Impact case study (REF3b)

Institution: University of Sheffield

Unit of Assessment: 2 - Public Health, Health Services and Primary Care

Title of case study: Changed clinical guidelines to improve the diagnosis of deep vein thrombosis (DVT)

1. Summary of the impact

Our research has led to the development of guidelines on the diagnosis of deep vein thrombosis (DVT), reducing the risk of death and saving resources by reducing unnecessary tests and treatments.

Meta-analysis and decision-analysis modelling studies undertaken at the University of Sheffield between 2005 and 2007 formed the basis of the National Institute for Health and Clinical Excellence (NICE) and the American College of Chest Physicians (ACCP) guidelines for diagnosing DVT. These guidelines determine the management of over 140,000 patients each year in the United Kingdom with suspected DVT, and many more in other countries.

2. Underpinning research

DVT is a potentially life threatening condition with an annual incidence of 124 per 100,000 population. Patients with DVT are at substantial risk of death if they are not correctly diagnosed and treated. The diagnostic assessment of DVT has changed dramatically over the last 10-20 years, from being inpatient-based using contrast venography to becoming outpatient-based using a variety of non-invasive tests. The development of clinical prediction scores, D-dimer blood testing, ultrasonography, computed tomographic (CT) imaging and magnetic resonance (MR) imaging, alongside older tests such as plethysmography, had until 2005 led to confusion over the best test to use and different testing strategies being used in different hospitals.

Between 2005 and 2007, researchers from the School of Health and Related Research (ScHARR) at the University of Sheffield, led by Professor Steve Goodacre, undertook an evidence synthesis project funded by the National Institute for Health Research Health Technology Assessment programme. The project aimed to estimate the diagnostic accuracy of tests for DVT and identify the most cost-effective diagnostic strategy. It consisted of systematic reviews, meta-analysis, decision-analysis modelling of cost-effectiveness, and a national survey.

Goodacre and Fiona Sampson (ScHARR, University of Sheffield, since 1996) undertook the systematic reviews of the diagnostic accuracy of tests, and with statistical support from Professor Alex Sutton of the University of Leicester, conducted meta-analysis to provide clinically useful estimates of sensitivity, specificity and likelihood ratios. The systematic reviews showed that individual clinical features were of limited diagnostic value, while the Wells clinical probability score (a structured patient assessment that estimates the probability of DVT) stratified proximal, but not distal DVT [R1]. D-dimer had good sensitivity, but limited specificity for DVT [R2]. Plethysmography techniques had modest sensitivity and specificity. Ultrasound had good sensitivity for proximal DVT, modest sensitivity for distal DVT, and good specificity [R3]. CT and MR imaging both had similar diagnostic accuracy to ultrasound, but these estimates were based upon limited data [R4,R5].

Professor Matt Stevenson (ScHARR, University of Sheffield, since 1996) developed the decision-analysis model to estimate the cost-effectiveness of diagnostic strategies for DVT. Goodacre and Sampson undertook the national survey and a literature review in 2005 to identify potential diagnostic strategies. They then applied estimates of sensitivity and specificity from the meta-analysis to the strategies to estimate the outcomes in terms of overall diagnostic accuracy.

Stevenson then used modelling to estimate the costs incurred and quality-adjusted life years (QALYs) gained by each strategy, along with the net benefit of each strategy assuming willingness to pay in accordance with NICE guidance. The analysis showed that the most cost-effective and feasible strategy involved a combination of Wells clinical probability score, D-dimer and compression ultrasound [R6].

In 2008-9, at the request of the ACCP Guideline Development Group, Goodacre updated the systematic reviews of CT and MR scanning and Stevenson used the decision-analysis model to estimate the risk of adverse outcome for various commonly used diagnostic strategies for DVT. The findings were published in 2012 in the ACCP Evidence-Based Clinical Practice Guidelines for the diagnosis of DVT.

3. References to the research

R1. **Goodacre S**, Sutton AJ and **Sampson F**. The value of clinical assessment in the diagnosis of deep vein thrombosis: a meta-analysis. Ann Intern Med 2005;143:129-139. doi: 10.7326/0003-4819-143-2-200507190-00012

R2. **Goodacre S, Sampson FC**, Sutton AJ, **Mason S** and Morris F. Variation in the diagnostic performance of D-dimer for suspected deep vein thrombosis: systematic review, meta-analysis and meta-regression. Q J Med 2005;98:513-517. doi: 10.1093/qjmed/hci085

R3. **Goodacre S, Sampson F, Thomas S**, van Beek E, Sutton AJ. Systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis. BMC Medical Imaging 2005;5:6. doi: 10.1186/1471-2342-5-6

R4. **Thomas SM, Goodacre SW, Sampson FC** & van Beek EJR. Diagnostic value of CT for deep vein thrombosis: results of a systematic review and meta-analysis. Clinical Radiology 2008;63:299-304. doi: 10.1016/j.crad.2007.09.010

R5. **Sampson FC, Goodacre SW, Thomas SM** & VanBeek EJR. The accuracy of MRI in diagnosis of suspected deep vein thrombosis: systematic review and meta-analysis. Eur Radiol 2007;17:175-181. doi: 10.1007/s00330-006-0178-5

R6. **Goodacre S, Sampson F, Stevenson M, Wailoo A**, Sutton AJ, **Thomas S, Locker T & Ryan A**. Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis. Health Technol Assess 2006;15 (10).

4. Details of the impact

Our research directly informed changes to national and international guidelines for the diagnosis of DVT. Diagnostic assessment is undertaken in the UK using NICE guidelines [S1] and internationally using ACCP guidelines [S2].

Impact in the UK

NICE published its DVT guideline in 2012 (Clinical Guideline 144) [S1], with the aim of reducing the current high toll of long-term ill health or death caused by venous thromboembolic diseases by clarifying - for the first time - what combination of tests and treatments results in the most cost-effective diagnosis and management of these conditions. Specifically, the guidelines provide an algorithm to guide DVT diagnosis in the NHS and evidence-based guidance on the use of clinical probability scoring, D-dimer and ultrasound in the diagnosis of DVT.

The estimates of sensitivity and specificity, and the evidence statements provided in the guidelines are based upon our meta-analyses of these approaches/methodologies. The NICE DVT guidelines recommend the algorithm identified in our analysis as being most likely to be cost-effective and feasible in the NHS.

Implementation of the NICE guidance will improve outcomes for patients with suspected DVT by reducing misdiagnosis and will result in more cost-effective care. NICE claimed that the clinical guideline would save lives by improving the diagnosis and management of blood clots [S3]. This will be achieved through NICE Quality Standard 29, Quality Statement 2 (Diagnosis of DVT), which promotes implementation of NICE Clinical Guideline 144 [S4].

NICE Clinical Knowledge Summaries provide primary care practitioners with a readily accessible summary of the current evidence base and practical guidance on best practice in respect of over 300 common and/or significant primary care presentations. The NICE Clinical Knowledge Summary for predicting who is at risk for DVT [S5] cites data from our meta-analysis [R1] and economic analysis [R6] to guide practitioners.

Around 140,000 people are investigated for suspected DVT each year in the UK. It is difficult to estimate the impact of new guidance on health outcomes and costs since practice varied substantially prior to implementation of the guidance [S6]. However, on the basis of our economic model we estimate that adopting the NICE recommended algorithm instead of using ultrasound for all cases would result in a net benefit of £42,919 per 1000 patients with suspected DVT (i.e. per year at a large hospital), assuming health outcomes are monetised with an estimated value of £20,000 per QALY.

International impact

ACCP guidance is produced in the United States and Canada, and is used in many other countries. Updated ACCP guidelines for diagnosing DVT were published in 2012 [S2]. Recommendations in the guidance for the use of Wells score, D-dimer and ultrasound all cited our meta-analyses. Furthermore, as a direct result of our research the ACCP Guideline Development Group asked us to provide updated systematic reviews of CT and MR scanning specifically for this guideline. We were also asked to use our decision-analytic model to estimate the probability of adverse outcomes for commonly used diagnostic strategies. These estimates were published in the ACCP guidance.

The ACCP and NICE take different approaches to providing guidance, but both based their recommendations on our analyses. Whereas NICE recommends a specific algorithm, the ACCP guidance provides physicians with estimates of the likely consequences of different diagnostic approaches and leaves the choice of strategy to the physician. Our approach to analysis allowed us to adapt our outputs to the needs of both organisations. For NICE we identified the strategy most likely to be feasible and cost-effective in the NHS. For the ACCP we estimated the likely consequences of alternative diagnostic strategies. These mean that our findings influenced practice in different ways and in different settings.

Impact on the clinical community

To increase the use of our research throughout the clinical community, the Chief Investigator for the project published an educational article for Annals of Internal Medicine in 2008 that provided advice on DVT diagnosis based on our analysis [S7] and provided content between 2007 and 2011 for the DVT module of the Physicians' Information and Education Resource run by the American College of Physicians, based on our analysis [S8]. We also presented our findings at a specially organised one-day conference for clinicians and at other conferences, such as the Annual Scientific Meetings of the College of Emergency Medicine and British Society for Haematology.

5. Sources to corroborate the impact

S1. National Institute for Health and Clinical Excellence. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing. NICE clinical guideline 144, June 2012, http://guidance.nice.org.uk/CG144. See Clinical Guideline pages 42-52, reference 85, and Appendices pages 82, 102, 144, 474-476, & references 170-173.

S2. Bates SM, Jaeschke R, Stevens SM, Goodacre S, Wells PS, Stevenson MD, Kearon C, Schunemann HJ, Crowther M, Pauker SG, Makdissi R, Guyatt GH. Diagnosis of DVT: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. CHEST 2012; 141(2)(Suppl) http://journal.publications.chestnet.org/article.aspx?articleid=1159488. See pages e356S, e383S, e384S, & references 14,15,56,71,144.

S3. National Institute for Health and Clinical Excellence. NICE clinical guideline set to save lives by improving the diagnosis and management of blood clots (press release, 20/6/2012) http://www.nice.org.uk/newsroom/pressreleases/VTEDiseasesGuideline.jsp

S4. National Institute for Health and Clinical Excellence. QS29: Quality standard for diagnosis and management of venous thromboembolic diseases. Quality statement 2: Diagnosis of deep vein thrombosis. http://guidance.nice.org.uk/QS29

S5. NICE Clinical Knowledge Summaries: Deep vein thrombosis (revised April 2013). http://cks.nice.org.uk/deep-vein-thrombosis#!supportingevidence1

S6. Sampson F, Goodacre S, Kelly A-M and Kerr D. How is deep vein thrombosis diagnosed and managed in UK and Australian emergency departments? Emerg Med J 2005;22:780-2.

S7. Goodacre S. In the Clinic: Deep Vein Thrombosis. Ann Intern Med 2008;149:ITC3-1-16.

S8. American College of Physicians: Physicians' Information and Education Resource website, http://pier.acponline.org/index.html