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Evidence into practice: evaluating a child-centred intervention for diabetes medicine management (EPIC)

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Evidence into practice: evaluating a child-centred intervention for diabetes medicine management (EPIC)

Planned investigation
The EPIC project is funded by the NIHR-SDO programme and commenced in April 2008 for three years. The research team comprises of experts in the field of diabetes care and qualitative research, including researchers with clinical trials expertise from the North Wales Organisation for Randomized Trials in Health and Social Care (NWORTH). The project will be seeking the support from the Medicines for Children Research Network (MCRN) and also support from the Diabetes Research Network (DRN).

Existing research: Why the need for the study?
A requirement of participative models promoting health, self-care and medicines management is provision of information to assist patients' choices so that they may engage fully and knowledgably in decision-making, and be aware of risks and benefits of treatment (Committee on Safety of Medicines, 2005; Department of Health, 1998; Henwood et al., 2003). There is little reliable evidence concerning the effectiveness of different types of provision of information for children, young people and their carers. There is even less evidence about types/formats of information which could empower children/young people to make decisions/choices about aspects of their care, where appropriate (Joghlin & Law, 2005).

Policy makers identify a need for health and social services providers to increase capacity, confidence and efficacy of individuals for self-care and to build social capital in the community. The requirement for prevention, early intervention and support for individuals for self-care, and promoting wellbeing for the wider population is underlined (Bradlyn et al., 2003; Department of Health, 2006).

Children's information is likely to be critical to developing the notion of self-care and wellbeing as children's autonomy increases with age. Information needs and `informed choice' are central to the Children's NSF (Department of Health, 2006), which makes specific reference throughout the ten standards to the requirement to provide high quality, age-appropriate, child-centred information in varying formats, including a standard on children's medicines.

Progress has been made on a UK strategy for service delivery and organisation of medicines for children/young people to facilitate not only a measurable increase in appropriately labelled and formulated medicines and conduct of trials, but also information for prescribers, carers and children (Department of Health, 2004). One outcome is the setting-up of the Medicines for Children Research Network (MCRN) which is already supporting the EPIC project's foundational work (in the form of support to the Information Matters Project (IMP) being undertaken by the principal investigators). It is hoped that the EPIC project will similarly be adopted by the MCRN.

The need for child-centred, age-appropriate information on medicines management is highlighted when viewed against the broader NHS policy

context. Children's health policy is centred on the notion of 'family-centred' care with family (especially mothers) providing a large proportion of care, with children taking on more responsibility for their healthcare as they gain autonomy. Indeed, the Children's NSF model of children's acute and chronic disease management has incorporated the notion of educating children/young people in age-appropriate ways to deliver aspects of their own healthcare, and specifically identifies parents as experts (Department of Health, 2006). The shift in focus to homecare and community settings requires complex arrangements for medicines and treatments and greater support for parents and children/young people who are administering increasingly complex medicines (e.g. subcutaneous and intravenous regimes) at home (Department of Health, 2006). Information relating to safety and administration issues is urgently required to support the contemporary delivery of healthcare.

The informed use of unlicensed medicines and off-label usage of medicines for children/young people is unavoidable if they are to access the most effective medicines (Department of Health, 2006), however comprehensive accessible and timely information about both risk and benefit and decision support are imperative if children/young people are to be active partners in decision-making about healthcare choices. Information around risk is provided by professionals and increasingly by adult and child patients themselves. Quality information is regarded as central to participative models of health citizenship which have emerged (Department of Health, 1998; Department of Health, 2001). However, there is uncertainty about the positioning of children/young people and their families within these models and what practical plans and processes exist for their successful implementation. Children's information is likely to be crucial to developing the notion of self-care as children's autonomy increases with age.

The illness trajectories of many childhood conditions now extend into adulthood. There is little information available for young people and their families around transition between child and adult service provision (Allen/Gregory/Lowes on SDO-funded exploration of transition from child to adult diabetes services), with many young people seemingly unprepared to manage their own care and live independently. Available standard patient information is often of poor quality. It may be hard to understand, and not easily accessible for young people and their families (Committee on Safety of Medicines, 2005).

Policies need to be placed within the context of children/young peoples' lives, illnesses they experience and what best suits their needs. Long-term conditions such as diabetes are commonly treated with medicines and children/young people increasingly take responsibility for their regimes over time, especially during school hours. Children/young people need to be involved with their families/carers and professionals in decision-making about their care-management, including understanding risks and benefits, and specific instructions to ensure optimum effect. Research has been aimed at identifying aspects of structured education programmes, for example comparing their effectiveness (see www.mhra.gov.uk), developing innovative curricula (Northam et al., 2005), and exploring acceptability to adolescents

and their parents and eliciting ideas on how they would set about designing education sessions (Howe et al., 2005). There is also work on psycho-educational interventions (Waller et al., 2005).

While the research illuminates important aspects of a neglected area of investigation it is clear that structured education programmes for children/young people are based on programmes designed for adults, notably the dose adjustment for normal eating programme (DAFNE). The HTA brief (HTA Brief 06/44) states such programmes have been shown to be effective in adults, however a trial is necessary to establish if they have a role to play for children/young people. Our searches also suggest that high-quality, child-centred information underpins the achievement of optimal glycaemic control with the aim of minimising acute readmissions and reducing the risk of complications in later life (NICE, 2004). There is insufficient evidence about the effectiveness of information underpinning diabetes education for children and young people (Knowles et al., 2006; Hampson et al., 2001; Clyne et al., 2007). Likewise tailored, child-centred information could equip children/young people with the knowledge to become expert in diabetes care (NICE, 2004; Waller et al., 2005).

Research aims
The aim of the research is to develop and evaluate an individually-tailored, age-appropriate information pack to support decision-making and self-care relating to insulin management and electronic blood glucose monitoring for children/young people aged 6-18yrs with type 1 diabetes, compared with available resources (if any) in routine clinical practice.

Research objectives
- Review gold-standard clinical guidelines, currently available information including findings from completed Phase 1 of current SDO/145/2007 (The Information Matters Project) to identify best practice, and types/formats of information most likely to assist age-appropriate decision-making and choices concerning blood glucose monitoring and insulin management.
- Develop an age-appropriate child-centred information pack for children/young people, to support appropriate use of blood glucose meters to optimise management of and concordance with their insulin regime.
- Explore the utility of the resource within different contexts in which children/young people manage their routine diabetes care (home, school, community) with and without support from parents or healthcare professionals, and in alternative settings.
- Explore how children/young people with and without their parents, teachers, nurses, doctors use (or not) the information pack to support decision-making; in particular how children/parents 'self-prescribe' the correct (or incorrect) dose of insulin.
- Identify similarities and differences between the resource developed for adolescents and those available within adult diabetes services.
- Evaluate the resource within the context of routine diabetes care in relation to patient outcomes (diabetes-specific, health-related quality-of-life concordance, acceptability, ease of use, and glycaemic control).
- Identify gaps in knowledge.

Design
The investigation is a mixed-method study informed by the `Promoting Action on Research Implementation in Health Services' (PARIHS) framework which has been widely used to inform design and evaluation of evidence-into-practice initiatives. To meet our objectives which are aligned with the phases of the MRC framework for RCTs of complex interventions a four-stage study has been designed:

- Stage 1. Review and, where appropriate, undertake further work to identify types/formats of information most likely to assist age-appropriate decision-making/choices related to children/young people with type 1 diabetes.

- Stage 2. Construct an exemplar information pack, piloting for variations as necessary.

- Stage 3. Conduct a pragmatic evaluation to assess utility, acceptability effectiveness and cost effectiveness of the information pack.

- Stage 4. Undertake data synthesis and comparative analysis.

As the study is using a four-stage design, there will be a need to recruit children/young people aged 6 -18years with type 1 diabetes within two different stages of the project (stages 2 and 3). During stage 2 children/young people will be consulted during the process of developing the information pack. During stage 3 the resource will be used during the randomized control trial in order to establish how helpful and effective it is.

Conceptual and methodological frameworks
Using the MRC Framework for evaluating complex interventions we propose to develop and refine an individually tailored and child centred information pack concerning blood glucose monitoring and insulin management and carry out a pragmatic randomized controlled trial of the information intervention versus usual (routine) practice for children and young people aged 6 to 18 years with type 1 diabetes.

PARIHS framework
The Promoting Action on Research Implementation in Health Services (PARIHS) framework will be used as the framework for translation of evidence into practice evaluation (Kitson et al., 1998). The framework has been theoretically and empirically developed to represent the interplay and interdependence of the many factors influencing implementation of evidence into practice. This is explained by a function of the relation between evidence, context and facilitation (Rycroft-Malone et al., 2002; Rycroft-Malone et al., 2004; McCormack et al., 2002). The hypothesis offered is that for implementation of evidence to be successful there needs to be clarity about the nature of the evidence being used, the quality of context, and, the type of facilitation needed to ensure a successful process. The framework has been used by others to inform the design and evaluation of evidence into practice initiatives (Harvey et al., 2002; Sharp et al., 2004).

The PARIHS framework is particularly relevant to this study because:

1. It aims to introduce a new information pack (evidence) into children's self-care regime and healthcare practice in order to improve blood glucose meter use and insulin management. Understanding the factors that influence its implementation and use will be important in determining the acceptability and feasibility of the information pack (facilitation) - this framework will provide a conceptual guide for mapping these issues.

2. Understanding how the information pack is used in different contexts where children/young people manage their diabetes will be key in the evaluation of its utility and contribution. Applying the framework will allow a focus on the key contextual variables mediating the implementation and use of the information pack.

3. It facilitates the gathering of individual (e.g. child/ practitioner/ carer) experiences as well as appreciating the fit with the broader context of care delivery.

Methods: Plan of Investigation

Stage 1. Literature review

Systematic review of literature, policy, best practice clinical guidance and management plans Building on completed systematic review findings from SDO/145/2007 to inform the proposed work we will extend the scope to focus in-depth on childhood diabetes and health information resource development. The extended systematic review of published and grey literature concerning childhood diabetes will be undertaken to inform the subsequent development and evaluation of the exemplar information resource with children, families and healthcare professionals.

The review will be conducted according to established principles of literature reviewing and will be an iterative process. Policy and practice literature will span the last 10 years and effectiveness literature the last 15 years. The childhood diabetes-specific research questions to be addressed are: a) What ideas underpin current policy (eg `expert patients', 'partnership' and self-care) and how are children positioned within these policies? b) To what extent are children's and families' information needs made explicit in best practice, clinical guidance and pathways through care? c) How does information impact on children's decision-making and the appropriateness of actual choices made? d) What principles underpin best practice guidance concerning the development of age-appropriate health information resources for children?

Electronic health databases, including the Cochrane Trial Register and Library, Medline, Embase, Cinahl, Assia, Psychlit, and HMIC etc. will be used. Hand searching will supplement electronic searching. Additionally, our existing connections with, for example MCRN, leading children's and diabetes charities, RCN Children's Forums and Royal College of Paediatrics and Child Health will be utilised to uncover grey literature and knowledge embedded in practice. References will be recorded and managed in ENDNOTE. Key issues will be extracted and summarised to form the basis of the findings. Findings will be synthesised and themed within and across the research questions and will be used to map out the main issues.

Integration and extension of critical discourse analysis of currently available childhood-diabetes information sources.

We will use completed SDO/145/2007 critical discourse analysis findings to inform the current work and extend the scope to focus in-depth on childhood diabetes. We will explore management of childhood diabetes and focus on blood glucose monitoring and insulin management as a key exemplar concerning medicine management, self-care and concordance. We will also look specifically for similarities and differences in the discourses and philosophies underpinning children's/young peoples' and adult care pathways and management plans to see how and in what ways medicine

management and self-care discourses/philosophies change at key stages across the lifespan. Information sources across all mediums and sectors (eg. NHS, pharmaceutical) will be sought. This work will establish what sources of diabetes information are currently available to children/young people and their families. We would also wish to identify the underlying assumptions of the information sources and their main messages, and we will assess their applicability in terms of age, disability, ethnicity and gender, and for those children living away from their families. Analysis of the content will identify whether key messages match clinical guidance on childhood diabetes management. Synthesis of integrated and extended contextual data to inform development of exemplar information resource Systematic review, discourse analysis findings and current evidence will be integrated using evidence-based principles and methods developed for synthesising diverse study designs within systematic reviews for public policy.

Focusing on diabetes, we will devise matrices that juxtapose currently available information for children and their families, children's information needs as identified in their management plans and care pathways against the evidence concerning children's identified information needs and preferred information choices of children and their families, and benchmarked standards for the presentation of age-appropriate health messages to inform development of an exemplar information resource.

Stage 2. The information pack development
Evidence from stage 1 (literature review and discourse analysis) will be used as an empirical bases for developing the information pack. The information pack will be designed during the second phase of the study in conjunction with children/young people, parents, healthcare professionals, and a children's medical illustrator. Children/young people should be included in this research because the relevant knowledge cannot be gained through research with adults (MRC: Medical Research Involving Children, 2004).

Qualitative interviews and focus groups
To establish the context for the development of the information pack and subsequent trial, we will conduct approximately 20 interviews and 3 focus groups to ascertain children's views and experiences of managing their diabetes in everyday contexts, explore their information needs related to managing diabetes, and where appropriate seek their views on currently available information packs and how they and their families manage the child's diabetes within the context of the family and other locations such as school. We will also seek to interview children and young people with type 1 diabetes who live away from their families in the short, medium or long term. In addition, approximately 20 healthcare professionals (nurses/doctors/pharmacists) drawn from fieldwork sites will be interviewed regarding clinical care pathways for children with type 1 diabetes.

A variety of approaches will be used to identify, approach and recruit children, young people, parents and healthcare professionals to take part in the various stages of the study. We will register the study with the Medicines for Children Research Network and Diabetes Research Network in order to utilise the

additional resources and expertise in gaining access to study sites and facilitating recruitment of children.

Focus group recruitment
Focus group potential participants will be approached by local clinicians with the support of MCRN nurses who will send out or give out in person study information packs on our behalf. Children, young people and/or their parents will be asked to return a contact sheet and the research team will then make direct contact with the child and family. Children/young people will usually have a minimum of a week to decide whether they want to take part.

Focus group potential participants will be recruited once they have read the information sheet and given their informed consent to taking part. Consent for focus group participation will usually be obtained by a member of the research team and /or with support from the MCRN research support nurse prior to participation.

Interviews with children and young people recruitment
We will use the same approach as described for the focus groups above. Plus in addition – to recruit hard to reach children and young people who in particular have lived for short, medium or long periods of time away from their families we will use a press release. In the case of young offenders we will seek to recruit those who have previously experienced custody but are not currently in custody. We have produced a press release for distribution by the press office at Bangor and Cardiff Universities. It is hoped that different media outlets will pick up and print/highlight the research and that potential participants will choose to respond directly to the research team. The first point of contact is the Research officers. Once contact has been made – potential participants will be sent a study information pack. If they are willing to consent the Research officer will make the necessary arrangements within the lone worker policy to recruit them. Potential participants are likely to have a minimum of a week to decide if they want to take part.

Healthcare professionals: recruitment for 'current standard practice' interview
Healthcare professionals in participating sites will be given a study information pack via their manager or centre administrator (delivered by hand or left in their pigeon hole). Healthcare professionals are likely to be in regular contact, and working with MCRN support nurses and research officers who may approach and recruit the healthcare professionals in person. Healthcare professionals can also return a contact sheet and the research team will contact them in person to gain their informed consent and make the necessary arrangements to meet. Healthcare professionals will have a minimum of 24 hours to decide whether they want to be interviewed. Consent will usually be gained by a researcher, or MCRN nurse prior to interview.

Obtaining children and young people's perspectives on various iterations of the information pack
Although not technically a research procedure, we aim to contact children/young people within current Data Protection legislation through press releases (see sample press release in Appendix 1) and the Roche children's

database and through press releases. The Roche database contains 8000 children and their families who have signed up to receive regular information, and access the Roche website and associated functions (chat rooms etc) for children with type 1 diabetes. Permission for this to happen has already been granted by Mark Samuels at Roche. Roche will forward and/or display an advert (see sample advert in Appendix 2) to children/young people with type 1 diabetes via their own database and/or website and newsletters. The advert will guide children/young people to the EPIC Project website - www.epicproject.info and they will be asked their consent (and parent/guardian consent if under 16 years of age) to take part in web-based activities such as choosing which image they like best out of a selection and commenting on various iterations of the information pack.

If appropriate, children/young people contacted via the Roche database may also be asked if they would like to take part in a face to face interview (see above).

Stage 3. Trial platform to evaluate the information pack in routine practice

In an iterative approach, building on stages 1 and 2, we will fine-tune a pragmatic evaluation to test the information pack in routine clinical practice.

Methods

Sample size calculation and effect size

A systematic review provides sample size calculations for studies of educational interventions targeting psychological effects and glycaemic control (HbA1c) for children with diabetes (Hampson et al 2001). They calculated a total of 130 randomized subjects in order to detect a 0.5 (medium) psychological effect size, with a power of 80% at the 0.05 significance level (assuming equal assignment in the two arms). They report that the effect size for psychological outcomes is more predictable with a median and mean of 0.38 and 0.35 respectively .therefore we will aim to detect an effect size of 0.4.

Proposed sample size

Our target sample size is 252 children/young people with type 1 diabetes (this is allowing for a 10% drop out rate). We will employ a 2:1 randomization strategy and randomise 168 children/young people into the intervention arm and 84 children/young people into the no intervention arm, stratified by age, gender and length of time since diagnosis (<2years and >2years).

Site selection and preparation

Depending on the size of site and number of children/young people with diabetes type 1, we envisage up to 10 sites (depending on current NHS re-organisation and amalgamation of Trusts) will recruit children and young people. We will be guided by clinicians (Gregory/Lowes) and the MCRN network who have an overall view of available of sites for trials and will have an overall strategic role in supporting research teams to facilitate site and participant recruitment.

The information pack will be individually-tailored and introduced by nurses/doctors in children's diabetes clinics during routine visits, therefore we will hold a launch event and workshops to familiarise healthcare professionals with the information pack in each participating site.

Recruitment:
Where appropriate consultants, nurses, or MCRN nurses will send an information pack to a child/young person attending a clinic visit one week prior to the clinical visit. During the consultation at the clinic, the consultant/nurse/MCRN nurse will ask them if they want to take part in the study. If the child/young person agrees to take part in the study, the consultant/nurse/MCRN nurse will take the consent.

Randomisation: Children age 6-18 years fulfilling the inclusion criteria and for whom appropriate consent(s) (proxy if appropriate) are obtained will be randomized using an independent web based randomisation service (NWORTH). 168 children/young people will be randomized into the intervention arm and 84 children /young people into the no intervention arm, stratified by gender, length of time since diagnosis (<2years and >2years) and age (stratification by age will be into the following age categories: 6-10; 11-15; and 16-18).

Inclusion criteria: Children age 6-18 years with type 1 diabetes.

EPIC Project exclusion criteria:

Exclusion Criteria for children / young people with:

1. needle phobia,

2. any significant social or emotional problems where such problems in the opinion of the clinical team are likely to impair a child's ability to take part in the trial,

3. any significant physical or intellectual impairment which in the opinion of the clinical team is likely to impair a child's ability to take part in the trial.,

4. an inability to communicate in an age appropriate way in written and spoken English

Children / young people should be entered into the trial where at all possible and should only be excluded if being in the trial would be detrimental to their social, emotional or physical health.

Planned interventions
Group 1 - Information intervention
The information pack will be individually-tailored and introduced by nurses/doctors in children's diabetes clinics during routine visits by children/young people between the ages of 6-18 years with type 1 diabetes.

Where appropriate parents will be provided with verbal and written guidance on supporting their child's use of the information pack.

Group 2 - Standard practice
Children age 6-18 years with type 1 diabetes receiving standard practice will be the practice as usual group. They will not receive the individually tailored information intervention. A manual of standard practice for each centre will be produced. This will help with the comparisons of outcomes at the end of the trial.

Data collection
Trial outcomes
Children/young people (if appropriate with support of, or proxy report by parents) will complete a baseline questionnaire recording sociodemographic variables, patient characteristics, and PedsQL (generic, diabetes and parent versions). The EQ-5D will be completed by parents (as a proxy measure) as well as the child/young person.

Follow-up questionnaires, focusing on process and outcomes will be administered at 3 months and 6 months (including data on health service use, episodes of diabetic ketoacidosis, and all hospital admissions for acute complications). Non-responders will receive telephone/postal reminders after two and four weeks.

Baseline and subsequent HbA1c measurements, blood glucose meter use, readings and insulin dose will be taken from routine test results and hand-held records when attending routine 3-4 monthly clinic visits. Routine test results will be collected by the clinicians/diabetes nurse specialists/MCRN nurses, or researchers where appropriate. Blood glucose meters will be checked for the previous 250 blood glucose records if considered appropriate by the clinician and if used as part of routine clinical practice.

Service utilisation and costs
Economic Evaluation
Murphy et al., (2006) strongly recommend that cost-effectiveness is considered as an outcome as none of the studies in their review of psycho-educational interventions with adolescents addressed it. We will therefore weigh up the costs and consequences of the different interventions (that involve resource use) from an NHS perspective.

Collection of service use and costs

All children/young people (with parents as appropriate) involved in the clinical trial will complete the Client Service Receipt Inventory (CSRI).
CSRI for diabetes (by proxy by parent, if appropriate).The CSRI will be adapted to record additional service use not already contained in the outcome questionnaire (Centre fro Reviews and Dissemination, 2002; Oliver et al., 2005). The CSRI for type 1 diabetes will be based on the prior work of Beecham, 1995 and Noyes et al., 2006). Contacts with NHS services will be

collected. Costs will be obtained from national sources. Activity will be collected for 6 months.

Process evaluation
Qualitative data
Interviews with children and their families
Following the intervention, sixty children/young people will be interviewed (40 from the intervention group and 20 from the control group) in order to gain further understanding about the usefulness of the new information pack/usefulness of materials used in existing routine practice.

Healthcare professionals' questionnaire
Healthcare professionals associated with the care of children/young people recruited to the trial will also be invited to complete a semi-structured questionnaire to determine acceptability and impact of the new information pack in practice.

Proposed outcome measures
Primary outcome measures
Choice of outcomes is guided by HTA commissioned systematic reviews recommending that HbA1c (glycaemic control measure) is not the appropriate primary outcome on which to assess benefits of an intervention designed to more directly effect behaviour/self-management. Therefore, the primary outcome
measure is diabetes self-efficacy and quality-of-life (Diabetes PedsQL).

Secondary outcome measures
Secondary outcomes include: HbA1c, generic quality of life, routinely collected NHS/child-held data, costs, service use, acceptability/utility.

Data handling
SPSS and Atlas Ti will be used for qualitative and healthcare professional questionnaire data handling.

Trial data management
Where feasible, we plan to use an electronic system (TrialSys®) in each centre to collect initial information prior to randomisation. Anonymised Data will be transmitted electronically and securely from each centre to the trial support unit (NWORTH). In sites where it is not practical or feasible to use TrialSys®, we will collect the same information prior to randomisation on a paper form.

Data analysis

Statistical analysis
Initial descriptive statistics will analyse characteristics and demographics of the sample at baseline. We shall compare outcomes between the two groups by analysis of covariance to adjust for possible differences in baseline measurements. This will be repeated at 3 and 6 months comparing

intervention and control groups. In addition, longitudinal analysis will consider any changes over time. These analyses will examine changes in the quality of life measures (paediatric EQ-5D, PedsQL generic and diabetes-specific health measures)
over baseline, both using a pairwise comparison, studying change on individuals, and a cohort analysis comparing overall change in group means.

Multiple regression analyses will be performed to identify factors which predict good outcomes within and between groups.

Cost effectiveness analysis
We will undertake a cost-utility analysis, whereby costs are in monetary terms and outcomes are in preference-based non-monetary units such as Quality Adjusted Life Years (QALYs). The area under the curve method will be used for calculating QALYs weighting survival by quality of life weights measured using the paediatric EQ-5D instrument. We will compare our findings with the unofficial NICE ceiling of £30,000 per QALY. Discounting will not be necessary given the time period.

Uncertainty
The bootstrap calculation is a useful statistical approach for examining the uncertainty in cost-effectiveness analysis. It is a non-parametric simulation method used when the underlying data has a skewed distribution. The bootstrap method can be used to provide an estimate of the probability distribution of the cost-effectiveness ratio, its confidence interval, or variance in the ratio.

Qualitative data analysis
Focus groups and interviews will be tape recorded and transcribed. Those undertaken to refine the information pack will feedback findings into the development process. The process analysis accompanying the subsequent evaluation will compare the experience of managing diabetes and insulin management and self-care processes between the intervention and control pathways. The predominantly deductive 'framework approach' will be used to categorise qualitative data based on the literature, the trial design, and the evaluation focus (Ritchie & Spencer, 1995).

Healthcare professional questionnaires
For the healthcare professionals' questionnaire, data will be analysed using descriptive statistics and open ended questions that will be subject to content analysis.

Stage 4. Data synthesis and comparative analysis
Data from stages 1 to 3 will be synthesised and subject to comparative analysis.

Ethical arrangements

Risks and anticipated benefits for trial participants

We are aware of the risk management and clinical governance procedures when developing individually-tailored information of this type. The research carries minimal risk and therefore is considered ethical according to the MRC Ethics Guide: Medical Research Involving Children (2004).

We will develop a specific clinical governance and risk management framework with clinicians (Lewis/Lowes/Gregory) to quality assure procedures and mitigate the risk of a child being given incorrect information.

Benefits

Children/young people with type 1 diabetes receiving the information pack developed for the EPIC project may benefit from receiving clear and concise information about how to monitor their blood glucose and manage their insulin intake. The children/young people in the control condition - practice as usual - will not benefit in the same way as they will not receive the individually tailored information pack.

Consent

Participants will be children/young people between the ages of 6 to 18 years. Children over the age of 16 can provide their own consent, however consent by proxy (from a parent or guardian) will have to be obtained for children under the age of 16 years. In seeking consent, we will follow current guidance from:

- 'Guidance on Patient Information Sheets and Consent Forms Version 3.2 May 2007 (NRES)'.
- Guidance from the Medicines for Children Research Network (MCRN)
- Guidance from the Diabetes Research Network (DRN)

Several types of consent forms and information sheets have to be considered and these have been created for the various aspects of the EPIC Project, including:

- *Consent forms and information sheets for parents and children for the different iterations of the information pack*
- *Consent forms and information sheets for parents and children for the information pack development interviews*
- *Consent forms and information sheets for parents and children for the information pack focus groups*
- *Consent forms and information sheets for parents and children for the randomized clinical trial of the new information pack*

Retention of trial documentation
It is planned that anonymised data will be kept securely for a period of ten years following the completion of the trial, subject to discussion with relevant Ethics Committees.

Retention of non-trial (information pack development) data
It is planned that anonymised data will be kept securely for a period of ten years following the completion of the project, subject to discussion with relevant Ethics Committees.

Confidentiality
Only members of the research team, study advisors, and relevant NWORTH staff will have access to the original data. Participants' personal details will be stored separately from the data, and will be kept in a separate file on a password protected computer at the Universities of Cardiff and Bangor. Each participant will be assigned an identification code, which will be used in all data storage files; these will not contain names or any other means of personal identification. All personal details will be deleted on completion of the study.

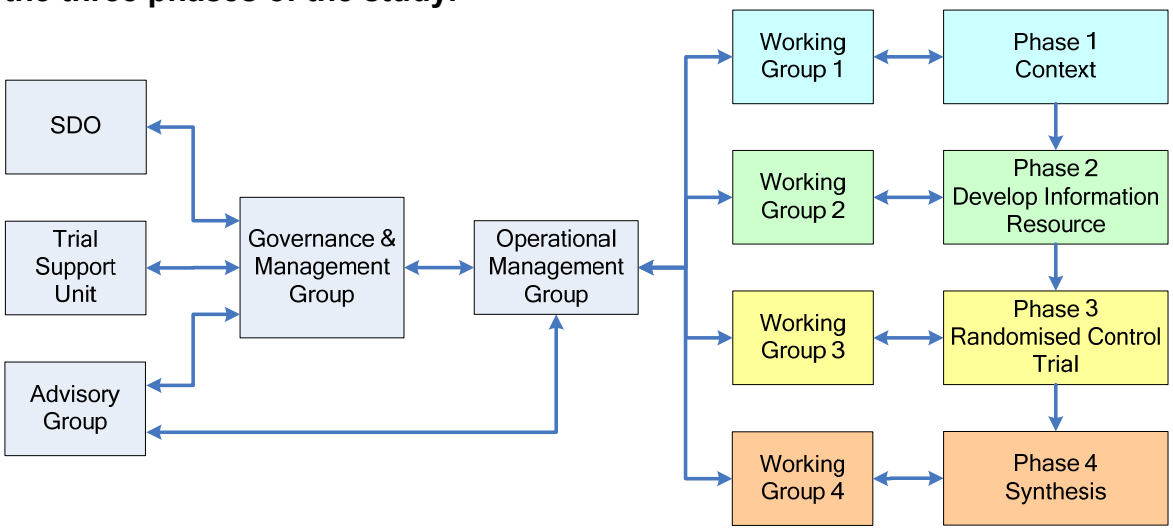
Management and research governance framework
The trial is sponsored by Bangor University, Sponsorship letter dated 22nd September 2008 (see Appendix 4).

The trial has been registered with ISRCTN: ISRCTN17551624. Registration with an ISRCTN allows trials to:

- Comply with international guidelines from the WHO, ICMJE and CONSORT organization
- Keep details of the research up-to-date: ISRCTN records can be freely updated on request, making sure they are not missed out by systematic reviewers
- Link trials to their results: Trial IDs can be quoted in article abstracts and indexed by PubMed, allowing publications to link back to their initial registration
- Maximise exposure for the research: ISRCTN content is fully and openly accessible and feeds automatically into the WHO international trial search platform.

Team management
Drawing on team members' experiences of managing teams, we have constructed a management and research governance framework to support the four phases of our study (1. context: review literature and current information 2. develop information pack, 3. randomized controlled trial, 4. synthesis), and to ensure cohesive and effective working between team members (see Figure 1). The framework is designed to maximise best utilisation of team members' skills in supporting the PIs and RAs and to facilitate timely delivery of reports to the SDO commissioners. Crucial elements to the framework's smooth operation are a) key groupings and b) processes for working together, as identified below.

Figure 1. Management and research governance framework to support the three phases of the study.



Key Groups

Group tasked with overall responsibility and governance (`Governance and Management Group')

Management and research governance will be overseen by a group composed of the co-applicants named on the bid, led by Anne Williams and Jane Noyes. Co-applicants were chosen to support this application on the basis that they each have established reputations in fields and expertise most relevant to the proposed research, including: systematic review skills, research skills, Trials expertise, experience of user groups/working with users, clinical expertise, policy knowledge, services planning and development, management and delivery, multi-agency/ disciplinary partnerships, networking and dissemination skills. In addition, co-applicants have specialist roles within relevant clinical research thematic networks (Brocklehurst, Gregory, Noyes) and professional bodies (Gregory, Jackson, Lewis, Noyes, Williams).

All co-applicants are experienced and effective communicators in their capacity as researchers, clinicians and managers. The majority of us have collaborated previously or are currently collaborating on other projects. While we each bring different discipline and professional perspectives to bear on the objectives we have set, we intend to promote team values with an inclusive approach where differing opinions are respected. Many of us have developed considerable confidence as team leaders in multi disciplinary/ multi agency settings. *The Governance and Management Group* will normally meet face-to-face twice a year, and will report to the SDO. Additionally, teleconference meetings will be called if required.

Group tasked with day-to-day management (Operational Management Group)

Day-to-day management of operational aspects of the programme will be the responsibility of the two PIs working with the two RAs employed for the duration of the study. Anne Williams will work with one RA based in Cardiff, meeting face-to-face on a weekly basis and Jane Noyes with one RA based in Bangor, also meeting face-to-face weekly. This core group of four researchers will be in close contact with each other via a secure web site and will meet

through video link/ teleconference at least every 2 weeks during the 36 months of the programme. They will meet face to face in the early stages to establish working relationships. Our experience suggests this increases effectiveness and efficiency. They will also be in contact with members of the *Working Groups*, *Governance and Management Group* and *Advisory Group* as detailed in the section `Working together effectively' below. Management of information will be critical to the day-to-day management of the study; common data bases and resources will be set up and maintained between Bangor and Cardiff in conjunction with the secure website. The precise division of labour between RAs will be agreed at the outset of the study depending on their particular skills.

Trial Management
Working group three in Figure 1 (above) has been convened as a Trial Management Group, Chaired by Lesley Lowes (co-applicant) that meets monthly by teleconference. Membership includes PIs (Noyes, Williams), ROs (Edwards, Spencer), trial statistician (Whitaker), and health economists (Tudor Edwards, Houndsome).

Trial Steering Group
A trial steering group (TSG) has been convened under the independent Chairmanship of Professor Tim Barrett. The TSG includes clinical, academic, parent and young person representation and will meet every six months in person and every six months by telephone conference.

Data Monitoring and Ethics Committee
An independent data monitoring and ethics committee (DMEC) has been convened and chaired by Dr Chris Foy (independent statistician), who will report to Professor Tim Barrett (Chair TSG). The DMEC will have 3 members (Chair, clinician, diabetes nurse). The DMEC will meet face to face every six months and virtually every six months prior to the TSG meeting.

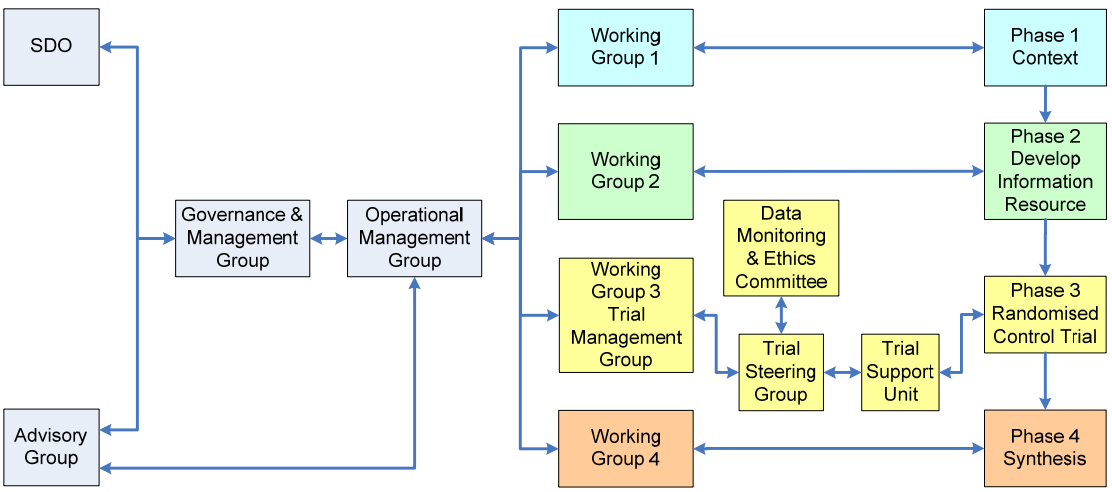


Figure 2. Trial governance and management arrangements.

Advisory Group
As we note in the proposal, we wish to involve at various stages of the study those from groups we have already consulted in preparing the research proposal - parents, children, young people - and others such as clinicians, managers and voluntary sector representatives. A number are working with us on SDO145/2007. The group will advise the *Governance and Management Group* on the overall conduct and relevance of the research and the *Operational Management Group* on implementing the research plan.

The Advisory Group will therefore be drawn from stakeholders with knowledge and experience relevant to the aims of the project. Previous experience of this type of research by the co-applicants suggests that collaboration, communication and transparency with key stakeholders from the outset will be crucial to the success of the proposed study. The *Advisory Group* will be kept informed of the progress of the project through regular electronic and paper dissemination processes and will, themselves, input information via a variety of media including email and the secure web-site (used successfully in other projects). The group will normally meet face-to-face twice a year, on occasion in conjunction with the *Governance and Management Group*.

The *Trial Support Unit* (North Wales Organisation for Randomized Trials in Health and Social Care; Director Russell – Co-applicant, Whitaker) will administer the trial and provide independent scrutiny.

Good clinical practice training of core research team
Good clinical practice training will be completed on 10th November 2008 at University Hospital Wales, Cardiff, organised by Cardiff and Vale NHS Trust Research and Development Office (see Appendix 5 for the good clinical practice training template).

Working together effectively
Based on previous experience and current models of good practice employed on projects by the co-applicants, we will set up **Working Groups**. These will give clarity to the roles and responsibilities of the co-applicants who have been costed into the price of the proposed research. They are planned to provide particular advice and guidance to the PIs and RAs in each phase of the study: 1. context: review of literature and current information 2. Development of the information pack, 3.randomized controlled trial, 4. Synthesis. Guidance will be related to varying aspects such as range of policy, best clinical practice, child/ user-friendly construction of question sheets and so on. Guidance on dissemination of findings will be a key aspect of their role. Individual members of the *Governance and Management Group* will lead activity in the working groups, working closely with the *Operational Management Group*. *Advisory Group* members will be called on for specific

expertise, including dissemination skills. Each working group will report to the *Governance and Management Group* via the *Operational Management Group.*

Working group	**Working Group members - Indicative**
1. Context: review literature and current information	Allen, Carter, Lewis, Lowes, Jackson, PIs and RAs.
2. Develop Information pack	Carter, Sharp, Gregory, Samuels, Lewis, Jackson, Rycroft Malone PIs and RAs.
3. Randomized Controlled Trial Now convened as the Trial Management Group – see section on Trial Management above.	Russell (with Whitaker and Trial Unit), Brocklehurst, Gregory, Lowes, Tudor-Edwards, PIs and RAs.
4. Synthesis	Core group with full team

The communication processes we have described will also allow for the sharing of knowledge and concerns about how the project is progressing and thus expedite timely intervention where there is anxiety that things may not be going ahead as planned. This in turn will alert the *Governance and Management Group* of individual performance, quality and organisational issues that could potentially undermine efficient working and quality of output. The proposed management and research governance framework will also allow for the support and development of people working on the project including junior colleagues, adopting a model of action learning and peer support/ supervision. We will review the framework at *Governance and Management Group* meetings to ensure it is working effectively and facilitating the delivery of high quality research outputs.

Project timetable and milestones

The project timetable and milestones are set out in Table 1.

Table 1 Project timetable and milestone

Stage	Activity
Stage 1 – April to October 2008	Project commences. Recruitment of Research officers. MREC approval and Initial Research Network approvals sought. Review literature. Review other existing information for children and their families.
Stage 2 – November 2008 to May 2009	Develop an age-appropriate information pack. We will ask children/young people, key family members and healthcare professionals to help us develop this information pack. Children will be recruited through the Roche database and possibly through Diabetes UK. Healthcare professionals will be recruited through the MCRNs and NHS Trusts. Conduct 3 focus groups with children/young people with diabetes.
Stage 3 –June 2009 – March 2012	Test the resource to establish how helpful and effective it is. 168 children/young people with diabetes will receive the information intervention; 84 children/young people with diabetes will receive routine care. Resource use will be collected from all children and where appropriate their parents for the economic analysis (self complete questionnaire and telephone follow up if appropriate). Interviews with 60 children and were appropriate their parents (40:20 intervention/control) will be conducted as part of the process evaluation. Semi-structured interviews with the healthcare professionals involved in the trial will be conducted (see Appendix 7 for flow chart)
Stage 4 – July 2011 – June 2012	Synthesise and comparative analysis. Subsequently report findings and make widely available. We will publish papers and organise a conference emphasising everyone's perspectives. This will ensure maximum impact of our findings amongst health service users, practitioners, managers and policy makers.
June 2012	Submission of the final report.

Expertise

Anne Williams and Jane Noyes (joint-PIs) have track-records in managing research programmes in patient/carer-centred service delivery and organisation, and health economics (Noyes). As joint PIs for SDO/145/2007, they have in place an operational management and research governance strategy, approved by the SDO, which they will extend to the proposed study to ensure the safe delivery of outputs.

Team-members with relevant skills and expertise are drawn from previous successful collaborations:

Peter Brocklehurst, as Chair of the Methodology Clinical Studies Group of MCRN will act as formal link between the research team and MCRN and facilitate additional links with the MCRN Endocrinology Clinical Studies Group. As an experienced Trial researcher, Brocklehurst will provide additional input and scrutiny into the running of the trial and data monitoring.

The study demands applied clinical expertise and research. **John Gregory** (Paediatric Endocrinology) and **Lesley Lowes** (Paediatric Diabetic Specialist Nurse) have a joint-research programme into delivering children's diabetes care.

As an academic clinician managing a caseload of children with diabetes, **John Gregory** will help facilitate recruitment and support the development of a robust risk management framework for the use of the information pack in practice. As an experienced Trial researcher, Gregory will provide additional input and scrutiny into the running of the trial and data monitoring. He will also provide cross-linking with another trial on which he is principal investigator into adolescent diabetes care, thereby adding value by sharing best practice and findings. Gregory through his membership of British Society of Paediatric Endocrinology has strong links with the MCRN Endocrinology Clinical Studies Group and will facilitate communication on behalf of the study. He also has links with the Diabetes Research Network.

As diabetes nurse specialist and academic, **Lesley Lowes** will provide advice on clinical governance issues and support the development of a robust risk management framework for the use of the information pack in practice.

Carol Jackson is a children’s pharmacist and will advise on current policy and practice in relation to administration of children’s medicines and the children’s BNF. She will advise and support on the development of appropriate risk management procedures with specific reference to medicines, and support the facilitation of translation of the information pack into practice with reference to pharmacy professionals.

Ian Russell is non executive director of the North Wales Clinical Trials Unit which will coordinate trial management and scrutiny. Russell will also oversee statistical aspects. He is also Professor of Clinical Trials, Centre for Health Information Research & Evaluation, Swansea University School of Medicine.

Rhiannon Whitaker is trials unit assistant director (NWORTH) and research statistician. The Trials Unit will develop randomisation procedures and provide an independent randomisation service, advise on data base development, data storage, and provide data as requested by the data monitoring and ethics committee.

Davina Allen's expertise in policy and research concerning transition from child to adult. Her extensive work on policy analysis from a sociological perspective and her depth understanding of theories informing current policy supports her role in advising on these matters in relation to children and young people with type 1 diabetes.

Cynthia Carter (specialist in children, communication and media) will advise on the development of the information pack in terms of content and intellectual structure from a media perspective.

As a member of the Wales Health Economics Group, **Rhiannon Tudor-Edwards** brings key expertise to the study. She will have overall responsibility for the health economics component of the trial.

Translating evidence into practice is critical to the research plan. **Joanne Rycroft-Malone** has extensive experience in knowledge translation and utilisation, and will guide translation of theoretical concepts and findings from SDO/145/2007 to practical application and evaluation in the current study.

As a children's researcher, lead nurse and clinical quality lead in a paediatric clinical trial, **Mary Lewis** will provide advice on clinical governance issues and support the development of a robust risk management framework for the use of the information pack in routine practice.

Mark Samuels (Roche) acting within the data protection act and Roche's Code of Business and Ethics will facilitate access to a database of 8000 children and young people using blood glucose monitors in the UK from which we will recruit to consult with in developing the proposed information pack. This data base will not be used in the pragmatic trial.

Jan Sharpe, a children's medical illustrator, will produce illustrations and support the design of the information pack.

Llinos Spencer, is a Researcher Officer on the EPIC Project, based at Bangor University, and is also the Data Manager for the EPIC randomised controlled trial. She will perform most of the data analysis under the supervision of Rhiannon Whitaker, research statistician.

Deborah Edwards is a Researcher Officer on the EPIC Project, based at Cardiff University, and is also the Trial Manager for the EPIC randomised controlled trial. She will perform trial management duties such as creating the step-by-step guide for the randomised controlled trial and maintaining the master trial files.

Service users
The research will produce findings to facilitate translation of information into practice for children/young people with type 1 diabetes, producing generalisable findings relating to other long-term conditions. Manufacturers' adult-orientated instructions for blood glucose monitors and the NICE guidelines on glycaemic and insulin management will be redesigned and individually-tailored in a child/young person-orientated way to support self-care choices, concordance with medication, correct insulin dose calculation and optimise prevention of long-term complications (4). Children will be consulted at all stages.

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