

Impact case study (REF3b)

Institution: King's College London
Unit of Assessment: 3B - Pharmacy and Nutritional Sciences
Title of case study: Managing hypoglycaemia to improve quality of life in people with diabetes
<p>1. Summary of the impact</p> <p>Research conducted at King's College London into the mechanisms underlying hypoglycaemia unawareness in type 1 diabetes mellitus (T1DM) and novel technology for reducing the risk of hypoglycaemia has led directly to innovative changes in the management of diabetes. These include UK and worldwide development and dissemination of the government-recommended 'Dose Adjustment for Normal Eating' (DAFNE) programme and on-going development of continuous subcutaneous insulin infusion (pump) therapy, now used by over 18,500 people with T1DM in the UK.</p>
<p>2. Underpinning research</p> <p>For people with type 1 diabetes mellitus (T1DM), therapeutic goals include achieving improved glycaemic control to minimise risk of chronic complications while avoiding hypoglycaemia. Research in this field at King's College London (KCL) has been led by Prof Stephanie Amiel (1995-present, Professor of Diabetic Medicine, Joint Head of the Diabetes & Nutritional Sciences Division), Prof John Pickup (1976-present, Professor of Diabetes and Metabolism), Angus Forbes (2008-present, FEND Chair of Diabetes Nursing) and Dr Pratik Choudhary (2010-present, Senior Lecturer).</p> <p>From 1998, KCL researchers collaborated with researchers in Sheffield, North Tyneside Hospital, and Dusseldorf's Heinrich Heine University, to develop and test an English language version of a structured education programme for people with T1DM: 'Dose Adjustment for Normal Eating' (DAFNE). DAFNE is a 5-day course in which participants learn to adjust near-physiological insulin dose regimens to desired food and exercise by using blood glucose monitoring reflectively to improve glycaemic control. The initial trial, with 141 adults, found a significant improvement in glycated haemoglobin (HbA1c, a risk marker for long term complications) and sustained positive effects on quality of life, treatment satisfaction and psychological wellbeing (1).</p> <p>KCL researchers further developed the programme into a 'hub-and-spoke model' where, while initial patient training still took place at large centres, diabetes teams from three smaller units were trained as DAFNE advisors to assess, recommend and follow-up DAFNE users. This was found to be a very feasible model of service provision for clinics where resources did not allow for a full DAFNE service. They again demonstrated improved control and reduced rates of severe hypoglycaemia and emergency service use (2). In a 2012 national audit of DAFNE centres, KCL researchers showed sustained improvements at one year in HbA1c and reduced episodes of severe hypoglycaemia, with a 43% improvement of hypoglycaemia recognition in those previously reporting unawareness. They also reported clinically relevant decreases in anxiety and depression (3).</p> <p>KCL researchers additionally developed, and are playing a major role in applying, continuous subcutaneous insulin infusion (CSII) therapy via a pump for diabetic people with recurrent severe hypoglycaemia despite optimised conventional therapy (including DAFNE). One 2005 study, involving 27 patients, showed that CSII produced a significant fall in HbA1c compared to multiple daily insulin injections (MDI), with a reduction in insulin dosage, glucose oscillations and severity and frequency of hypoglycaemia (4). Another study, with 40 patients, found that people who may be excluded from CSII due to compliance issues when controlling their diabetes on conventional therapy can responsibly use CSII when guidance is provided by a specialist diabetes service. This led to reductions in severe hypoglycaemia and extremes of high blood glucose (5). KCL researchers have also produced several widely-used meta-analyses including one in 2002 on 12 randomised controlled trials that compared CSII (n = 301) to MDI (n = 299) and showed a lower mean blood glucose concentration and HbA1c levels with an average reduction of 14% in insulin dose (6). Continuing studies have showed that severe hypoglycaemia rates could be reduced by pump therapy compared to MDI, with a greater reduction in those with higher initial severe hypoglycaemia rates on MDI (7) and especially with the addition of novel glucose monitoring devices (8).</p>

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3. References to the research (indicative maximum of six references)

1. Amiel S, Beveridge S, Bradley C, The DAFNE Study Group, et al. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial. *BMJ* 2002;325(7367):746-49. Doi: <http://dx.doi.org/10.1136/bmj.325.7367.746> (372 Scopus citations)
2. Rogers H, Turner E, Thompson G, Hopkins D, Amiel SA. Hub-and-spoke model for a 5-day structured patient education programme for people with Type 1 diabetes. *Diabet Med* 2009;26(9):915-20. Doi: 10.1111/j.1464-5491.2009.02796.x (4 Scopus citations)
3. Hopkins D, Lawrence I, Mansell P, Thompson G, Amiel S, Campbell M, Heller S. Improved biomedical and psychological outcomes 1 year after structured education in flexible insulin therapy for people with type 1 diabetes: the U.K. DAFNE experience. *Diabetes Care* 2012;35(8):1638-42. Doi: 10.2337/dc11-1579 (11 Scopus citations)
4. Pickup J, Kidd J, Burmiston S, Yemane N. Effectiveness of continuous subcutaneous insulin infusion in hypoglycaemia-prone type I diabetes. *Pract Diab Int* 2005;22(1):10-14. Doi: 10.1002/pdi.732 (17 Scopus citations)
5. Rodrigues IAS, Reid HA, Ismail K, Amiel SA. Indications and efficacy of continuous subcutaneous insulin infusion (CSII) therapy in Type 1 diabetes mellitus: a clinical audit in a specialist service. *Diabet Med* 2005;22(7):842-49. Doi: 10.1111/j.1464-5491.2005.01539.x (28 Scopus citations)
6. Pickup J, Mattock M, Kerry S. Glycaemic control with continuous subcutaneous insulin infusion compared with intensive insulin injections in patients with type 1 diabetes: meta-analysis of randomised controlled trials. *BMJ* 2002 23;324(7339):705. Doi: <http://dx.doi.org/10.1136/bmj.324.7339.705> (271 Scopus citations)
7. Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. *Diabet Med* 2008;25(7):765-74. Doi: 10.1111/j.1464-5491.2008.02486.x (127 Scopus citations)
8. Choudhary P, Shin J, Wang Y, Evans ML, Hammond PJ, Kerr D, Shaw JA, Pickup JC, Amiel SA. Insulin pump therapy with automated insulin suspension in response to hypoglycemia: reduction in nocturnal hypoglycemia in those at greatest risk. *Diabetes Care*. 2011;34:2023-25. Doi: 10.2337/dc10-2411 (43 Scopus citations)

Key grants

- 1999-2000. Roberts S, Heller S, Amiel SA. The effects of brief intensive training in self-management of Type 1 diabetes mellitus - the dose adjustment for normal eating trial (DAFNE). British Diabetic Association, £166,869
- 2003-5. Amiel SA (CI). Protecting against severe hypoglycaemia by manipulation of glucose sensing and cortical function. Diabetes UK, £98,241
- 2004-6. Amiel SA (CI), Reid H, Turner E. DAFNE A hub and spoke initiative. Diabetes UK, £54,517
- 2004-7. Amiel SA (CI), Williams SCR, Brammer M, Zelaya F. Central Glucose Sensing in Health and Disease. Wellcome Trust Project Grant, £440,952
- 2006-12. Pickup JC (CI), Birch DJS. Nanometrology for Molecular Science, Medicine and Manufacture. EPSRC/HEFCE, £4.3 million
- 2007-12. Amiel SA (CI), Ismail K, Docherty J, Thomas S, Edmonds M, Costa D, Patel A, Turner E, Gulliford M, Treasure J, King M, Stahl D. Non-pharmacological approaches to improving diabetes outcomes. The National Institute of Health Research, £1,925,329

4. Details of the impact (indicative maximum 750 words)

Dose Adjustment For Normal Eating (DAFNE): One of the major goals for people with type 1 diabetes mellitus (T1DM) is glycaemic control. To address how this can be attained, the 'Dose Adjustment for Normal Eating' (DAFNE) programme – a skills-based structured education patient program in intensive insulin therapy and self management – was set up as a collaboration between King's College London (KCL), King's College Hospital Diabetes service, Sheffield University and North Tyneside Hospital. From its successful trial showing improved outcomes in T1DM, DAFNE was initially rolled out to 10 centres, funded by the Department of Health. It is now delivered in 77 UK centres.

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Prof Amiel of KCL oversaw this, chairing the first DAFNE National Executive from 2002-2011. The executive coordinates training for DAFNE educators, provides teaching tools and quality assurance (including peer review) and monitors the curriculum through a national audit of outcomes. Up until July 2013, the UK centres have trained 900 UK healthcare professionals and 27,983 UK adults with T1DM in 4,045 courses. There is an active DAFNE User Group with its own website (DAFNE On-line) providing the patient voice. The original 2002 UK DAFNE study (Amiel 2002), along with follow-up studies by KCL including Rogers H 2009 and Hopkins 2012 are cited on the professionals' DAFNE website in providing their evidence base (1a). A number of follow-up investigations have shown that the DAFNE programme can lead to sustained benefit, including a mean improvement from baseline in glycated haemoglobin (HbA1c) and improvements in quality of life that remained significant at 44 months (1b) and demonstrated cost effectiveness (1c).

Use of DAFNE in the UK: DAFNE is the only nationwide structured education programme for adults with T1DM recommended as an exemplar by the National Institute for Health and Care Excellence (NICE) in their 2003 Health Technology Appraisal (HTA) (2a). This HTA is included in a number of current NICE documents, such as the 2011 Quality Standard on Diabetes in Adults (2b) and their T1DM Patient Pathway (2c). DAFNE is also named by the NHS as one of only two "national patient education programmes designed to give people the skills and confidence to manage their condition" in their National Service Framework (NSF) document regarding standards for diabetes care. The NSF aims to "set clear quality requirements for care ... based on the best available evidence of what treatments and services work most effectively for patients" (2d). DAFNE has also become a NHS Evidence Quality, Innovation, Productivity and Prevention (QIPP) case study. Such case studies are provided by the Department of Health as examples of recommended NHS care (2e).

Use of DAFNE overseas: Further afield, the UK programme has trained healthcare professionals in new centres in Ireland and Australia (OzDAFNE, which now trains teams in New Zealand and Singapore) (3a), Kuwait, South Africa, Nigeria and Spain. The International Diabetes Federation described the success of DAFNE in these centres in their journal *Diabetes Voice*. This publication is distributed worldwide to over 200 national diabetes organisations, healthcare professionals and funders including governments in over 160 countries (3b).

Continuous subcutaneous insulin infusion therapy: While DAFNE has been very successful for a large number of people with T1DM, for some however, diabetes control and hypoglycaemia can remain problematic even after DAFNE. Continuous subcutaneous insulin infusion (CSII) via pump therapy is a KCL-led innovation that can help such people. NICE's 2008 technology appraisal of pump therapy recommends it for adults and children with T1DM where multiple daily insulin injections (MDI) results in disabling hypoglycaemia (4a). This appraisal is based on an assessment by Cummins E, et al. 2007 that acknowledges Prof Pickup as one of the originators of CSII and cites Pickup 2002, 2005 and Rodrigues 2005, when discussing the evidence of effectiveness (4b). A 2010 HTA update to this assessment also concluded that pumps can be advantageous over MDI. This cites these KCL studies and Pickup 2008 and uses these as the basis for reporting in several sections including assessment of treatment costs (4c). NICE's 2009 commissioning guide draws heavily on the 2008 technology appraisal. This guide "provides support for the local implementation of NICE guidance through commissioning and is a resource to help health professionals in England to commission an effective insulin pump therapy service" (4d). Both these NICE documents utilised expert opinion from KCL Professors Amiel and Pickup. The reports have also been quoted in the Diabetes UK recommendation that CSII "should be offered as a treatment to people with T1DM as part of a cohesive and comprehensive diabetes service" (4e).

Further use of CSII: KCL work on CSII has also informed several UK guidelines including the NHS Technology Adoption Centre's 'How To Why To' guide (that cites Pickup 2002 and Rodrigues 2005). The guide is based on the experiences of three 'pump-naive' services mentored by diabetes teams from KCL working at the King's Health Partner hospitals King's College, Guy's and St Thomas's (5a,b). The guide had a major impact on roll-out of insulin pump therapy across UK, with an increase in adult pump use from 2% in 2008 to up to 6% in 2012. This has resulted in improved glycaemic control and better quality of life for 13428 adults and 5094 children (19% of all those with

T1DM) now using these pumps (5c).

5. Sources to corroborate the impact (indicative maximum of 10 references)

1) Dose Adjustment For Normal Eating (DAFNE): <http://www.dafne.uk.com/>

- a. Evidence base for DAFNE:
<http://www.dafne.uk.com/uploads/443/documents/PU07.002,%20Version%209%20-%20The%20Evidence%20Base%20-%20June%202012.pdf>
- b. Speight J, et al. Long-term biomedical and psychosocial outcomes following DAFNE (Dose Adjustment For Normal Eating) structured education to promote intensive insulin therapy in adults with sub-optimally controlled Type 1 diabetes. *Diabetes Res Clin Pract* 2010;89:22-9. Doi: 10.1016/j.diabres.2010.03.017.
- c. Shearer A, et al. Cost-effectiveness of flexible intensive insulin management to enable dietary freedom in people with Type 1 diabetes in the UK. *Diabet Med*. 2004;21:460-7. Doi: 10.1111/j.1464-5491.2004.01183.x

2) Use of DAFNE in the UK

- a. Heath Technology Appraisal HTA 60. April 2003. Guidance on the use of patient-education models for diabetes: <http://www.nice.org.uk/nicemedia/live/11496/32610/32610.pdf>
- b. Quality Standard QS6: Diabetes in Adults. March 2011: <http://guidance.nice.org.uk/QS6>
- c. T1DM Patient Pathway:
<http://pathways.nice.org.uk/pathways/diabetes#path=view%3A/pathways/diabetes/managing-type-1-diabetes.xml&content=view-node%3Anodes-patient-education-models>
- d. NHS National Service Framework: Standards for Diabetes Care:
<http://www.nhs.uk/NHSEngland/NSF/Pages/Diabetes.aspx>
- e. Department of Health Quality and Productivity Proven Case Study. Improving the quality of care for patients with type 1 diabetes: Dose adjustment for normal eating (DAFNE):
<http://arms.evidence.nhs.uk/resources/qipp/899091/attachment>

3) Use of DAFNE overseas

- a. About OzDAFNE (from Diabetes Australia's Victoria branch):
<https://www.diabetesvic.org.au/type-1-diabetes/oz-dafne>
- b. IDF. Diabetes Voice 2011;56;19-28: https://www.idf.org/sites/default/files/attachments/DV_56-SI2.pdf

4) Continuous subcutaneous insulin infusion therapy: NICE

- a. NICE Health Technology Appraisal 151. July 2008. Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus:
<http://www.nice.org.uk/nicemedia/live/12014/41300/41300.pdf>
- b. Cummins E, et al. Clinical and cost-effectiveness of continuous subcutaneous infusion for diabetes: updating review. A technology assessment report commissioned by the HTA Programme on behalf of NICE: <http://www.nice.org.uk/nicemedia/live/11729/38223/38223.pdf>
- c. Cummins E, et al. Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: systematic review and economic evaluation. *Health Technol Assess* 2010;14(11): <http://www.hta.ac.uk/fullmono/mon1411.pdf>
- d. Insulin pump therapy service for people with diabetes. Commissioning Guide. February 2009: http://www.nice.org.uk/media/37C/67/290312_Insulin_Pumps_cmg_update_for_PDF.pdf
- e. Diabetes UK position statement on Insulin Pump Therapy. Sept 2011:
http://www.diabetes.org.uk/About_us/Position-statements--recommendations/Position-statements/Insulin_pump_therapy/

5) Further use of CSII

- a. NTAC 'How to, Why to guide':
<http://www.ntac.nhs.uk/HowToWhyToGuides/ContinuousSubcutaneousInsulinInfusion/Insulin-Infusion-Evidence-Base.aspx>
- b. NTAC report:
http://www.ntac.nhs.uk/web/FILES/InsulinInfusion/nhs__1276991568_FINAL_DATA_REPORT.pdf
- c. Audit of pump use:
http://www.diabetes.org.uk/Documents/News/The_United_Kingdom_Insulin_Pump_Audit_May_2013.pdf