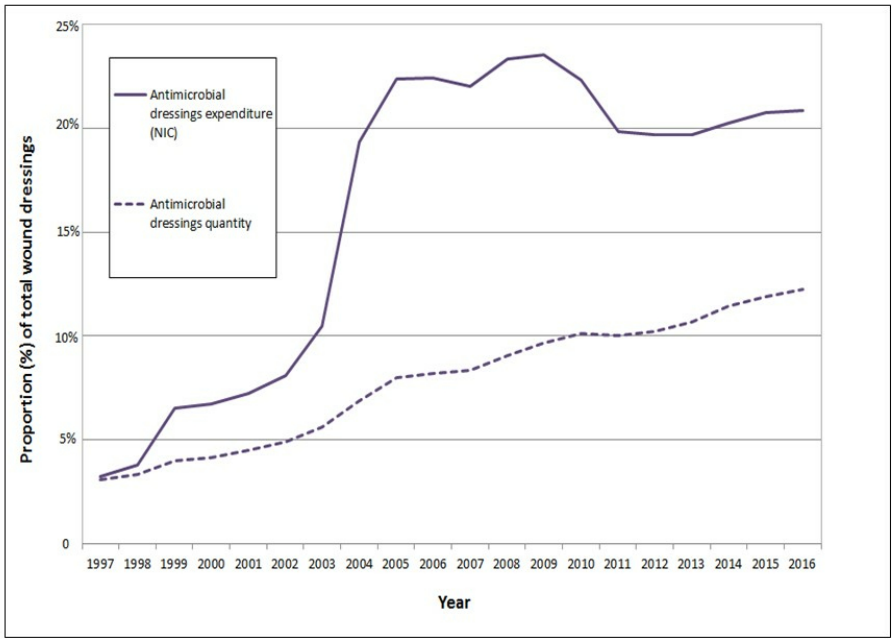

Figure 3. The quantity and Net Ingredient Cost (NIC) (total expenditure) per annum of antimicrobial dressings as a proportion of all dressings prescribed in the community in England (1997 to 2016)

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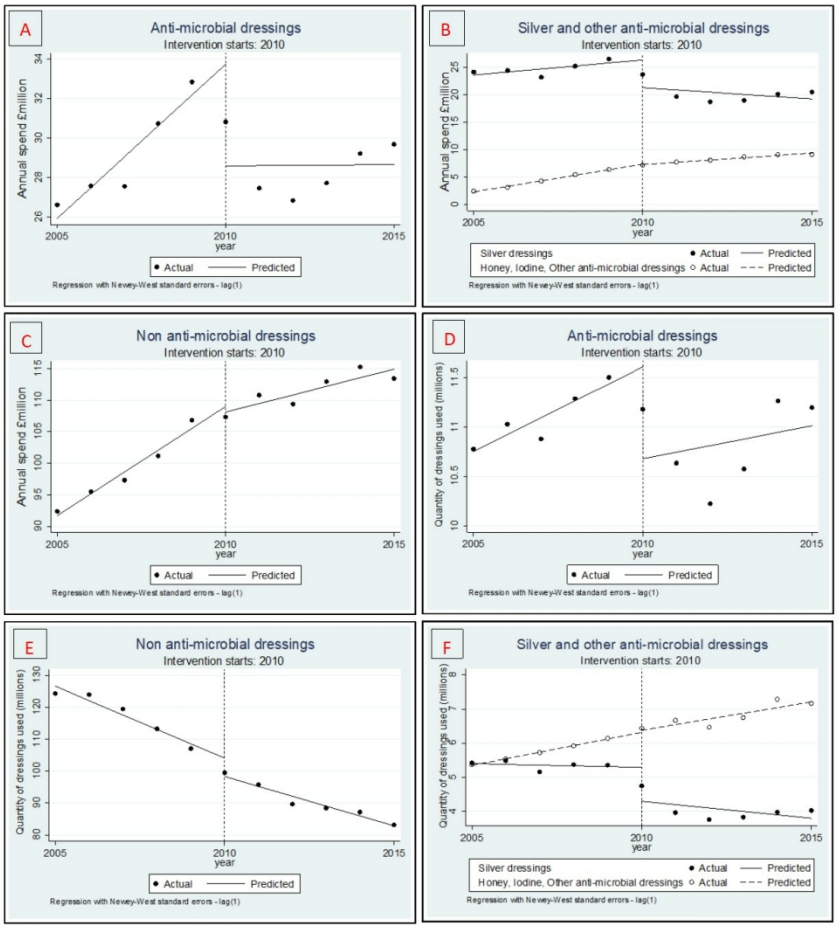

Appendix 1. Interrupted time series analysis of annual costs and usage of antimicrobial dressings and non-antimicrobial dressings from 2005 to 2015

104x148mm (300 x 300 DPI)