Final Report of the Paediatric Metabolic Sub-group for Children and Young People's Health Support Group

A review of health services for children with inherited metabolic disease

Paediatric Metabolic Review Group
June 2006

Table of contents ***Page No.***

Appendices

Executive Summary

Patients with inherited metabolic disease require rapid diagnosis, expert management and ongoing care for a lifelong condition. The UK review recommended that a critical mass of tertiary consultants should provide this expertise in conjunction with local teams.

In Scotland, it is estimated that there will be 10-20 new paediatric cases per year. The prevalence and survival data are poor but an estimate from the Glasgow clinic population indicates a twenty five percent survival rate. This equates to approximately 5 new cases annually transferring into adult services. (Adult services were not considered by the subgroup but anecdotal evidence suggests that many adults are still attending paediatric units, as there are no established services for adults in some areas). Patients can be managed locally in outpatient settings with access to local multidisciplinary teams (MDT). However rapid access to inpatient care and assessment is also necessary especially in newly diagnosed cases or those with acute crisis.

Therefore the service model of local expert MDT with back up from a core group of expert clinicians working across Scotland is recommended to ensure that all children receive high quality assessment and management on a 24 hour basis. An option to achieve this was selected and should be implemented.

The recommendations of the report include:

- A core group of experts should link with local expert MDT. The preferred option will achieve this and should be implemented.

- A managed clinical network should be commissioned nationally to educate clinicians in detection and management of these rare conditions and develop standards of care and clinical pathways. A database should be implemented to identify children and adults with IMD and measure outcomes.

- There should be close working and collaboration between Universities and the NHS to aid research and training in this important area.

- Each health board/region should examine adult services to determine if they are equipped to handle adults with IMD. Transition arrangements should also be put in place.

- In addition, a representative from the NHS Scotland should work with the proposed UK advisory group to maintain an overview and guide strategy implementation.

Background

In 2004, a group of metabolic clinicians submitted a paper on paediatric metabolic services in Scotland to the Scottish Executive Health Department (SEHD). The paper highlighted a number of issues that the paediatric metabolic service in Scotland faced together with suggested ways to tackle these issues. [(1)] NSD was asked by SEHD to examine some of the points raised in the paper. Therefore in May 2005, NSD met with the clinicians to discuss possible ways to resolve these. However it became clear that the problems were regional and national and that there was a lack of consensus about some aspects of the service model. The SEHD, Child and Young People's Health Support Group (CYPHSG) had already identified paediatric metabolic services as a candidate for review in January 2006. However it was decided at the July 2005 meeting to bring forward the review and consider regional and national issues in this review.

Stakeholders were invited to attend a meeting in December 2005 to detail the main issues for their services and discuss possible options to address the problems faced by the service at a regional and national level (**Appendix A** details the subgroup membership)

In parallel with the work in Scotland, a UK wide review of metabolic services started in June 2005. Dr Hilary Burton of the Public Health Research Unit in Cambridge led this review and the report was published in November 2005. [(2)]

A progress report was written by the paediatric subgroup for the meeting of the CYPHSG on 26th of January 2006. A subsequent meeting of the subgroup in February and March 2006 led to an option appraisal and final recommendations. This report will draw together the work and present the final conclusions of the paediatric metabolic subgroup.

Part one of the report will detail:

1. Epidemiology

2. National UK report summary
    a. Areas under consideration
    b. Results
    c. Recommendations

3. Current service issues for Scotland
    a. General Categories
    b. Structure of the services
    c. Issues raised by clinical teams
    d. Screening issues

4. Classification of the workload
    a. Subgroups
    b. PICU
    c. University and research

5. Conclusions

Part two of the report will describe:

1a. Managed Clinical Network
1b. Options to improve service delivery
1c. Option appraisal process
1d. Option Appraisal results
1e. Costs

Part three of the report details conclusions and recommendations.

1. Epidemiology

Inherited Metabolic Disease (IMD) is a diverse group of over 500 conditions with varying presenting features. They can cause multiorgan disease with severe physical and mental impairment and death in childhood or early adulthood. They are individually rare but collectively quite common. The literature suggests that IMD occur in 1 in 2,500 to 5,000 live births. [(2)] This would equate to a figure of between 10-20 new cases per year in Scotland. (Based on 51, 803 births for year ending March 2004, ISD figures). Many of these conditions require lifelong monitoring and management. This has significant implications for adult services. However the prevalence and survival data for adults and children is poor. One Italian study estimated that 11% of patients with IMD survive into adulthood. [(2)] However this is thought to be a minimum estimate as it is expected to increase with newborn screening programmes and improved management. [(2)] The Glasgow clinic population data indicate a survival in the range of 25% (personal communication Dr Peter Galloway). Using the incidence figure of 1 in 2,500 births and survival figure of 25% this equates to 5 new cases per year transferring to the adult service.

Over the past few years there have been advances in biochemistry, genetics and improved clinical management. For example the newborn screening programme already offers highly effective screening for PKU, which benefits from early effective dietary intervention. All these factors have increased the need for patients to have access to specialist teams with experience in managing these conditions.

The commonest conditions are phenyketonuria PKU, medium chain acyl CoA dehydrogenase (MCADD) and Lysosomal Storage Disorders (LSDs). A group of highly expensive drugs have been developed to treat some of the LSD. The cost of these drugs has recently been the focus of much debate and a formalised risk share among Scottish NHS Boards. [(3)]

2. UK review of Metabolic Services

The British Inherited Metabolic Disease Group (BIMDG) highlighted their concerns about the ability of services across the UK to meet the needs of patients with IMD and their families. This led to a review by Dr Hilary Burton of the Public Health Genetics team in Cambridge and financially supported by the Department of Health. Scotland was also invited to take part through Dr Ros Skinner and questionnaires were sent to all the lead clinicians in Scotland for completion.

2a) The areas that the UK review examined included:

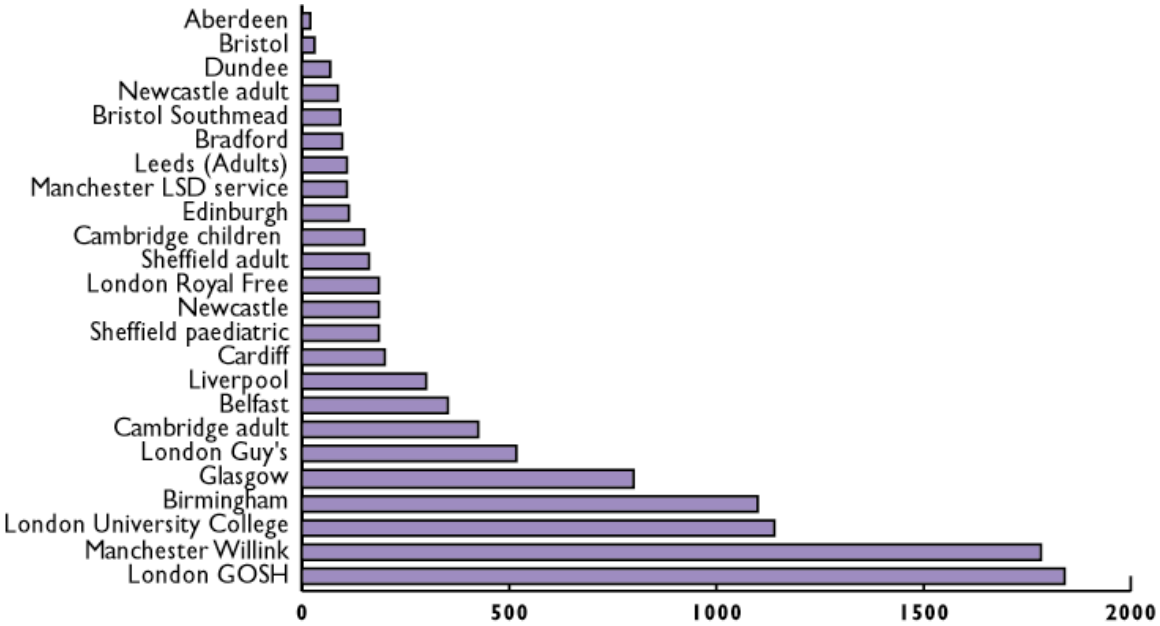
1. Where are the teams?
2. Do they have comprehensive clinical teams?
3. Clinical provision in relation to population size
4. Critical mass of patients
5. Importance of laboratory services

2b) The key findings showed:

- Effectiveness: estimated 9,000 patients in the UK are not in specialist care
- Efficiency: services were too thinly spread with a lack of critical mass
- Accessibility: long distances with no shared care
- Equity: geographical, disease and age related inequalities
- Relevance: services had not been properly planned
- Acceptability: services thought to be deficient by patients and professionals; no formal education for nurses and dietitians; emergency care on goodwill basis; 831 adults attending children's clinics

The figure below details the number of patient attending the services across the UK and is taken from the Nov 2005 UK report. [(2)]

Figure One Critical Mass: Implications for clinical governance



** Glasgow figures represent total number on the database for the service. Actual Number attending the service is 324.*

2c) Recommendations

The review offered the following recommendations:

- A UK wide formal strategic advisory group to maintain an overview and guide strategy implementation

- Formal and explicit commissioning arrangements for IMD that reflect the need to generate critical mass of patients to support comprehensive service provision balanced with reasonable geographical accessibility

- Reconfiguration of specialist clinical services through development of networks that ensure: access to a complete clinical team including doctors, nurses, dietitians and where possible, psychologists, emergency cover on a 24 hour basis; formal arrangements with other supporting specialties; and longer term robustness and continuity.

- Development by networks of formal supporting arrangements on a regional basis, including as appropriate outreach, shared care, education and support for other health professionals.

- Continued strengthening of the biochemical laboratory services, maintaining integration with clinical services and with molecular and cytogenetic laboratories and including training and manpower, provision of equipment, and safeguarding of highly specialist tests

- Robust manpower planning, resources and development for formal training for all involved specialties on a UK wide basis. Development of courses in IMD at Masters level for dietitians and nurses

- Support and close work with voluntary groups to assist them in providing information about specialist services to their members and participate in education for health professionals and patients.

3. Current services in Scotland

The next section will focus on the professional viewpoint of the services available in Aberdeen, Dundee, Edinburgh and Glasgow. It will highlight areas that work well and gaps. Most of the comments were taken from the meeting of 9th of December. Some comments are from May 2005 meeting and from the lead clinicians' paper submitted to the SEHD. Many of the findings and conclusions mirror those found in the UK review. There are, however, areas that require further discussion.

3a) General Categories

The clinical teams were asked to categorise the key patient groups. All agreed with the following broad categories of patients that comprise the workload for paediatrics:

Category A. Outpatient Care

- Children (and adults) with PKU – this is a large group, which can be managed by specialist dietitians with input from the consultant when required and is very amenable to protocol-driven care.
- Outpatients with other rare disorders

Category B. Degenerative disorders –children with progressive loss of skills, e.g. neurodevelopmental problems and cardiac problems

Category C. Urgent IP care – NICU/HDU and IP care
Many of the clinical teams represented had generic and personalised protocol-based care in place. Many children can be managed appropriately in HDU care

Category D. PICU care – this is only available in Glasgow and Edinburgh

The bulk of the workload is in categories A-C of this grouping.

An example of the case mix was given in the Edinburgh lead clinician's paper where the current caseload comprises:

- 44 patients with PKU
- 10 patients with fatty acid oxidation
- 6 patients with galactosaemia
- 55 patients with various other rare inborn errors of metabolism
- There are about 10-20 admissions per year of patients with known conditions and 3-6 referrals from ITU.

The broad categories for adults were summarised as:

1. PKU, Galactosemias etc
2. Acute care with decompensation requiring possible admission to adult ITU
3. Complex cases – e.g. LSDs

There are clinical services in Glasgow and in Aberdeen for adults with IMD but in many other areas in Scotland there is only paediatric care available. Many IMD patients require long-term care. A case study in the UK report showed that good dietary advice and compliance for a pregnant woman with PKU lead to the delivery of a healthy child while a similar patient lost to follow up and subsequent poor dietary compliance had a severely handicapped child. [(2)]

3b) Structure of the services

The clinical teams described the structure of the hospital services in each city. Table 1 summarises some of the key features of each service.

Table 1 – Structure of Paediatric (& Adult) Metabolic Services in Scotland

Centre (& referring areas)	Availability of Consultant paeds	Availability of Dietitians	Availability of Adult services	PICU, HDU and NICU	Other Features
Aberdeen Grampian/ Northern Isles	Yes, though will retire Sept 06. Succession plan to take over the service with gastro consultant with biochemistry degree is currently under discussion.	Yes, takes part in adults and paeds service. Holds clinics.	Yes, run by Diabetologist. Adult patients in remote areas managed by email and telephone advice	1. HDU,NICU on same site. Advice given by on site consultant. 2. Stabilise and transfer complex cases to Glasgow	Share care with neurologist Can liaise with obstetrician and midwife Biochemical advice available Genetics services see some patients as well
Dundee **Tayside areas**	Yes, University appointment with commitment to NICU PhD in metabolic disease and if grant approved may need successor. Seeking regional solution with Grampian	Yes, part time dietitian	Provided by paediatrican/biochemist and dietitian Multi-disciplinary clinics with paed/bioch and dietitian.	Patients have own protocols when seeking emergency tx Complex patients link with Glasgow Plans for joint consultation in Dundee with Glasgow consultant	Telemedicine help link the service 10 years to evolve model University has a major research interest in metabolic disease
Edinburgh Lothian/Fife	Yes, formally trained specialist employed by MRC – unfunded 1 or 2 sessions per week. Being withdrawn by MRC. This could be serious for Lothian. The MRC specialist advises and links with consultant paediatric endocrinologist who provides IP and OP support and management Multidisciplinary approach	Yes, dietitian work with protocols and take lead on PKU patients with advice from docs as required	No adult service- represents approx 25% and seen by paeds	PICU admissions (variable between 3-6 per year). Managed on site Patient have individualized protocols to seek help Need to form links with NICU – on another site and no referrals received since the move of Obstetrics to the new hospital.	Pharmacy helpful and involved in service; Biochemical service very useful Good links with neurosurgery in PICU
Glasgow – referrals from all areas in Scotland except Edinburgh	Yes, formally trained paediatrician and an adult biochemist specialist who are increasingly working together. A second paediatric specialist post was advertised and successfully recruited in March 2006. The new consultant will start in summer 2006.	Yes, plans to change service model with flexible approach and PKU management	Yes, adult clinics available with part time dietician	PICU admissions – approx 20 per year On site NICU with advice	Joint pregnancy & pre pregnancy service at QMH with obstetricians; Weekly PKU, metabolic and new patient clinics

3c) Issues raised by clinical teams

There were a number of additional issues raised by the clinical teams. These can be summarised as follows:

1. **Efficiency**
    a. On call issues – there was a problem as many areas were reliant on a single clinician. Each area would phone the relevant specialist who may be on holiday at the time.
    b. The service is heavily dependent on too few staff with low critical mass
    c. Many of the local specialists (LB, MB & RH) would welcome a 24-hour on call service where they could seek advice. MB mentioned the paediatric liver service as a model where most cases are managed locally but there is always advice available from the liver unit in London.
    d. The numbers are variable year on year and hence the service model should take account of this.
2. **Effectiveness**
    a. There is a lack of knowledge about IMD as it is perceived as very complex.
    b. Protocols would help increase knowledge and education in peripheral units but the specialist clinicians do not have time to develop these.
    c. There is a significant need for education of clinicians in investigation, detecting, managing and referring cases of metabolic diseases
3. **Acceptability**
    a. Terminal care is also an issue for many children/young adults. The development of links between local/national specialists and hospices may need further thought.
4. **Accessibility**
    a. Some areas wished 'in reach' sessions – e.g. local clinicians may go to Yorkhill and do joint clinics (RH) as well as outreach sessions with the 'tertiary' clinician traveling to regions to do joint clinics and see complex patients with the local teams.
    b. Adult and transition services are not available in many areas

5. **Sustainability**
    a. In Edinburgh, there is a general paediatrician who provides care to children with IMD. The service is, however, also reliant on a specialist who is currently employed full time by the Medical Research Council (MRC). The MRC have recently written to the clinical director of the Lothian service and indicated their intention to cease this arrangement. This would have consequences for the service in Edinburgh, which relies on this expert to manage complex cases (e.g. PICU) and help run the service. In Dundee, the University funded clinician currently undertakes metabolic clinics. There may need to be plans for a successor if a grant application is approved.

3d) Screening issues

The national newborn screening laboratory is located in Glasgow. All results are recorded and the laboratory has systems in place to ensure that all children found to have a positive result are referred to local clinicians. However it can be an onerous task to identify the appropriate service. Dr David Aitken outlined the issues for the newborn screening programme. These included:

- The PKU screening programme had been established for over 40 years. There were around 6-8 PKU cases per year from around 55,000 births
- Screening for Galactosaemia was discontinued in 2003. The establishment of the UK National Screening Committee had formalised the screening tests selected and it may be that new tests will be carried out in the future if found to be appropriate. For example MCCAD screening.
- New technology e.g. Tandem Mass Spectrometry (TMS) has enabled much faster screening to be carried out for a wider variety of conditions. This may impact in the future;
- It would be beneficial to formalise referral pathways to the metabolic services when a child is found, on screening, to have a metabolic condition
- Great Ormond Street is developing a dataset to encourage a UK wide audit programme for screening services. Therefore a database of all screen detected cases and their outcomes would be useful to screening service as well as clinical use.

The aim of the second half of the meeting on the 9th of December was to explore some models of care, which may alleviate some of the problems outlined above. The following section highlights issues raised and draws out the areas which most people agreed with and other areas where there is further work to be done in seeking a consensus.

4. Classification of the workload

It may be beneficial to go back to the classification, which clinical teams felt was appropriate.

4a) Subgroups

The workload can be divided as follows:

Group A. Outpatients

- PKU patients – may be mainly managed by specialist dietitians with advice from specialist general paediatricians as required.
- Children already diagnosed with rare metabolic problems and the aim is to manage and keep out of hospital.
- Babies referred by screening programme e.g. new cases of PKU.

Group B. Children referred with degenerative disorders – e.g. cardiac, progressive loss of skills/functions.

Group C. HDU/NICU – many children are managed in HDU in local areas or first picked up in NICU.

Group D. PICU – this is a relatively small though important element of the workload and may represent acute decompensation of known cases or children who present for the first time. (E.g. an estimate 1PICU to 6HDU admissions)

Therefore the children who fall into categories A, B and C can be managed locally with a variety of service models depending on complexity. These include:

- Managed locally by dietitian – e.g. PKU patients with protocols/standards etc with advice from local clinician.
- Managed by Multi Disciplinary Team (MDT) locally.
- Managed locally by local clinician with advice by telephone from centre available to get over acute period or transfer if appropriate.
- Managed locally with outreach or in reach from a tertiary expert who may review patients jointly with local team in an outpatient clinic.

4b) PICU Patients - Category D

There are approximately 20 admissions per year to Yorkhill and between 3-6 admissions to Edinburgh PICU. Patients who are not known to have an IMD often require acute inpatient care and may present with very acute symptoms. Examples of these clinical conditions that may require PICU admission are detailed below.

- **Neurological**: acutely and severely altered conscious level where deterioration and depression are likely, and are unpredictable, and where breathing may be compromised;
- **Endocrine and Metabolic**: severe ketoacidosis, with compromise of the circulation or brain and nervous system; potential or actual severe metabolic derangement, fluid or electrolyte imbalance; acute deterioration requiring respiratory support, acute dialysis, haemoperfusion, management of raised intracranial pressure, or drugs to support the circulation or blood pressure.
- **Multisystem**: established organ disease or organ failure, who experience acute deterioration or secondary failure of another organ.

Referral Pathways to PICU include:

- A small number of babies, known to be at high risk will be delivered in an obstetric unit where there is immediate access to specialist care;

- Consultant to consultant referral between consultant responsible for patients care and consultant in charge of PICU

- Patients transferred by Paediatric Retrieval teams. Some critical problems will require treatment to be started before or during transfer

4c) University Research and training

Dundee University has a major interest in metabolic disease research. It is important to link research with the patient populations which will ultimately benefit the patients, the university and ensure a good training of clinical personnel the NHS and universities work together to achieve this.

Conclusions

Following the UK needs assessment and the meetings of the subgroup, there were a number of conclusions which could be drawn. Inherited Metabolic Diseases are rare. They require rapid diagnosis, expert management and ongoing lifelong care. In order to provide optimum care, the following conclusions can be drawn:

- All Professionals (many of whom may see only a few patients with IMD in a working lifetime) require education and training in ensuring that rapid investigation, diagnosis and initial management is achieved in the acute phase.

- The current multidisciplinary teams provide local care for patients with IMD to ensure access at a geographical level for lifelong chronic conditions. However these teams require back up from a critical mass of specialists to advise and, in some cases, jointly managed very complex or acute conditions.

- Yorkhill have been successful in recruiting an additional paediatric specialist who is due to start in the autumn of 2006. Therefore there are 3 clinicians who provide tertiary expertise. In addition, there is an MRC specialist who provides support to the Edinburgh service. There is, therefore, potential to develop a Scottish specialist service which could support regional teams.

- As IMD is rare and complex, there would be benefit in linking with colleagues in England both at a strategic level to share good practice as well as enhancing links at an operational level with super specialist units for very rare conditions.

- There should be a unified but stratified service in Scotland with local provision and support available from experts, ideally on a 24-hour basis for acute emergencies and more elective support for joint consultations for complex patients. This relies on local units with MDT and a critical mass of experts.

- The NHS and Universities require formal links to ensure both training and research is mutually supported.

- Adults with IMD are attending paediatric clinics due to lack of local services. This has two effects:

    - It overloads paediatric services.
    - It is more appropriate for adults to attend adult based OP and IP services.

The issues outlined above have to be addressed by a two-pronged approach: a managed clinical network and a service component with local teams backed up by a critical mass of experts. Once these principles had been established, the next phase of the work was to develop options which would meet these requirements.

Part two – developing a plan to improve service delivery in Scotland

1a) Managed clinical network

At all the meetings of the subgroup and at the CYPHSG there was overwhelming support for a national managed clinical network It was agreed that the key aims of the network should include:

a. Education for clinicians with varying levels of experience in IMD in the detection, investigation and management of metabolic illness;
b. Development of standards, care pathways and protocols of care;
c. Information on the quality of the care of children with metabolic illness to ensure a optimal outcomes and adherence to treatment standards;
d. Developing links with the parents, children and the voluntary sector to ensure their views/needs are taken into account and inform service planning;

It was agreed that one of the experienced network managers would draft an application for a national managed clinical network and the group would offer comments. The final draft is attached in **appendix B** for information. There was no point adding the MCN to the option appraisal process as it would add little value in distinguishing between the options.

1b) Service Delivery

Options to improve service delivery

The subgroup met in February and March 2006. The focus of the first meeting was to outline a range of options to address some of the issues facing the service and comply with the principles outlined in the previous section. The main aim of the meeting in March 2006 was to score the options and select the most appropriate one.

Options:

The options were agreed on 2nd of Feb. There were some modifications suggested by members of the group in the weeks following the meeting. The final options agreed were:

1. Status Quo

2. Full time Tertiary specialist in Edinburgh with links to South East with parallel tertiary service in Glasgow. The Edinburgh tertiary specialist would take over the duties of the general paediatrician with an interest in Edinburgh. Outreach provision from each service in Edinburgh and Glasgow to Dundee and Aberdeen would be organised by each centre.

3. General Paediatricians in Edinburgh, Dundee and Aberdeen with an interest in metabolic disease with outreach/inreach from tertiary clinicians in Glasgow.

4. Half time tertiary specialist appointed by Lothian but work within the clinical network of tertiary consultants in Scotland to:

    a. Plan outreach/inreach with secondary care specialist consultants in Edinburgh, Dundee and Aberdeen
    b. Joint clinics and review meetings with Scottish clinicians
    c. On call cover with 24 hour access for secondary care specialist and cover for PICU
    d. This option would retain a 0.5 general paediatrician with an interest in Edinburgh

1c) Option appraisal process

A meeting of the subgroup was convened in March 2006. The focus of this meeting was to:

a. Agree criteria to score the options
b. Weight the criteria
c. Score the options

The criteria were discussed in detail and examples from previous option appraisals were used. The agreed criteria with definitions and methodology are detailed in **Appendix C**. The scoring sheet together with the weights attached is shown in **Appendix C.**

1c) Option appraisal results

The overwhelmingly preferred Option was 4. It was agreed that if there were significant difficulties implementing this option then option 3 would represent a 'fall-back' or second best choice. The final scores are shown in table 1 and individual scores are detailed in **Appendix D**.

Table 1 – Option appraisal scores

Option	**Option 1** **(Status quo)**	**Option 2** **(Edinburgh and Glasgow parallel centres with outreach)**	**Option 3** **(Glasgow centre with outreach)**	**Option 4** **(Integration with tertiary critical mass with outreach)**
Score	**459**	**6790**	**6880**	**9955**

This option would also address many of the issues facing the service and is consistent with the principles detailed at the end of section one. There would be a cost to the NHS as the half time salary of the Lothian tertiary specialists has been funded by the MRC and this is no longer sustainable under any option. Therefore this option is using the resources in a different way. The recruitment of an additional specialist in Glasgow during this review has also helped ensure that the metabolic services in Scotland will be much more sustainable.

The preferred option requires the three consultants from Yorkhill together with the half time consultant from Edinburgh to work together as a Scottish tertiary team to:

- Plan outreach/inreach services with the local multidisciplinary teams
- Provide on call cover to deal with acute emergencies from secondary care and PICU

Costs

It is expected that the MCN will be funded from best use of current resources so this is cost neutral. This has been a policy developed by the National Services Division over the past year and has been applied successfully to other networks. There will be a small budget for educational meetings etc in the region of a few thousand pounds per annum

However in order to make the preferred option a reality it is necessary to transfer funds to the MRC for half of the time of the tertiary specialist to secure this expertise for the NHS. For planning purposes this equates to approximately £60,000. This is, of course, subject to change when specific contracts/salary is considered. This should be considered by SEAT.

Therefore the total cost is £60,000. It is felt that this represent a cost effective option which.

Recommendations

This review has considered the UK needs assessment and examined the issues facing the Scottish Service. This is a small, specialised service which requires strategic planning on a national level to support delivery at a regional/local level. The review has considered a number of ways of tackling these issues which will provide a good clinical, sustainable service. There are five areas for recommendations. They are as follows:

1. **A national MCN application should be developed for submission to the National Services Advisory Group. The key aims of the network should include**:

- Education for clinicians in the detection, investigation and management of metabolic illness;
- Development of standards, care pathways and protocols of care;
- Develop information of children with metabolic illness to ensure a high standard of outcomes and adherence to treatment standards;
- Link with parents, children and the voluntary sector to ensure their views/needs inform service planning;

2. **There should be a unified but stratified service in Scotland with local provision and support available from a tertiary core of experts, ideally on a 24-hour basis for acute emergencies and more elective support for joint consultations for complex patients. This relies on local units with MDT and a critical mass of experts. This may be achieved by adopting and implementing option 4 which is detailed below**.

   There should be a clinical team of tertiary clinicians comprising the 3 clinicians at Yorkhill and a half time tertiary specialist who should be appointed by Lothian. This team will work closely with secondary care specialists and the multidisciplinary team to:

   - Plan outreach/inreach with secondary care specialist consultants in Edinburgh, Dundee and Aberdeen (and other areas as required);
   - Joint clinics and review meetings with Scottish clinicians;
   - On call cover with 24 hour access for secondary care specialist and cover for PICU;

3. **There should be close linking with the English advisory group at a strategic level and the super specialist units at an operational level.**

   This would enable:

- Organisation of sustainable on call rotas;
- The development of protocols and the service model;
- Linking with super specialist units and organize referral pathways;
- Linking with England over the issue of cost and clinical effectiveness of expensive treatments;

- Development a UK network of information on outcomes and adherence to standards of care;

4. Development of research and training to achieve sustainable succession.

The NHS and Scottish Universities should link together to support the development of a strong research base which will aid the patients of the future and robust teaching programmes for clinicians of the future.

5. Needs assessment for adult services

The transfer of adults with IMD should occur at the earliest, safest opportunity from paediatric services to adult services. Therefore boards/regions with no identified adult metabolic services should review the options to provide this service and ensure robust links with tertiary centers are in place to provide specialist advice.

References

1. FitzPatrick D on behalf of the SIMDIG (Scottish Metabolic Disease Interest Group); Proposal for the National Provision of Biochemical Genetic Services in Scotland.
2. Burton Hilary; Metabolic Pathways, Networks of Care. Nov 2005
3.Evans Deidre; Papers for NHS BCE Meeting 13 April. Enzyme Replacement Therapy - Proposed Financial Risk Share

Appendix A – Subgroup membership (those marked in italics took part in the option appraisal exercise)

Dr David Aitken, Consultant Clinical Scientist, Yorkhill Division (DA)
Dr Jennifer Armstrong, CPHM, NSD (JA)(Chair)
Dr Ian Auchterlonie, Consultant in Medical Paediatrics, NHS Grampian
Dr Ian Bashford, Principal Medical Officer, SEHD
Dr Louise Bath, Consultant Paediatrician, RHSC, NHS Lothian (LB)
Dr Jim Beattie, Clinical Director in Medicine, RHSC, Yorkhill(JB)
Dr Michael Bisset, NHS Grampian (MB)
Barbara Cochrane, Dietician (BC)
Dr Zoe Dunhill, Clinical Director, RHSC, NHS Lothian (ZD)
Dr David Fitzpatrick, Honorary Consultant Clinical Geneticist, RHSC (DF)
Dr Peter Galloway, Consultant Clinical Biochemist (PG)
Charlotte Giles, PA / Project Support, NSD (CG)
Professor Robert Hume, Maternal & Child Services, NHS Tayside (RH)
Dr Morgan Jamieson, Medical Director, Yorkhill Division (MJ)
Dr Jean Kirk, Consultant Biochemist, RHSC, NHS Lothian (JK)
Heather Knox, Regional Co-ordinator, West of Scotland Planning Group (HK)
Ms Sheena Laing, Chief Dietitian, RHSC, NHS Lothian (SL)
Dr Zelda Mathewson, CPHM, NHS Tayside (ZM)
Jamie Redfern, General Manager, Yorkhill Division (JR)
Dr Peter Robinson, Consultant in Metabolic Medicine, Yorkhill Division (PR)
Kathleen Ross, Chief Dietician, NHS Grampian (KR)
Robert Stevenson, CYPSG Co-ordinator, SEHD (RS)
Professor George Youngson, Consultant Paediatric Surgeon, NHS Grampian

Appendix B APPLICATION TO NATIONAL SERVICES DIVISION

A National Service for the introduction of a Managed Clinical Network for Inherited Metabolic Disease

1. Name and Location of Proposer (tbc)

2. Parties supporting the Application

This application has the unanimous support of the National Paediatric Metabolic Review Group. (listed on page 9 of this submission).

3. Introduction

3.1 Inherited metabolic diseases result from genetically determined defects in body chemistry and more than 500 different IMD's have been identified.

They are individually rare, but collectively add up to a great burden of illness and demand for health care.

Some are detected by newborn screening and dietary treatments, PKU for example has been an outstanding public health success.

3.2 Delivering effective services for IMDs is challenging for many reasons.

- Some require very urgent intervention to prevent severe mental and physical handicap or death.
- They may require highly specialised drugs, complex dietary manipulations, interventions from many medical specialities (neurology, nephrology, cardiology, surgery and transplantation).
- Diagnostic assessment and monitoring often requires highly specialised biomedical and molecular tests.
- New technologies will increase the numbers identified with IMDs.

3.3 Scotland's population is geographically dispersed. A managed clinical network will play an important part in ensuring that best practice is available to all, irrespective of where they live.

3.4 Carers and patients face challenges from coping with these rare, severe and chronic diseases such as:

- Carers and Patients have difficulty finding useful information regarding the specific disease.
- Carers and Patients often have to learn to provide complex treatment regimes.
- Carers and Patients have to recognise and deal with acute crisis that can occur at any time; they may have to deal with many other specialists if their child has involvement of multiple organ systems.

- Carers and Patients will need to understand the familial aspects of the condition, which can result in difficult reproductive choices.
- Parents energies may be almost totally consumed by coping with a child with a severe disability, and all that this entails in terms of everyday life, education and work opportunities.

3.5 Specialist services for IMD are essential to provide more effective and high quality care. Such care should be judged on:

- Decrease in mortality
- Decrease in morbidity
- Reduction in disability
- Prevention of harm to family members
- Prevention of damage to unborn child
- Reproductive choice
- Improved overall quality of life (reduction of handicap)

3.6 Legislation supports the rights of children, young people and adults to access services that will enable them to fulfill their developmental potential and maintain a reasonable quality of life whilst managing a chronic medical condition.

3.7 Since 1994 informal networking has taken place among professionals in Scotland caring for children and adults with IMD. However it has not been possible to focus on the patient journey, or set or audit specific standards of care or influence the planning of metabolic services for children and adults nationally or regionally. Patients and carers have not been actively involved in the planning of the service.

4. Incidence and Prevelance

4.1 There are over 500 known IMDs and, probably, many more that are yet to be discovered. IMDs can be categorised by their typical age and mode of presentation:

- Detection via the newborn screening program
- Neonatal intoxication – classically where the baby is well for the first 24-48 hours and then develops a metabolic acidosis and/or hyperammonaemia
- Neonatal neurological presentation – often a floppy baby with seizures
- Aberrant response to fasting in early life (0.5-3yrs), sudden catastrophic illness often associated with an intercurrent viral infection
- Single organ failure – most commonly liver or heart
- Neurological deterioration during childhood or early adult life
- Multiple malformation syndromes

Many IMDs produce multisystem disease with severe physical and mental impairment, which can lead to death in childhood or early adulthood. They are individually rare but collectively have a live birth incidence of 1 in 2,500 to 5,000. This would equate to a figure of between 10-20 new cases per year in Scotland. (Based on 51,803 births for year ending March 2004, ISD figures). The commonest single condition is phenylketonuria (PKU) with an incidence of 1 in 6500 to 8500 live births (6 to 8 new cases annually).

4.2 In the UK including Scotland, the lack of a national register of patients with IMD has significantly hampered clinical research and practice as well as the planning, procuring and monitoring of services for patients with these conditions. Reliable Scotland wide incidence and prevalence figures are not therefore available.

4.3 However, the following statistics give an indication of the rarity of these diseases. It should be noted that the figures below do not indicate prevelance but only the numbers of patients who attend clinics.

The West of Scotland has approximately 324 patients known to the service.

	PKU	Fatty Acid Oxidn	Galactosaemia	Others	Totals
Yorkhill Clinics	84	12	7	90	193
Adult Female/Maternity	50	-	-	10	60
GRI Adult Clinic	38	2	4	15	59
Late Diagnosed	12	N/A	N/A	N/A	12
TOTALS	184	14	11	115	324

Aberdeen has approximately 36 patients known to the service.

	PKU	Fatty Acid Oxidn	Galactosaemia	Others	Totals
Adults	12	5	2	0	19
Children	14			3	17
TOTALS	26	5	2	3	36

Edinburgh, Fife and Borders have approximately 115 patients known to the service.

	PKU	Fatty Acid Oxidn	Galactosaemia	Others	Total
Combined Clinic	44	10	6	55	115

Edinburgh receive all the newborn screening referrals for Edinburgh, Fife and the Borders.

Tayside has approximately 67 patients known to the service.

	PKU	Fatty Acid Oxidn	Galactosaemia	Others	Total
	12	5	1	49	67

Scotland Wide

The most frequent disorder is PKU with around 6-8 new cases detected each year in Scotland through the newborn screening programme.

PKU Children attending the 4 main centres of Scotland – March 2006 (excluding patients over 18 years)

	0-5 years	6-11 years	11-18 years	Total
Aberdeen	3	1	10	14
Dundee	1	2	7	10
Edinburgh	8	8	11	27
Glasgow	25	24	35	84
TOTAL	37	35	63	**135**

4.4 Greater awareness and new laboratory techniques will identify more cases including previously unrecognised cases, which present in adulthood rather than childhood. The development of new and better treatments has also meant that more children will survive into adulthood. This creates an increasing demand on specialist paediatric and adult services to provide continuing management.

4.5 Due to the specialist nature of the IMD service, the relative rarity of the conditions and rarity of clinicians with specialist knowledge on IMDs, most adults in Scotland are managed by clinicians working in paediatric health services. In the West of Scotland alone there is estimated to be around 200 adults with late diagnosed PKU and there is a need to provide a dedicated service to this group in order to best meet their needs. An integrated IMD service throughout Scotland, integrating childrens' and young people's IMD services and adult PKU services is considered the best approach to utilise scarce resources and expertise in this highly specialised area of the health service.

4.6 As children survive into adulthood with conditions which are prone to acute decompensation (eg MSUD – Maple Syrup Urine Disease, MMA – Methyl Malonic Aciduria, OTC – Ornithine Transcarbamylase Deficiency), the ability to admit them to appropriate beds and support them acutely is stretched if based upon paediatricians whose work is in different hospitals in three of the four main sites in Scotland.

5. Current Service Provision

5.1 **West of Scotland.**
Adult, children and young people's metabolic services are provided by (see clinic breakdown above);

- 0.7 wte Consultant Paediatrician (Peter Robinson, Yorkhill)
- 1.0 wte Consultant Paediatrician (Bernard Schwahn, Yorkhill, due to start in August 2006)

- 0.1 wte Consultant Medical Biochemist (plus 0.9 wte dedicated to metabolic biochemistry laboratory work) (Peter Galloway, Yorkhill)
- 0.05 wte (unfunded) dietician based at Glasgow Royal Infirmary
- 1 wte Clinical Dietetic Specialist (Chief III) based at Yorkhill (Barbara Cochrane)
- 0.4 wte Senior 1 Dietician based at Yorkhill Division
- 0.3 wte specialist midwife at QMH

RHSC Childhood PKU clinic		**Weekly**
	Childhood general metabolic review clinic	Weekly
	New Patient childhood metabolic clinic	Fortnightly
QMH	*Female/Maternal PKU Clinic*	*Weekly*
GRI	Adult metabolic clinic*	Weekly
	Late treated PKU clinic	3 monthly or monthly

* includes monthly paediatric/adult transition clinic

Plus

- 2 Dietetic sessions per month at each of Ayrshire Central and Ayr Hospitals
- < 1 session per month in Dumfries
- 2 dietetic sessions per month at Crosshouse Hospital, Kilmarnock

If a current proposal to establish a dietician led PKU service was accepted, this would free up approximately 60 sessions per year of Peter Robinson's time, allowing him to concentrate more time to other areas within the metabolic service.

5.2 **Edinburgh, Fife and Borders**

1. The weekly medical IMD clinic is led by Dr FitzPatrick with Dr Louise Bath as the link paediatrician. There is dietetic and laboratory support at this clinic.
2. Dr FitzPatrick is an MRC Clinician Scientist with only 3 (official) clinical sessions (unfunded by the NHS)
3. The weekly PKU clinic in Edinburgh is dietetically led.
4. There is no separate adult clinic therefore adult patients attend the paediatric clinics.
5. With current resources medical input to the IMD service in Edinburgh is not sustainable in the short to medium term.

5.3 **Aberdeen**

- Adult Services – Clinic run by Dr Donald Pearson plus adult dietetic support.
- Children's Services –Dr Ian Auchterlonie retires in September. Dr Michael Bisset will take the lead as a "Paediatrician with an interest" and will be undertaking further training. Ms Kathleen Ross, Chief Dietician, will lead the service to PKU children.
- Twice Monthly children's clinic held at RACH.

- Biochemistry and clinical genetics support for all patients.

5.4 **Tayside**

- Consultant Paediatrician (clinical Service 0.2 wte; academic 0.5 wte;)
- Consultant Biochemist (clinic 0.1 wte; 0.4 laboratory metabolic work);
- Paediatric Dietician (clinical service 0.25-0.3 wte)
- 1 clinic per week with a single combined consultation with Consultant Paediatrician, Consultant Biochemist and Paediatric Dietician for children and adults including pregnant mothers.

5.5 There are no dedicated IMD Nurse Specialists within Scotland.

6. Nature of the problem that a National MCN is expected to address/alleviate

6.1 **Care Pathways** – With regard to IMDs that are likely to produce acute clinical decompensation, there is currently no construction of, updating or audit of IMD care pathways. With the anticipated expansion of IMD screening in the population, and the subsequent additional demand on services, the development of robust care pathways is essential to ensure identified patients are appropriately referred.

6.2 **Service integration and equity of access** –The limited resources for service delivery, training and laboratory analysis could be more effectively utilised. Lack of integration impedes training and service developments to occur.

6.3 **Fragmentation of Specialist Services –** IMD services are provided over a range of sites throughout Scotland by highly skilled but limited numbers of staff. The geographical nature of Scotland makes it difficult to offer quality services to this small, but highly demanding group of patients with complex needs.

6.4 **General Services –** In addition, children present to a number of professionals who may have little experience in how to recognise, investigate and manage these conditions. The referral pathways and share care pathways are not well worked out.

6.5 **Management of PKU cases identified through newborn screening** – A particular national responsibility exists in the management of PKU as this has been part of the national newborn screening program in Scotland for nearly 40 years. This screening program exists because effective dietary therapy is available for this condition. National and international guidelines have existed for more than 10 years regarding best practice for dietary therapy and biochemical monitoring in phenylketonuria (PKU). As mentioned above it is currently impossible to determine how well Scottish patients are being managed due to lack of basic information. Indeed we currently have no national plan for any aspect of management of follow-up for PKU in Scotland.

6.6 **Audit** – There is no mechanism for national audit in any IMD. This is particularly disturbing in PKU where the regular biochemical monitoring facilitates effective audit of any intervention. Lack of audit severely hampers medium and long term audit of outcome data for current and future IMD detected through the national newborn screening programmes.

6.7 **Recruitment, retention and training of metabolic laboratory, dietetic and medical staff**.

(a) Laboratory Staff - There is a demographic bulge that means that in the years from 2000-2015 the majority of highly experienced senior Clinical Scientists and Biomedical Scientists providing the Paediatric metabolic service reach retirement age. In addition, there is a high ongoing requirement for formal and on the job training for all grades of laboratory staff. The Network may highlight training issues and link with National Education Scotland and with the strategic advisory group in England to inform training requirements.

(b) Dieticians - Dietetic services are generally very stretched within the NHS in Scotland and it is crucial to build on the excellent experienced personnel in post to ensure adequate future provision of an expanded role for dieticians in the management of PKU. There is potential to redesign the service to utilise the resources more effectively.

Specialist medical training in this area has only recently been formalised in paediatrics and adult medicine. The Network may be able to disseminate expertise to other professional groups.

6.8 **Planning for the future** – there is no national strategy to prepare and plan for the clinical consequences of the future expansion of newborn screening to include fatty acid oxidation disorders or other conditions. The introduction of tandem mass spectrometry will dramatically increase the number of different IMDs that can be detected through newborn screening and thus increase the number of urgent presentations to paediatric IMD services.

6.9 **User issues** – patients and carers have increased expectations of care and access to information. Users are currently not involved in planning services.

6.10 There is **potential inequity** in the availability and use of high cost therapies.

6.11 **Service efficiency** –There is currently no mechanism for distributing emergency care protocols to help non-specialists detect, diagnose and institute early management of treatable IMDs. Improvements in detection, diagnosis and early management will result in considerable service improvements which may translate into clinical outcomes.

6.12 **Research** – There is currently no integrated research strategy in IMD which focuses upon Scotland's needs and respect to the diagnosis, treatment and understanding of specific metabolic conditions.

6.13 **Identify Patients** – There is currently no formal surveillance and notification procedure within Scotland for specific IMDs which would allow monitoring of trends or identification of areas of high incidence.

6.14 **Conclusion**

There is a lack of planning, resourcing and commissioning to provide comprehensive services to Scotland's population. This has meant that many patients do not have access to IMD services. Those that do most frequently find the services overstretched, limited in scope and unable to offer care tailored to their individual needs.

7. Benefits a MCN would bring to patients

7.1 Establishing a national Managed Clinical Network would support the provision of a long term integrated framework for clinical, dietetic, laboratory and pharmaceutical

aspects of the diagnosis and management of IMDs across Scotland. A Managed Clinical Network would facilitate the following:

- The promotion of education and training for professionals on the recognition and initial management of metabolic disease.
- Development of a multi-disciplinary network throughout Scotland. A useful model to develop may be the informal work of SIMDIG (see below).
- National care pathways for children identified with PKU through the new born screening programme to ensure all children receive the treatment they require.
- National standards on the diagnosis and management of children identified with IMD.
- Establishment of information on all IMD patients in Scotland and to develop a patient register.
- The development and dissemination of personalised care plans for all patients at risk of metabolic decompensations.
- The use of modern techniques to augment local services in addition to conventional peripheral clinics (e.g. video conferencing, web based information)
- The development, co-ordination and review of Scotland wide standardised emergency protocols and care pathways.
- Audit Programmes to examine clinical effectiveness of services.
- Partnership with voluntary groups and patients to assist them in accessing appropriate information about specialist services and to participate in the Managed Clinical Network directly. This may inform the planning of services from a user perspective.
- A consistent, clinically based approach to the use of high cost therapies. This may ensure that a national approach is taken which reduces 'postcode' prescribing and takes account of national recommendations.

7.2 As part of the Managed Clinical Network implementation, a quality assurance plan will be agreed with relevant partners including Quality Improvement Scotland. This plan will include disease specific standards, clinical governance structures, and structures for annual reporting.

7.3 A vital component in ensuring the implementation and maintenance of a successful Managed Clinical Network will be communication. As such a great deal of effort within the first 2 years will be placed on developing a communications strategy.

8. Managed Clinical Network – Structure and Implementation Plan

8.1 As noted earlier there already exists a multi-disciplinary relationship between specialist tertiary and secondary care clinical staff working within metabolic medicine both regionally and nationally. This is currently organised around the Scottish Inherited Metabolic Disease Interest Group (SIMDIG). This group meets informally and has not had the time to develop these pathways. This existing Group would be the starting point to establish a National MCN Steering Group.

8.2 The administrative/managerial base for the Network – to be decided.

8.3 The Lead Clinician who will provide clinical leadership/sponsorship through the submission/subsequent implementation period of the network - to be decided.

8.4 **Managed Clinical Network - Set Up Plan**

During the first year the MCN will:

- Establish a National Steering Group and its Terms of Reference.
- Agree roles and responsibilities of key Network stakeholders.
- Agree Network membership.
- Within 3 months develop a MCN development plan detailing specific timescales and priorities for year 1.
- Establish working groups and/or individuals with responsibility for taking forward the elements of the Development plan.

9 Managed Clinical Network- Goals For the First Two Years

9.1 A national Managed Clinical Network would provide long-term support for the provision of an integrated clinical, dietetic, laboratory and pharmaceutical approach to the diagnosis and management of IMDs across Scotland. A Managed Clinical Network would include the following as priorities in the first two years:

- Establish guidelines for identification, investigation and management in the acute and long term IMD patients
- Identify clinical pathways and shared care for both newly diagnosed patients and established patients.
- Work with NHS QIS and the English strategy group to produce standards.
- Introduce and audit dietician-led care plans for PKU
- Develop care plan and diagnostic algorithms to inform the acute management of patients.

10 Conclusions

National Services are asked to support this submission for an integrated nationally managed clinical network for metabolic medicine - integrating children's, young people's and adult health services. This request is based on a number of broad principles including:

- The individual rarity, diverse range and complexity of IMDs and the requirement for specialist clinical knowledge.
- The difficulties in strategically planning IMD services under current fragmented planning structures;
- The severe disability and chronic illness that untreated or poorly managed metabolic disorders can produce in many patients;
- The suitability of the Inherited Metabolic Disorders service within Scotland to successfully implement and maintain a managed clinical network.
- The clinical benefits to the patient, which can be accrued from a successful implementation of a managed clinical network for metabolic disorders in Scotland.

11 Support

The following professionals support the proposal for a Managed Clinical Network in metabolic medicine in Scotland.

This application is supported by:

Signed: _____ Date:

Designation: _____

Signed: _____ Date:

Designation: _____

Signed: _____ Date:

Designation: _____

References:

A needs assessment and review of services for people with inherited metabolic disease in the United Kingdom. Hilary Burton, November 2005.
Proposal for national provision of Biochemical Genetic services in Scotland. Dr David FitzPatrick and SIMDIG

Appendix C

1. Definition of Criteria

Structure

- **Clinical sustainability** - staff retention and recruitment and support to the staff providing the service and succession

- **University and Research** – the extent to which the option supports the research and improves academic performance. Training - continuity of education for local staff, who are not experts. Specialist training for future exerts – e.g. specialist MDTs

Process

- **Flexibility**

  The service needs to be adaptable in order to accommodate changes in the provision of the service as and when required. Options should be scored in relation to the relative ease with which they could accommodate changes in:

  - Case-mix and activity
  - Technology & techniques
  - Comprehensiveness

  For example further development in screening, treatment

- **Equity of access**

  Ability of the patient to managed locally with access to specialist advice and access to multidisciplinary team

  Access to specialist care and advice for all Scotland children - e.g. PICU/HDU

- **Continuity of care -** *Continuity of care is a multi faceted concept used in a series of different ways including continuity across organisational boundaries; continuity of personnel; continuity of information and continuity over periods of time. (Freeman et al, 2000, http://www.sdo.lshtm.ac.uk/continuityofcare.htm)*

- **Support to & from other specialties** e.g. NICU. Support to & from wider specialities.

Outcome

- **Meet national clinical standards** - which option will allow us to develop and meet national standards more easily

- **Clinical effectiveness** –

  Ability to diagnose conditions rapidly and initiate treatment to avoid sequel are:

  - Short-term outcomes to discharge (e.g. complications) Optimum diagnosis and treatment for life long conditions – avoid mortality and long term morbidity and genetic counseling for the family

  - Long-term outcomes (e.g. survival) In assessing options the full spectrum of care should be reduce long term learning disability.
  - Training arrangements for all staff and involvement in research would also be included under clinical effectiveness. *"The extent to which specific clinical interventions, when deployed in the field for a particular patient or population, do what they are intended to do - that is, maintain and improve health and secure the greatest possible health gain from available resources."* NHS Executive (1996).

  - **Patient acceptability** – access to service and journey and how good care is and satisfaction

2. Methodology

Once the criteria were agreed, the subgroup was asked to:

1. Weight each of the criteria;
2. Score each of options against the criteria;

Weighting of the criteria

A variety of proposals for weighting the criteria were discussed. The agreed method was as follows:

High – 15
Medium – 10
Low – 5

The weights were then assigned to each of the criteria and agreed by the group prior to scoring.

Scoring of the options

The methodology for scoring was also discussed and the group agreed a scale ranging from 0(very poor) to 10 (excellent).

A scoring sheet was then used to score the options.

Appendix C - Options Appraisal Scoring sheet with attached weights

Name _____

Weight High = 15 Med = 10 Low = 5	Score 0 = v. poor 10 = excellent	**Option 1** **Status quo**	**Option 2** **Parallel tertiary**	**Option 3** **GP & 1 centre**	**Option 4** **Tertiary network & GP**
	Total				

Structure

	Weight				
Clinical sustainability	15				
University and research	5				

Process

Flexibility	15				
Equity of access	15				
Continuity of care	10				
Support from & to other specialties	10				

Outcome

Meets national clinical standards	10				
Clinical effectiveness	15				
Patient acceptability	10				

Appendix D

Individual	Option 1	Option 2	Option 3	Option 4
A	280	615	660	925
B	220	405	740	945
C	235	295	390	715
D	390	450	340	840
E	405	665	735	800
F	500	560	580	760
G	525	720	635	705
H	290	675	570	830
I	585	785	685	925
J	305	495	495	665
K	320	565	695	910
L	540	560	355	935
Total	**4595**	**6790**	**6880**	**9955**