Institution: University of East Anglia		
Unit of Assessment: 3 - Allied Health Professions, Dentistry, Nursing and Pharmacy		
Title of case study: Safe administration of medicines to people with enteral tubes		
Period when the underpinning research was undertaken: Sep 2008 to Dec 2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Prof. David Wright	**Role(s) (e.g., job title):** Professor	**Period(s) employed by submitting HEI:** 2003 – to present
Period when the claimed impact occurred: 2015 to 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

Enteral tubes (ET) bypassing the mouth are utilized where patients are unable to swallow. ETs are used to deliver food and drink directly into the intestines and can also be used to administer medication. However, most therapeutics are not formulated for ET delivery, and it is therefore often necessary to manipulate medicines (e.g. crush tablets) to enable medicines to be passed through an ET. Such practice voids the safe drug use licence and results in the unlicensed administration of medicines.

UEA research has highlighted that people with ETs are at very high risk of medication error due to the need to manipulate medicines prior to administration. This research led to **Professor David Wright** advising (in 2014) the Medicines & Health Regulatory Agency on licensing processes and a subsequent revision to its licensing standards.

In collaboration with Rosemont Pharmaceuticals, this research led to the development and licencing of thirteen new liquid drug formulations for ET administration across the UK, which have supported Rosemont Pharmaceuticals sales to grow by 230% (from GBP18,0000,000 to GBP42,000,000) between 2004 and 2019.

2. Underpinning research

Swallowing difficulties (dysphagia) arises from numerous medical conditions associated with ageing e.g., Parkinson's disease, dementia and stroke. Different grades of clinical dysphagia affect more than 1 in 6 people over the age of 65. This inability to swallow results in a significant proportion of this population receiving their food and medicines via ETs. Within hospitals, ETs are also used when patients are unconscious and unable to receive food and liquids by mouth. For these patients the formulation of the drug in a liquid form is as important as the medication itself (**3.1, 3.2**).

Research by **Professor David Wright's** research group in the School of Pharmacy at UEA has highlighted that whilst healthcare professionals focussed their attention on nutrition and hydration, appropriate and safe administration of medicines was often overlooked. The research identified that when nurses were required to administer medicines via enteral tubes, the standard practice was to either disperse tablets and capsules in water or administer a liquid medicine prior to administration (**3.3, 3.4**). Such practices were performed outside of the medicine's license and were associated with significant increases in risk in medication error and with the potential for increased risk of ET blockage, which can necessitate new tube insertion by surgical procedure. Furthermore, due to the wide range of options available when choosing to undertake unlicensed administration, the process was found to vary significantly depending on the administrator (**3.2, 3.5**).

UEA research specifically identified that administration of medicines to patients with dysphagia was not optimal (**3.2, 3.3**). Several factors conspired here, including inadequate knowledge of how

to administer medicines, and lack of skill in mixing medicines for ET delivery (**3.3, 3.4**). This research highlighted that, excluding time errors, the normalised frequency of medicine administration errors for patients with dysphagia was 21.1% compared with 5.9% for patients without (**3.3**). Furthermore, the results highlighted that there was a significantly increased risk of medication errors ($P < 0.001$) for patients with dysphagia (excluding patients with enteral tubes). In dysphagia patients with enteral tubes, there was a further increase in the risk of medication error ($P < 0.001$) (**3.3**).

The main concerns with respect to administration of medicines via ETs were found to be tube blockage and loss of active ingredient on the tube during administration. The research identified that the principal reason for these outcomes was the limited availability of licensed medicines suitable for administration via ETs (**3.2**)**.** A key recommendation of the research was to administer drugs in formulations that are specifically designed not to block ETs in an unaltered state. These recommendations would decrease the risk of errors and, furthermore, the possibility of additional (avoidable) surgical procedures would be significantly reduced.

Key conclusions of the UEA research are that improvements in interprofessional communication are needed to improve medicine administration to dysphagic patients, and that there is a need for continuing professional development in medicine administration to provide greater understanding of the contra-indications of combining medications and of the significant legal implications of altering formulations.

3. References to the research

The underpinning research outputs have all been published in competitive, international, peer-reviewed journals and form part of a larger body of such published work. Citation numbers are from Google Scholar (12/2/21).

UEA authors highlighted in **bold**

3.1 Kelly J, **D'Cruz G**, **Wright D.**
Patients with dysphagia: Experiences of taking medication.
Journal of Advanced Nursing. (**2009**); 66(1): 82–91.
DOI: 10.1111/j.1365-2648.2009.05145.x Citations: 85

3.2 Kelly J, **D'Cruz G**, **Wright D.**
A qualitative study of the problems surrounding medicine administration to patients with dysphagia.
Dysphagia (**2009**); 24(1): 49-56.
DOI: 10.1007/s00455-008-9170-3 Citations: 63

3.3 Kelly J, **Wood J**, **Wright D.**
Medication administration errors in secondary care older person's wards: A multi-centre observational study.
Journal of Advanced Nursing (**2011**); 67(12): 2615–2627.
DOI: 10.1111/j.1365-2648.2011.05700.x Citations: 80

3.4 Kelly J, **Wright D.**
Medication administration errors and their severity in secondary care older person's ward: a multi-centre observational study.
Journal of Clinical Nursing. (**2012**); 21: 13-4.
DOI: 10.1111/j.1365-2702.2011.03760.x. Citations: 28

3.5 Kelly J, Eggleton A, **Wright D.**
An analysis of two incidents of medicine administration to a patient with dysphagia.
Journal of Clinical Nursing. (**2011**); 20(1-2):146-155.
DOI: 10.1111/j.1365-2702.2010.03457.x Citations: 17

4. Details of the impact

Effecting safer drug administration to patients

Nurses, midwives and health visitors are advised not to crush medication. However, there are occasions where a patient is unable to swallow solid oral dosage forms. In such instances, it may be necessary to crush tablets or open capsules. Crushing medication or opening capsules prior to administration results in unlicensed administration. Under the Human Medicines Regulations (2012) only licensed prescribers can authorise the administration of unlicensed medicines. It may therefore be illegal for other healthcare professionals (HCP) to open a capsule or crush a tablet before administration without the authorisation of the prescriber. Where such administration results in harm to the patient, then the manufacturer has no liability for any harm that ensues, and if the unlicensed administration is unauthorised by the prescribing doctor then liability may lie solely with the administering HCP.

In 2019, **Wright** chaired a national working party to develop clinical guidelines for use by healthcare professionals when administering medicines via ETs (**Source 5.1**). In line with Medicines and Health Regulatory Agency (MHRA) recommendations, these guidelines state:

> "*When choosing a new drug, follow due diligence and use clinical judgement: – medicines licensed for administration by enteral feeding tube should be used first line.*"
> (**Source 5.1 page 4**)

Chief Pharmacists from NHS hospital trusts have confirmed that this is being implemented in contemporary NHS practice:

> *"Best practice and advice from the MHRA dictates that we always use a licensed product where one exists… Given the option of a licensed versus unlicensed product, professional standards and responsibilities for quality assurance will always guide us to use the licensed one, even if there is a cost implication. Having a licensed liquid available to us gives assurance that it can be administered safely via an enteral tube"*
>
> *"It is always preferable to use a licensed liquid preparation, if this is available. The reasons for this are that the licensed preparation will be on the commercial market and are therefore readily available at short notice. Licensed medicinal products will also have been tested to ensure that it is a standardised preparation that is clearly labelled and will reliably deliver the stated dose within the shelf life of the product."*
> (**Source 5.2**)

In 2013, **Wright** secured funding from Rosemont Pharmaceuticals to develop education and training materials which supported the relaunch of the swallowingdifficulties.com website. This is an online go-to for patients and HCP to obtain information and guidance on dysphagia and liquid medicines. The website has received over 1 million international webpage views (with users split equally across the EU, USA and Asia with smaller percentages from Africa and Oceania). Information specifically for patients is accessed 40% of the time, with 20% information for prescribers. (**Source 5.3**)

The education grants also facilitated the development and delivery of a massive open on-line course (MOOC) entitled "Dysphagia: Swallowing Difficulties and Medicines". The MOOC seeks to disseminate best clinical practice to patients, carers and healthcare professionals administering medicines to people with dysphagia. The MOOC is delivered over five weeks and has been accessed by over 30,000 patients and healthcare professionals from 181 countries and dependencies. (**Source 5.4**)

Developing the first licensed liquid medicines for ET administration

UEA researchers collaborated with the senior management team at Rosemont Pharmaceuticals – a specialist company that manufactures and sells liquid medicines globally – on a strategy to license specific liquid medicines for ET administration.

> "*In 2005 we invited Prof Wright to present his findings at a Rosemont round table event, at which he recommended the company to consider licensing liquids specifically for administration via enteral tubes - at the time no liquid medicines were approved for this route of administration.*" (**Source 5.5**).

In order to deliver this business plan, senior regulatory team members from Rosemont, with **Wright** as an expert witness, were invited to MHRA in 2014 to discuss and agree a new process for the licensing of liquid medicines for administration via the ET route (**Source 5.6**). Research undertaken by Wright (**3.6**) was used to underpin and inform the methods used by Rosemont to secure their ET administration licenses (**Source 5.6**).

> "*The work originally done by Rebecca White who was Prof Wright's PhD student investigating how to set up the testing rig and advice on the types of tubing and materials, plus techniques used to administer drugs via feeding tubes helped Rosemont develop a sound method of testing, that gave robust and repeatable results*."
> (**Source 5.6**)

Importantly, the research undertaken in the **Wright-Rosemont** collaboration contributed to the MHRA benchmark used when considering license approval of other liquid medicines for ET approval that are submitted by other companies.

> *"As a result of the discussion, the MHRA was confident that the proposed approach would not only provide an appropriate way of testing to allow assessment by the regulatory authorities, but would also set the bar for the testing that would be required for all marketing authorisations, requiring that route of administration."*
> (**Source 5.6**)

Having secured MHRA agreement for the proposal, Rosemont were the first company to apply for, and secure, UK licencing approval to market and supply liquid medicines for ET administration to dysphagia patients. Rosemont currently has thirteen licensed liquid medicines including seven drugs at different doses that embrace a broad range of therapeutics used to treat many of the most common diseases, ranging from high blood pressure and infections to epilepsy and pain.

As the UK's largest specialist liquid medicine manufacturer, Rosemont used the licenses for these new products to maintain its market share **(Source 5.5)**. According to Rosemont, specific licensing for ETs:

> *"...has allowed us to retain customers and reduce the severe price erosion, because we have added something clinically useful to these products."*
> (**Source 5.5**)

The importance of **Wright**'s research to Rosemont's development of licensed liquid medicines is recognised by the company

> *"…Prof Wright played a pivotal role in Rosemont's decision to be the first company to develop and license formulations for enteral tube administration. Our work with prof. Wright since 2004 has provided a solid platform for Rosemont to drive product sales and disseminate clinical best practice in medicines administration to patients with dysphagia. In this time period, the sales of Rosemont liquid medicines have more than doubled from £18m to*

£42m, representing a significant increase in our company turnover" (**Source 5.5**).

There is evidence of other companies licensing their medicines for administration via the ET route in recent years. For example, Colonis Pharma, Bayer, and other pharmaceutical manufacturers have secured UK licensing for ET administration of their products. In 2018, ITF Pharma secured FDA approval for ET administration of riluzole in patients with amyotrophic lateral sclerosis in the United States (**Source 5.7**).

Improving healthcare outcomes with mitigated risks, legal challenge and cost

Unlicensed administration of crushed tables or capsule powders via ETs can cause drug delivery to inappropriate sites for drug absorption (stomach vs lower intestine) and unintended drug interactions, for example, between different drugs, between drug and feeds or between the drug and tube (**3.1-3.5**). The development of new licenced products, applicable to a broad spectrum of symptoms/conditions, is ensuring that these medicines are being delivered with optimal efficacy, and thus realising their full therapeutic potential.

Crushed tablets can cause ETs to block (**3.1-3.5**). The availability of ET-specific formulations, developed through the **Wright-Rosemont** collaboration, obviate these blockages. Avoiding ET blockage removes surgical (and post-surgery infection) risks and reduces hospital costs associated with clinical management of tube blockage and reinsertion.

In summary, increased availability of medicines licensed for administration via ET simplifies practitioner decision-making, reduces the opportunity for error in the preparation of unlicensed medicines through e.g. tablet crushing and removes the possibility of legal challenge. Thus, the development, licencing and increased availability of ET-specific formulations are improving patient care and protecting thousands of nurses, midwives and health visitors from potential legal action.

5. Sources to corroborate the impact

5.1 Medicines management of patients with enteral feeding tubes. Available from Guidelines.co.uk (Downloaded 15.09.20).

5.2 NHS Chief Pharmacists testimonials (dated September 2020).

5.3 Website and usage statistics for the period 01.08.2013 - 31.07.2020 for swallowingdifficulties.com.

5.4 MOOC statistics showing global reach and number of participants for the UEA Dysphagia course.

5.5 Testimonial from External Affairs, Rosemont Pharmaceuticals (dated December 2019).

5.6 Testimonial from Head of UK Pharmacovigilance, Rosemont Pharmaceuticals (Dated November 2020).

5.7 Prescribing information for Metaformin Colonis, Vitrakvi, Inovelon, Captopril, Desitrend, Gabapentin Colonis and Levothyroxine from medicines.org.uk (accessed on 15 February 2021) and TIGLUTIK (riluzole) oral suspension, from accessdata.fda.gov (accessed on 28 January 2021).