New South Wales

Special Commission of Inquiry into Healthcare Funding

Submission Number: 17

Name: Genetic Metabolic Disorders Service, SCHN

Date Received: 31/10/2023

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30th October 2023

Parliamentary Special Commission of Enquiry into Health Funding

Dear Mr Richard Beasley

Metabolic Genetic Services in NSW – SCHN – Westmead and Randwick

The genetic metabolic disorder service (GMDS) was established formally at the Children's Hospital at Westmead a 1995 and was deliberately co-located with the state-wide newborn-bloodspot screening (NBS) lab and confirmatory Biochemical Genetics (BG) lab. When tandem mass spectrometry (TMS) newborn screening was introduced in 1998, this allowed rapid identification and treatment of babies with life threatening rare metabolic genetic disorders. The changing scope of GMDS was world leading at the time, but as more children with life threatening conditions were treated prospectively, the growth in patient numbers and complexity increased substantially. GMDS differs from clinical genetics service because we have provide ongoing treatment of our patients in contrast to the consultative nature of clinical genetics. Further expansion of newborn screening has been recommended by the federal government for adrenoleukodystrophy and other metabolic disorders such as Pompe disease, MPS1 and MP2 are currently being considered.

I have worked as part of this service from the early days in 1996 through till now and the complexity a range of conditions that we now manage has altered exponentially over that time. When I first started, most patients with Pompe disease and MPS, that we saw died. Nowadays we have treatments for most conditions identify identified by TMS as well as enzyme replacement therapies for MPS disorders and Pompe Disease. While early identification for the severest forms is of huge benefit, there will be long latent asymptomatic periods for many of these individuals extending potentially to adult life, meaning long-term specialist surveillance by our team will be required.

The attached strategic plan was associated with the brief SCHN TRIM/ 18/3701 was the last detailed analysis of our service that we provided to SCHN executive. It mapped activity, strategy, policy and models of care. At the time three clinical genetics specialists contributed to the on-call service at SCHN – Randwick but they felt that the ongoing treatment of patients with rare disorders was beyond their scope of practice, and they withdrew from the on-call roster. That has meant that the service at Westmead has provided an on-call service to both paediatric hospitals at Westmead and Randwick with clinical services at both sites. Rather than purposefully designing a clinical service for severe rare disorders, the team have had to provide support at either site when required, when staff have left or been redeployed. We are proud to be genuinely integrated into both children hospitals at Westmead and Randwick but compliant safe on-call practices for on-call specialties are not being adhered to per item 23 of the Henry review for NSW Health in 2019. It should also be noted that GMDS operates as a state-wide service providing specialist advice to doctors in NSW and ACT. The activity of nurses, dietitians and doctors in interpreting biochemical, genetic and clinical information as well as partnering in life-saving treatment or re-directing care is not measured effectively in the hospital records of SCHN, thereby vastly under representing the true service GMDS provides to children in NSW and ACT.

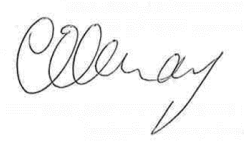
The table below represents the service when mapped in 2018, the enhancements made and ideal requirements now. It should be noted at the time that we predicted that we would fall behind demand in genomics therapies and this has come to pass with commercially sponsored trials for the rare

disorders we treat, preferentially selecting other states rather than NSW. Our most reliable data in the Rare Voices Australia report of 2021 was from our specialist dietitians who only provide service to see patients accepted into our service at SCHN. They give advice only to those patients who have a genetic metabolic affecting a nutritional metabolic pathway. The benchmark from services in USA and UK indicate that the ratio of patients to specialist dietian should be in the order of 1:125 and our diet team currently manage twice that number. The numbers indicate fraction of whole full time equivalent (FTE), before and after a request in 2018.

	2018	**Request 2018**	**2023**	**Request 2023**
Medical- Staff Specialist FTE	3.8	4.8	3.8	5
Medical – JMO FTE	0.5	2	1.5	2.5
Social Work level 3	0.3	1.3	1	1.5
Dietetics	0.36 level 6 0.5 level 5 1.0 level 4 0.4 level 2	0.36 level 6 0.5 level 5 1.0 level 4 0.3 level 3 1.0 level 2	0.36 level 6 0.4 level 5 0.6 level 4 1.2 level 3	0.36 level 6 0.5 level 5 2.0 level 4 1.0 level 3 0.5 level 1/2
Nutrition Education Assistant	0. 5 temp funding	0.5 FTE permanent funding	0.5 permanent funding	1
Nursing	1.4 CNC CHW 0.6 CNC SCH	2.0 CNC 1.0 Nurse practioner	0.6 NP 1.4 CNC	1.6 NP 2.0 CNC
Genetic Counsellor	0	1.0 level 4	0	1.0 level 4
Administration	1.2 (level 3)	2	1.2	2
Psychology	0	0	0	0.5
Neuropsychology	0	0	0	0.5

When evaluating the RVA white paper on rare metabolic work force, it should be noted that because our specialty is not AHPRA recognised and is in other countries, all Australian services require enhancement and should not be benchmarked against each other. Victoria has recently had its adult and paediatric services reviewed although outcomes are awaited. I enclose a comparator from Ireland in 2014 – with about 1.75 times the population our current service staffing lags well behind theirs from 9 years ago.

Kind regards



Carolyn Ellaway
Genetic Metabolic Disorders Service
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Genetic Metabolic Disorders Service (GMDS) – SCHN

Business Case

Executive Summary

The purpose of this business case is to describe the future model of care for GMDS within the Sydney Children's Hospitals Network.

The Genetic metabolic disorders service (GMDS) encompass the management of a variety of individually rare life threatening, genetic conditions.

The following is a summary of the agreed service priorities for consideration:

- Genetic metabolic disorders will be managed by one Network Service across two sites
- SCHN GMDS key clinical staff will provide care across both Westmead and Randwick sites
- Patients at critical risk of decompensation will be managed at Westmead due to requirement for immediate biochemical samples (Severe MSUD; Severe OTC, PA)
- One Network Medical on-call service

The following is a summary of the workforce enhancement priorities:

1. 1.0 FTE staff specialist to be recruited nationally / internationally.
2. 1.0 FTE Metabolic Fellow working across SCHN - Provisional Fellow Level 4.
3. Dietician permanent 1.0 FTE level 3 (current 0.4 FTE permanent level 3 at Randwick and 0.4 FTE level 2 temp at Westmead) – enhancement 0.6 FTE level 3.
4. Training grade dietician 1.0 FTE level 1 / 2 (per award) – new post.
5. Social Worker 0.3 FTE permanent level 3 and 0.7 FTE temp level 2 – to become permanent 1.5 FTE level 3 in 2018
6. Nutrition Education assistant-0.5 FTE- to become permanent 0.6 FTE in 2018
7. Admin support currently 1.5 FTE level 3 – enhancement 1.0 FTE level 3.
8. Creation of 1.0 FTE nurse practitioner for SCHN Randwick.
9. Clinical nurse consultant 0.6 FTE temporary enhancement 2017 / 18 – made permanent.
10. Creation of 1.0 FTE Genetic Counsellor level 3 for GMDS-SCHN.
11. Creation of research coordinator (Level 9 registered nurse) and 1.0 FTE research fellow temporary 1 yr. from donated funds.

Additional recommendations for future implementation:

- Formalise SCHN Paediatric Metabolic Services as a State-wide Service: NSW Paediatric Genetic Metabolic Disorders Service.
- To work with Research to creating a clinical trial infrastructure to support such approaches to novel therapies.
- To enhance transitional care at interface with state-wide adult metabolic service based in Westmead Hospital using novel transitional services across the network and state.

Background

Genetic metabolic disorders (GMDs) or inborn errors of metabolism (IEM) are a diverse range of conditions, which vary widely in their presentation and management according to which body systems are affected (Bhattacharya et al 2015). IEMs are a collection of disorders that lead to severe disruption of metabolic processes in the body, leading to an accumulation of unwanted toxic products or deficiency of products that are essential for normal bodily functions. Patients with IEM's require input from a specialist multi-disciplinary team, including at least medical, nursing and dietetic input integrated closely with the specialist biochemical laboratory team. This can only occur with experienced staff operating above entry level practitioners in order to facilitate effective management. (Burton and Sanderson 2005; Burton et al 2007)

Case for Change

The burden of care for families is intense because they do not have standard resources to avail. As a consequence, healthcare professionals have to create bespoke plans for each patient. SCHN-GMDS has therefore traditionally provided a model of patient centred care, incorporating biochemical data, genomic information and social and nutritional information, with targeted community services in providing a comprehensive treatment plan for patients. *This is the reality of personalised medicine*.

Advances in genome technology have led to precise identification of genetic metabolic disorders and survival of hitherto untreatable conditions, such as Pompe disease (with natural history of 90% mortality) (Kishnani et al 2006), and MCAD patients who previously had a 25% mortality rate (Wilcken et al 1994) at initial presentation. With early treatment, Pompe patients can survive long-term (Kishnani et al 2009) with MCAD having virtually no mortality nor neurological morbidity when identified by newborn screening and treated (Wilcken et al 2007).

Due to increasing number of patients and staff departures, the GMDS as a whole has been managing crises for a sustained period, without the capacity for developing protocols, standards or systematically enhancing care. The medical and multidisciplinary team need more time to undertake these integral functions.

The demographic in Sydney and NSW is changing, with projected population growth. SCHN-GMDS needs to be positioned to face these challenges, both now and into the future. There is a high consanguineous population in certain parts of Sydney leading to manifestations of rarer, complex genetic metabolic disorders, and more challenging social and cultural management compared to 20 years ago. SCHN-GMDS delivers resource intense personalised medicine, with outcomes comparable or better to equivalent centres across the world.

Vision

The SCHN offers a world class therapeutic service for children with Metabolic Disorders and their families through the provision of timely, interdisciplinary care. The SCHN GMDS service is involved in translational research utilise novel technology for assessment and trial of novel therapies.

The service is applied as a state-wide service. With judicious investment, the network will be able to deliver the promise of genomic targeted therapy utilising experienced practitioners in the field. SCHN-GMDS remains committed to finding therapeutic treatments for all disorders that are identified in order to help children 'live their healthiest lives'. In this context, the service can not only be a leading national clinical service but also attract international investment for novel clinical trials.

National Context

A 'collective' submission has been made to the National Health Minister (February 2018) by a group of metabolic specialist physicians (Victoria, NSW and QLD) highlighting the key issues facing genetic metabolic services in Australia. In summary the key issues represented are:

The lack of a strategic and planned approach to the future of genetic metabolic medicine within Australia

1. An increasing number and complexity of patients due to combination of population growth, newborn screening, novel diagnostic technologies such as whole genome sequencing and novel therapies
2. A lack of trained specialist genetic metabolic medical staff:
3. In paediatric centres this is collectively a result of inadequate funding for training positions, planned and imminent retirements in a number of senior practitioners and the lack of recognition of Genetic Metabolic Medicine as a speciality by AHPRA.
4. There is a growing need for adult services due to medical advances improving morbidity and mortality rates
5. Insufficient funding to support succession planning and training for nursing and allied health teams
6. The rapidly growing gap between research funding and translational genomic medicine delivery in clinical care delaying the opportunity for patients to be commenced or trialled on new treatments.

NSW Context

NSW Health Genomics Strategy; SCHN-GMDS needs to be aligned with the NSW Health genomics strategy in strengthening its foundations across the network to provide an adaptable, high quality, contemporary service. The NSW Health Genomics Strategy has the objective of prioritising translational research for implementation in the public health system with treatment being a primary objective. SCHN-GMDS remains the only dedicated paediatric therapeutic genetic service in NSW.

Prior to 2000 genetic testing was not widely available, thus metabolic patients may not have been diagnosed. Novel genomic technologies have led to more referrals of patients with *genetic variants* of a metabolic gene rather than a biochemical issue (Wright et al 2010) which subsequently require investigation, understanding and explanations of genetic variations (including variants of unknown significance and incidental findings) related to genomic investigation. Genetic testing requires extensive pre and post-test genetic counselling. Currently only the staff specialists in the team can do this.

SCHN

The Sydney Children's Hospitals Network was formed in 2012, and has made significant progress towards the formation of a specialist network of services providing healthcare and support services for children and families. The most recent SCHN Strategic Plan (2017-22) identifies the need to improve our streams of clinical care provision across the Network and capitalise on the Network with regard to opportunities for patient outcomes and research. GMDS Randwick and Westmead

need to consolidate, in order to provide an effective state-wide service in a rapidly changing genomic and therapeutic environment. Temporary staffing arrangements complicate the stability of service provision and there remain significant risks to GMDS services in NSW. The strategy to provide an integrated SCHN service per TRIM REF SCHN 16-2269 has been partially implemented.

SCHN Metabolic Organisational Structure

SCHN currently has 2 site based services providing clinical care for patients with Genetic Metabolic Disorder Services (GMDS). The structure of the current services is mapped in Figure 1. Specialist medical care at the Randwick site is currently being provided by a Medical Specialist (0.2FTE) who is primarily based at the Westmead campus.

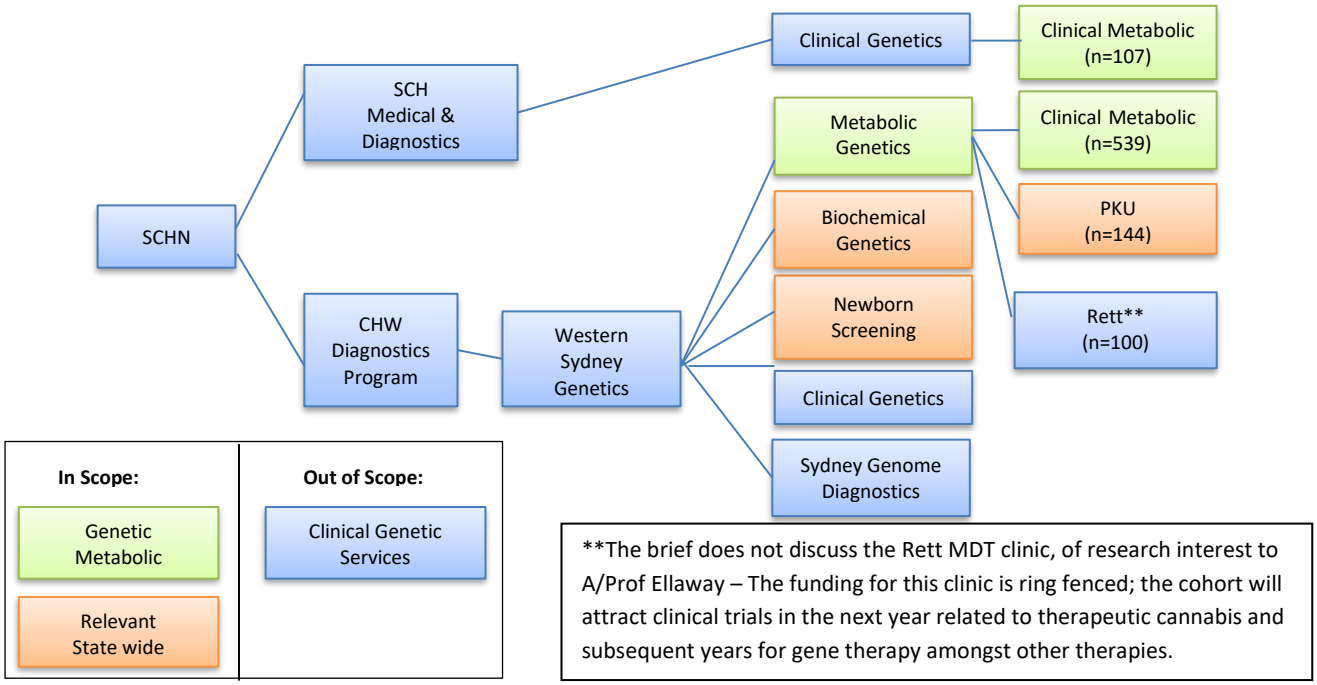


Figure 1: Structure of current SCHN Genetics Services, with Genetic Metabolic Disorders Services currently instrumental in delivering timely clinical services for patients with life threatening genetic metabolic disorders.

GMDS at the **Children's Hospital at Westmead** is one of the core units of the Western Sydney Genetics Program (WSGP) and sits within the Diagnostics Program at CHW. The CHW GMDS team provides the state-wide service for patients with Phenylketonuria (PKU) and 120 other inborn errors of metabolism, and is co-located with the state-wide Biochemical Genetics (BG) Laboratory and the NSW Newborn Screening (NS) Services.

The clinical service for genetic metabolic patients at the **Sydney Children's Hospital Randwick** is physically collocated in the Bright Alliance Building with the Clinical Genetics service and falls within the Medical and Diagnostics Program.

Current Model of Care

Figure 2 summarises the generic model of care for patients with IMD (Inherited Metabolic Disorders) with a high-level indication of the variations at each of the defined phases of the patient journey

Figure 2: Generic Model of Care

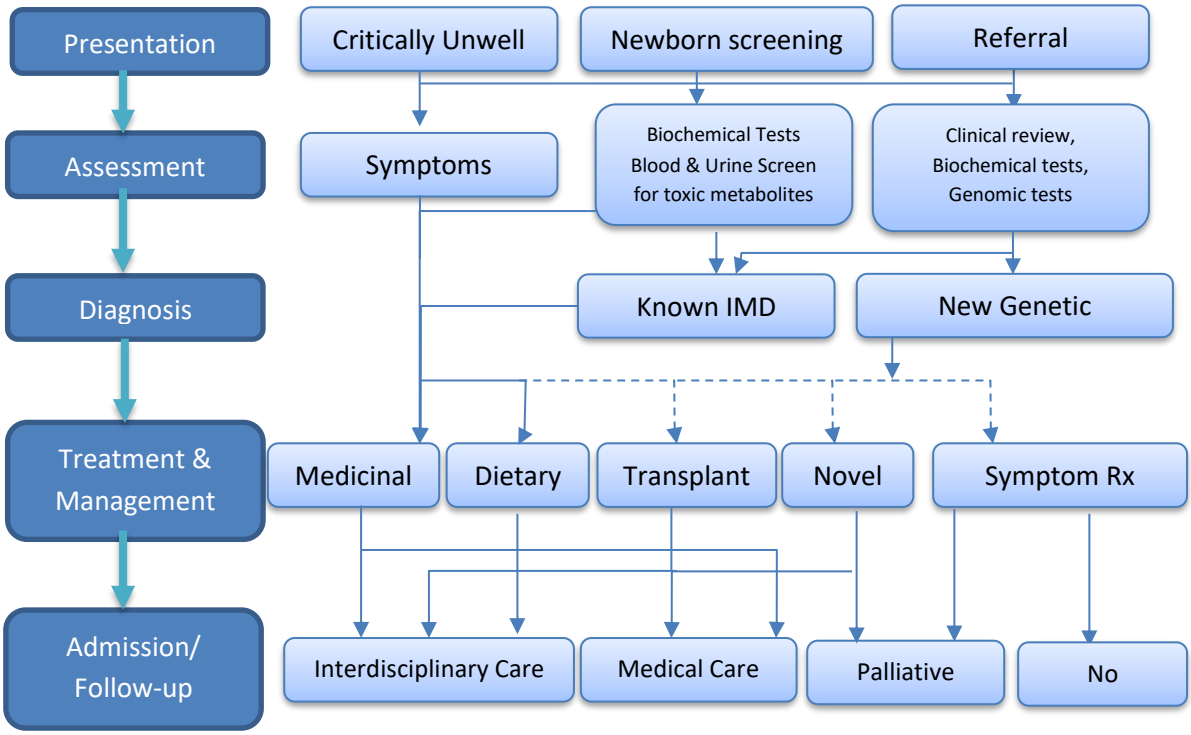


Table 1a: Services for GMDS patients are delivered through a combination of inpatient, outpatient, integrated, ambulatory services and health care in the home.

	CHW	SCH
Inpatient	Admitted under -GMDS staff specialist as AMO1 for management of acute metabolic deterioration. -Other Specialty area with 'GMDS' AMO2 for planned procedures etc **Specific conditions requiring immediate specialist laboratory assessment and at risk of decompensation admitted to CHW**	Patient Admitted under -General Medicine if present as acutely unwell with phone or in-person consultation from GMDS -Other Specialty area for planned procedures
Ambulatory • **Day only** • **Care by Parent**	Admissions As Above -Day only admissions for medical procedures including Enzyme Replacement Therapy under GMDS team -Care by Parent utilised as required for admission of rural and regional patients who require investigations, management/education and therapy over more than one day. E.g. new diagnosis, multi-team review (for MPS patients)	
Outpatient	2 interdisciplinary outpatient clinics per week -up to 3 GMDS Specialists - Currently 2 consultants; 1 paediatrician; 0.5 fellow. -up to 2 dietitians, 2 nurses and 2 social workers	1 outpatient clinic per week -up to 1 consultant, dietician and nurse
Outreach	Services to Hunter withheld due to staff shortages since 2016	
Integrated	Shared care with local paediatricians and GPs. (medical/dietetic/nursing/social work) Phone support provided for admissions to other hospitals (medical/dietetic/nursing) Local Health Districts providing Enzyme Replacement Therapy (medical/ nursing)	

Table 1b: Summary of the high-level variations to the patient journey that are possible at each phase of the patient journey.

Phase of Care	Possible Variation	Description
Presentation	Critically unwell	Build-up of toxic metabolites resulting in metabolic crisis with symptoms requiring urgent medical and/or dietary intervention.
	Newborn Screening	Specific conditions identified through formal newborn screening program allowing early intervention and prevention of poor outcomes
	Referral	Referral for investigation of symptoms
Assessment	Symptoms	Routine assessment of presenting symptoms
	Routine Laboratory findings &specialised Biochemical Genetics	Specialist laboratory tests for blood and/or urine metabolites present in excess or not present are utilised to screen for the presence of an IMD and/or to monitor treatment effects.
	Genetic Sequencing	Screening for genetic mutation – known or unknown condition
Diagnosis	Known IMD	IMD previously identified genetic mutation or variant of condition effecting the same enzyme process
	New Genetic Mutation	Mutation or gene previously unreported
Treatment and Management	Medicinal	Commence medication: to block the effect of toxic metabolite of reduce production of metabolite; direct effect or as cofactor for enzyme or enzyme replacement therapy
	Dietary	Modified diet therapy through which macro or micronutrient intake is required to either suppress production of toxic metabolite or increase presence of required agent. Varied dietary management for each different clinical condition requires intensive assessment and education for families, specialised and prescription food products
	Transplant	Organ transplant options considered for conditions affecting prognosis such as liver, kidney and haematopoietic stem cell transplantation.
	Novel Therapy	Treatment of new or variant gene / mutation causing symptoms. Treatment identified as experimental due to dearth of clinical/research findings to support therapeutic use. Ethics submission recommended for new or experimental therapy
Admission & Follow up	Interdisciplinary care	Monitoring and adjustment of medicinal and/or dietary therapy. The complexity of many metabolic conditions requires a range of specialty consultations, broad group of allied clinicians and nursing, along with specialist laboratory services. Care coordination by nurses in MDT.
	Medical care	Medical only management
	Palliative care	Some genetic metabolic conditions are not able to be cured and many have a life limiting impact on patients.
	No therapy	Where Genetic conditions are novel and/or no known therapy is available, or the genetic variant does not have a known or identifiable effect on health

Due to the nature of this patient cohort, the pathway to care for an individual patient, often has a unique combination of the possible variations, and the sequence often not linear in nature. The following cases are examples of the complexity of the genetic metabolic cohort (Cases 1-3).

Case 1: Newborn Screening

In 2017, a newborn baby was referred from a hospital on the NSW south coast to Canberra for a surgical cause of vomiting. When the baby was in the helicopter, a metabolic doctor was contacted and advised transfer to CHW based on calculations from the blood gas (anion gap). Within hours of arrival a diagnosis of severe Methylmalonic aciduria (MMA) was made, and life-saving treatment was started. The child is now normal at 5 months. The diagnosis was made by reconciling the newborn screen result, the baby's clinical condition and the confirmatory urine metabolic screen simultaneously. It could have been very different if the child did not get to CHW time – these patients often die.

Newborn screening patients can fall into one of three pathways: a) acute care in NICU or PICU e.g. MSUD, MMA and PA; b) Short admission for investigation ego PKU and c) urgent outpatient review e.g. MCAD. Once the acute phase is treated, the patients are managed in an outpatient interdisciplinary model (at varied levels of intensity depending on the condition and age of the child)

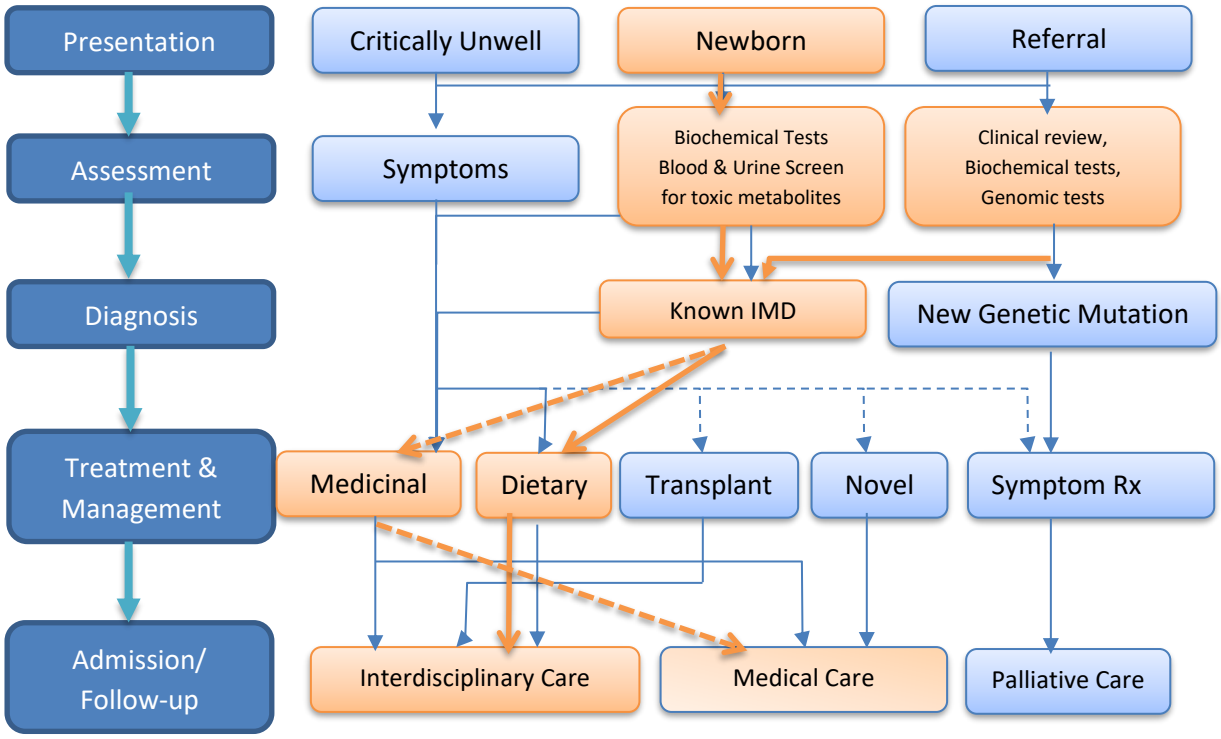


Table 2: Inpatient data for PKU, MCAD and Galactosaemia patients 2016-2017
(*Most MCAD admissions around NSW are not in SCHN, but in regional hospitals with management advice provided 24/7 by GMDS-SCHN*)

Year	Condition	Unique MRN	Episodes	NWAU Average	LOS Average (d)	Max NWAU	Max LOS (d)
2016	PKU	7	9	1.4	1.4	4	5
	MCAD	3	4	0.77	1.5	1.3	3
2017	PKU	5	7	1.1	1	1.2	1
	MCAD	10	13	1.2	3.3	7.6	10
	Galactosaemia	2	4	1.8	3	2.9	8

Maple syrup urine disease (MSUD) may be recognised on newborn screening or present acutely later in life depending on severity of the condition.

MSUD is one of several metabolic conditions in which fasting, eating a high protein load or becoming 'catabolic' especially when unwell presents a high risk of acute decompensation or rapid deterioration at any age requiring admission.

Table 3: Inpatient data for MSUD patients 2016-2017

Year	Unique MRN	Episodes	NWAU Average	LOS Average	Max NWAU	Max LOS	Non- GMDS Admitting Specialties
2016	7	16	5	6.4	44.5	40	Gastroenterology Gen Surgery
2017	4	12	11	11	92.4	110	Gastroenterology Gen Surgery Gen Med

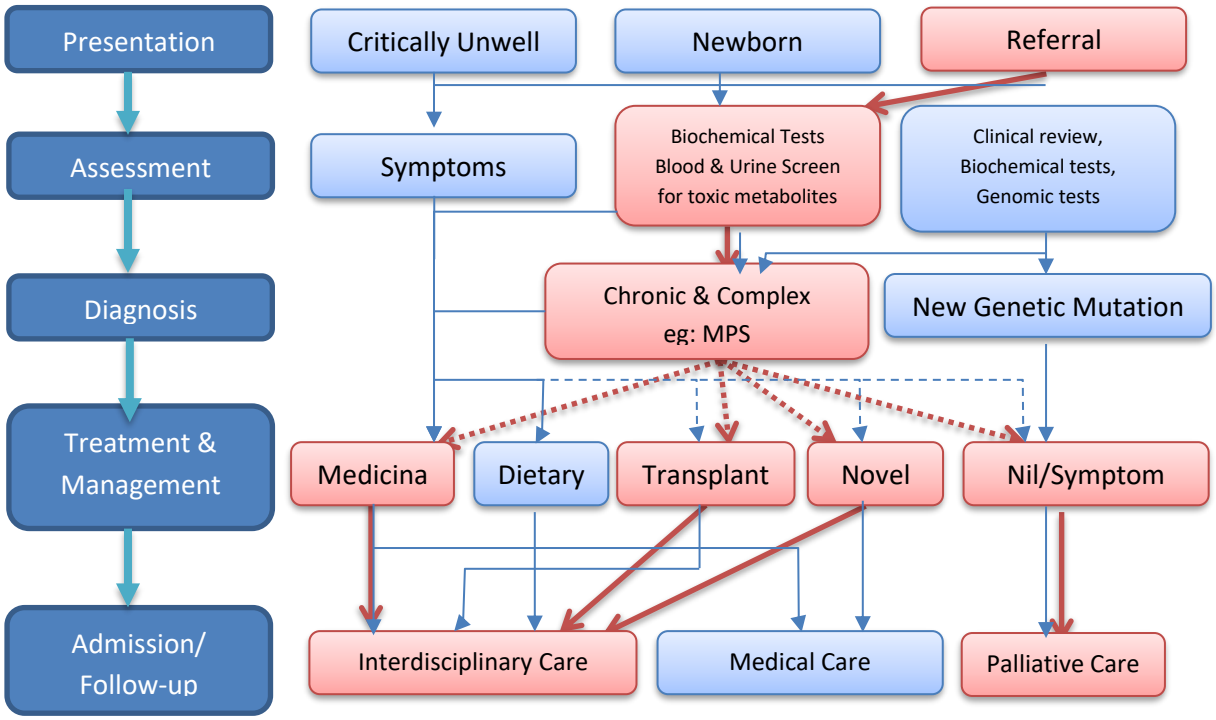
Along with MSUD there are a group of metabolic conditions who are at risk of immediate decompensation and becoming critically unwell including MMA, PA, OTC, ASA, CPS, GA I, and MADD

The Interdisciplinary model referenced later is applied to these newborn screening cases. This usually incorporates an intense specialised diet based on diagnosis, requiring senior dieticians with a thorough working knowledge of dietetic principles. Dietetic mistakes could lead suddenly to catastrophic consequences; hence providers need to be highly skilled. The senior nursing team engage in disorder education for the family, pre-empting processes for subsequent acute admissions, monitoring requirements and liaise with local medical and healthcare services. All conditions are genetic, and there may be genetic implications for the family which is currently counselled by staff specialists. Breaking all this news to a family with a newborn baby, can often destabilise a family, particularly for rare diseases without established community awareness, supports or networks. Hence the social adaptation of the family to the news and how it can be managed is an imperative task of the social worker.

Case 3: Complex Chronic Conditions

Will is a 3.5 year old boy living in a housing commission flat with his 20 year old mother. Will has been seeing a paediatrician since the age of 8 months for global developmental delay, a cardiac condition, chronic diarrhoea, severe hearing loss, poor swallow requiring modified diet and thick fluids, spinal deformities and respiratory stridor with airway obstruction requiring overnight CPAP.

A urine metabolic screen was positive for GAGS by the NSW Biochemical genetics laboratory at CHW. Upon speaking with the paediatrician, the Metabolic Consultant identified that Will was likely to have MPS II and arranged an inpatient admission for definitive diagnosis. Treatment could be bone marrow transplant, enzyme replacement therapy, or consideration of symptomatic treatment with palliative care. Regardless of the treatment path, management Will is likely to require long term monitoring for multiple associated morbidities including seizures, cervical spine stenosis and cardiomyopathy.

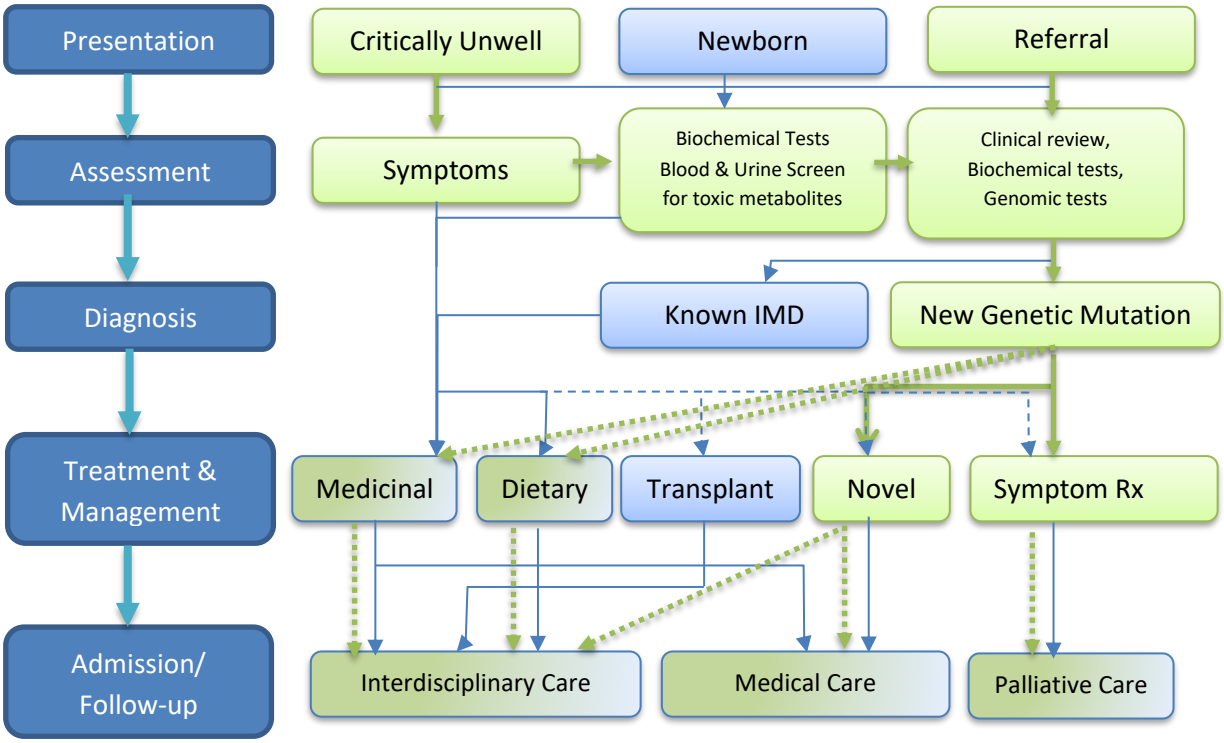


GMDS oversee the co-ordination of care for this complex and chronic diagnosis, which requires input from a broad range of specialists including; Respiratory Medicine, ENT, Anaesthetics, Orthopaedics, Cardiology, Ophthalmology, BMT and Allied health. Care coordination is typically performed by senior nurses with supervision from staff specialists.

Table 4 Inpatient data MPS disorders 2016 and 2017 MPS patients have a large number of episodes for a small cohort of patients; reflective of treatment with Enzyme Replacement therapy along with long admissions for more complex acute illness or bone marrow transplant in a smaller number.

Year	Unique MRN	Episodes	NWAU Average	LOS Average	Max NWAU	Max LOS
2016	34	349	0.44	1.12	5.5	6
2017	34	351	0.84	1.97	57.2	128

Case 4: Novel Gene or Genetic Mutation.



Finding a novel genetic disorder often comes with the hope that an intervention will make a difference to the lives of patients. In 2017, four referrals were made to GMDS specifically for treatment of novel disorders. This is over and above requests of novel treatments for known disorders.

The options available to patients found to have a novel disorder are; i) commencing a bespoke treatment and self-regulation by a clinician, ii) investigator led clinical trial with ethics approval or iii) no treatment offered for these patients.

The preferred option of treatment with novel therapy through investigator-led clinical trials is a resource intensive initiative and requires research ethics submission, literature review, consultation with international specialists, and development of trial protocol for assessment, monitoring and intervention.

Senior staff specialists need to supervise clinical trial activity, as the conditions are rare and complications of therapy may be unusual. Staffing for GMDS at senior level has been compromised by the departure of 2 senior professors in 2016 into full time clinical research – one as a genomic researcher at Murdoch Children's research Institute and the other at our Kids Research Institute. Whilst one of these roles was replaced, the incumbent has not been able to contribute to the clinical service since July 2017. This has put additional strain on the 2 remaining senior specialists to supervise novel therapy implementation.

In order to fulfil the potential of national and state genomic objectives, SCHN-GMDS proposes creating a clinical trial infrastructure to support such approaches to novel therapies.

Activity

A summary of the current reported level of metabolic activity across the two main hospital sites within the SCHN, Westmead and Randwick.

Table 5: Demographic Profile of Patients accessing GMDS services (2013-2017)

(not including 97 Rett patients at CHW)

	CHW	SCH	SCHN
Active Patients (n) (as of DATE)	618	103	721
Average Age (years)	9.1	7.7	8.9
• Metro LHDs	439	85	524
• Rural and Regional LHDs	153	10	163
• NSW	2	1	3
• ACT	19	7	26
• Interstate	2		2
• OS	3		3

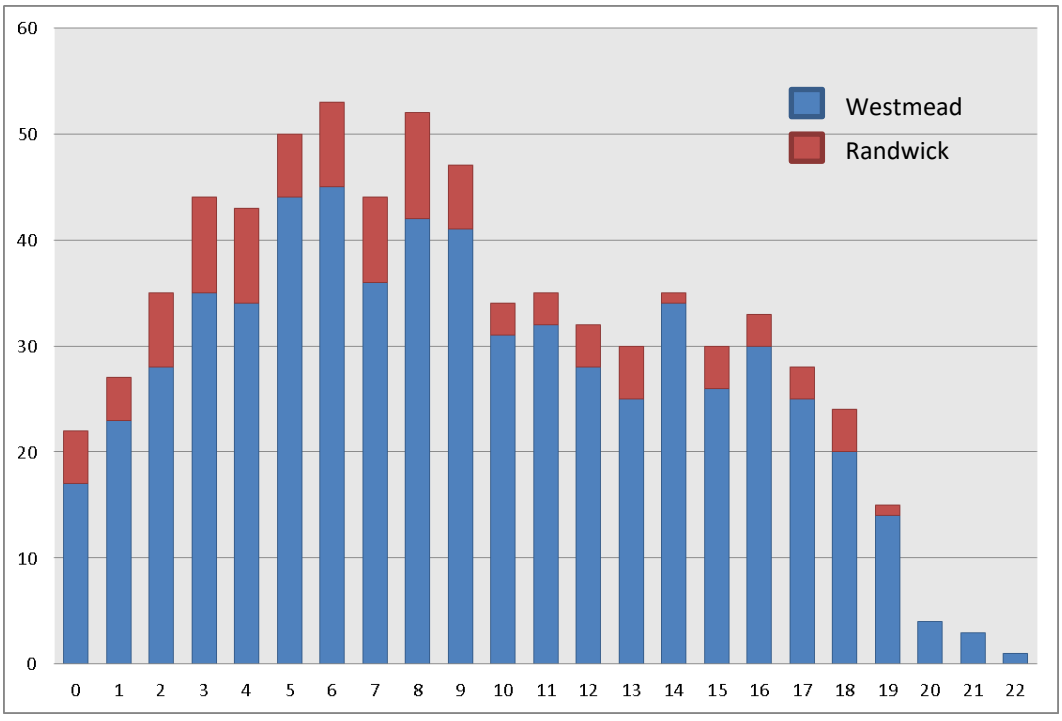


Figure 3: Age Distribution of GMDS patient cohort (2013-2017)

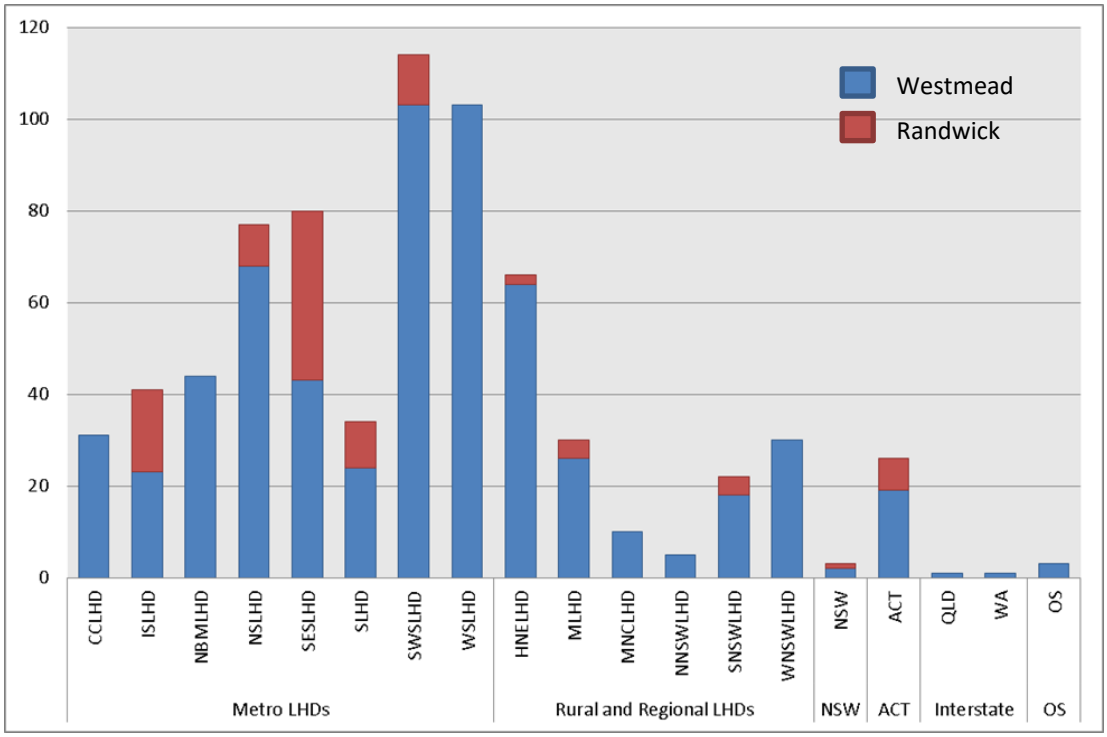


Figure 4: Geographical Profile for GMDS Patient Cohort SCHN

Whole genome sequencing has led to precise identification of genetic metabolic disorders, which has in turn resulted in an increased knowledge of conditions and thus an increased number of referrals for investigation since 2010. Over the past two years, the GMDS service has received approximately two hundred and seventy referrals each year, more than 100 more per year than 10 years ago.

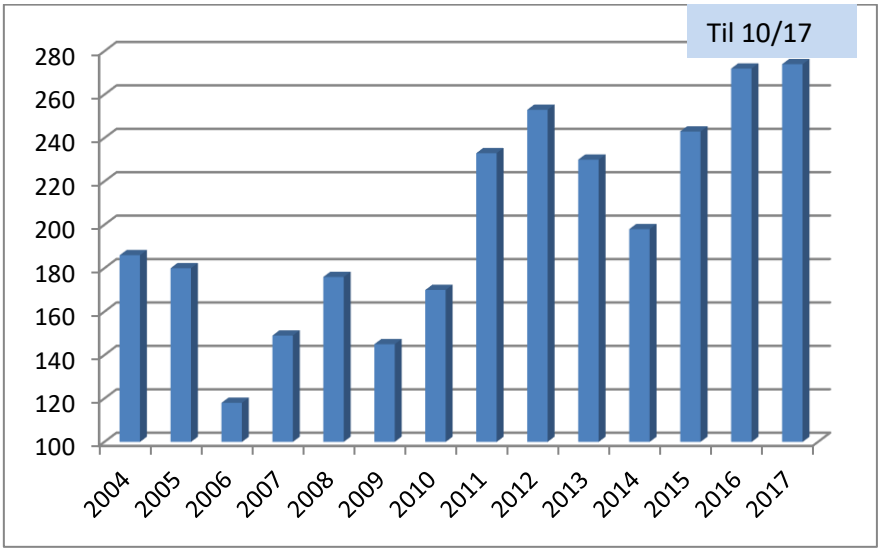


Figure 5: Referrals to GMDS-Westmead 2004 -17 (written and consultation requests). Source intake data lists.

Inpatient Activity

Table 6: Summary of Inpatient Activity by Facility

	CHW		SCH	
Year	2016	2017	2016	2017
No Patients (Unique MRN)	113	127	26	25
Episodes	660	642	59	91
Average LOS (Days)	2.1	3.4	3.8	2.1
Sum of LOS (Days)	1385	2173	223	188
Average NWAU	1.13	1.59	1.95	1.05
Max NWAU	51.41	92.16	46.56	16.95
Estimated Combined Admission Cost	$ 4,142,125.45	$ 3,407,439.41	$ 1,029,757.88	$ 228,535.55

Data limitations (likely under-representing activity)

A) Activity mapped to GMDS is limited to SCHN– based on MRN of patients serviced who have been admitted in 2 years. Hence services outside of SCHN not identified.

B) Static data used for retrospective analyses ie a cohort at a given time meaning that patients that came in and of service over the search period may not be presented including those that were treated extensively and died, transitioned or discharged from clinical service.

C) Limitation – unable to track AMO1 vs AMO 2 and frequency of consults ie 1-2 times per day for unwell metabolic- some patients may be seen 4 or 5 times a day in acute phase.

Figure 6: CHW Inpatient Average Length of Stay compared with number of separations by financial year 2005 – 2015

The increase in inpatient separations since 2010 is reflective of the improved identification of patients with genetic conditions. The reduced average length of stay is likely to be due to a number of factors including day only admissions and increased phone management of patients at home by MTD, meaning that sick patients have treatment changes at home managed by GMDS.

Table 7: Summary of NAPOOS for Metabolic Patients (By Unique MRN) by Facility, Professional Group and Calendar Year (2013-2017)

CHW		2013	2014	2015	2016	2017
Medical	Metabolic Medicine	1452	1312	1335	1691	2022
	Medical Specialists Other			6	454	433
	Surgical Specialist Care				117	145
	Medical Junior		182	348	738	140
Nursing	Nursing	207	403	221	1410	1653
Allied Health	Dietetics	566	710	435	2132	1937
	Social Work		1	4	113	191
	Physiotherapy				159	220
	Occupational Therapy				132	184
	Other Allied		1		260	377
CHW TOTAL		**2225**	**2609**	**2349**	**7206**	**7302**
SCH		**2013**	**2014**	**2015**	**2016**	**2017**
Medical	Metabolic Medicine	84	73	73	170	185
	Medical Specialists Other				114	87
	Surgical Specialist Care				7	25
	Medical Junior				5	15
Nursing	Nursing	75	52	54	164	220
Allied Health	Dietetics	50	42	46	146	132
	Social Work		1		51	45
	Physiotherapy				31	77
	Occupational Therapy				42	13
	Other Allied	2			89	66
SCH TOTAL		**211**	**168**	**173**	**819**	**865**

Outpatient Activity: Core Team

Figure 7: All NAPOOS Activity by calendar year 2013-2017 for Key Disciplines in Metabolic Clinical Team for a) CHW and b) SCH

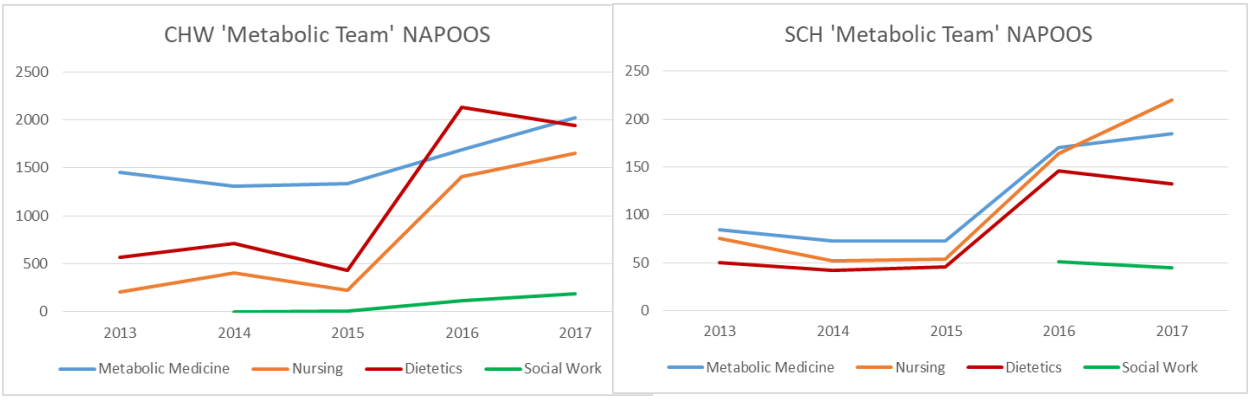


Table 8 : Summary of NAPOOS for Metabolic Patients (By Unique MRN) by Facility.

Nursing and dietetic services have vastly increased taking burden off medical team although it is likely that medical data from telephone under-represented in 2016 and 17.

Professional Group and Calendar Year (2013-2017)

MEDICAL		2013	2014	2015	2016	2017
FACE TO FACE	CHW	761	930	1021	1256	1247
	SCH	84	73	73	170	185
TELEPHONE	CHW	680	371	299	214	143
EMAIL	CHW	11	11	15	221	632

DIETETIC		2013	2014	2015	2016	2017
FACE TO FACE	CHW	431	476	247	672	597
	SCH	47	41	45	132	117
TELEPHONE	CHW	113	191	125	996	968
	SCH	1			12	13
EMAIL	CHW	22	43	63	464	372
	SCH	2	1	1	2	2

NURSING		2013	2014	2015	2016	2017
FACE TO FACE	CHW	119	175	83	1016	1295
	SCH	69	52	54	141	181
TELEPHONE	CHW	77	184	100	307	280
	SCH	6			20	32
EMAIL	CHW	11	44	38	87	78
	SCH				3	7

Table 9: Summary of NAPOOS (Tier 2) Outpatient Activity by Facility and Specialty Area for Metabolic Patients (identified by unique MRN) for 2016-17 calendar years

	2016		2017	
Medical Specialities	**CHW**	**SCH**	**CHW**	**SCH**
Dermatologist		3	2	
Neonatologist	2		4	
Ophthalmologist	47	13	57	11
Cardiologist	59	10	22	6
Endocrinologist	23	4	14	4
Gastroenterologist	69	5	70	1
Haematologist	3		2	
Immunologist / Allergy Specialist	7		6	
Infectious Diseases Physician	1			
Medical Oncologist	54	32	96	6
Neurologist	37	24	32	39
Palliative Care Specialist	23	2	15	1
Paedodontist	2			
Pain Management Specialist			1	
Rehabilitation Specialist	43	10	52	9
Renal Medicine Specialist / Nephrologist	15		13	1
Respiratory Specialist	21		24	1
Rheumatologist	4		2	
Sexual Health Specialist	3			
Sleep Medicine Specialist				2
Urologist		3		2
Surgical Specialties				
Neurosurgeon	1	1	3	
Oral & Maxillofacial Surgeon	1	2	2	7
Orthopaedic Surgeon	87		105	6
Otorhinolaryngologist (Ear, Nose & Throat)	16		17	
Paediatric Surgeon	10	2	17	9
Plastic & Reconstructive Surgeon	2	2	1	3

Table illustrates the broad range of Medical and Surgical specialty areas across the Network who are required to provide care to the complex Cohort of Metabolic Patients.

Table 9: Summary of NAPOOS (Tier 2) by Facility and Procedure Type for Metabolic Patients (identified by unique MRN) 2015-2017

Procedure Clinic Activity	Dental	Minor Medical Procedure	Parenteral Nutrition Delivery	Enteral Nutrition Delivery	Ventilation
CHW	33	20	74	21334	639
SCH		50		3017	

Medical On Call

At SCH on-call cover has been provided by Clinical Genetics Services. Several staff specialists have opted not to participate in the on-call roster as this falls outside the scope of practice of most Clinical Geneticists. One Clinical Geneticist left SCH partly because of the onerous GMDS on-call commitment. The SCH service has historically only received 0.5 FTE dedicated staff specialist funding and 0.4 FTE dietetic support, with all other resources informally provided by Clinical Genetics staff. This has been an incredibly generous commitment of the SCH service to support a group of patients with high needs, but remains an unsustainable long-term model with sub-optimal governance.

In 2015, CHW had 4 consultants providing on-call service 1 in 3. In 2016, two of these staff left with one replacement and subsequent to July 2017, this replacement has not contributed to the clinical service. This has left the consultant workforce vulnerable with only 2 specialist consultants providing on-call services. The recruitment of a general paediatric staff specialist has helped provide on-call provision but they still require supervision. This means that the 2 remaining specialists still provide a 1 in 2 on-call service which is not sustainable. The model was implemented across the network with clinical 2 genetics consultants providing cover but this too is not sustainable as the clinical geneticists are operating outside their normal scope of practice.

Research

The therapeutic landscape continues to become more accessible to more patients. Gene therapy is now a reality in Australia with MPS IIIa gene therapy trials having commenced in Adelaide. Professor Ian Alexander, SCHN-GMDS has developed gene therapy for OTC deficiency, a severe often fatal neonatal disorder. (Lisowski 2014).

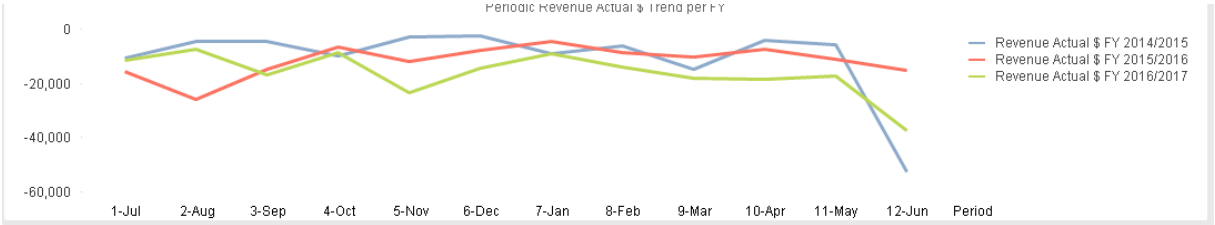
The capability of performing clinical trials in SCHN-GMDS does not exist, with products developed by our team not being utilised for translational research in Sydney. Opportunities for research involvement have been taken up by the SA and Victorian metabolic services. The huge media interest of the Charlie Gard case in UK could easily occur within SCHN. GMDS- Randwick has already been approached to utilise the controversial nucleoside therapy advocated for Charlie Gard (Garcia-Diaz et 2014). In response to this type of enquiry, onerous literature searches, contact with overseas physicians, trial protocol assessment and potential implementation need to be carefully considered.

Since October 2013, GMDS - CHW has participated in commercially sponsored trials for LSD patients. This has allowed the appointment of a part-time research nurse and fellow from “soft money” to help manage trial patients. The GMDS staff specialists are unable to commit to further clinical trials due to time constraints hence the research fellow position has lapsed.

In the last 6 months, the service has been approached formally with 6 contract disclosure agreements (CDAs) to conduct clinical studies, some of which are novel therapeutics. There are a number of informal discussions that have also occurred related to gene therapy for MPS, Rett syndrome and ALD, RNA therapy for MMA, small molecule therapy for Creatine transporter defect, PKU and CDG type 1A. Hence the service is not braced for this research therapeutic onslaught. A research infrastructure is urgently required. This will lead to further investment of clinical research at SCHN and NSW, rather than other states or countries.

Cost Benefit Analysis

SCHN-GMDS is a state-wide resource for genetic metabolic investigation and treatment. Consultations occur from a wide range of sources. These include parental requests, specialist referrals, laboratory result interpretation and from the state-wide newborn screening service and Biochemical Genetics laboratory. Feedback from TRIM REF SCHN 16-2269 was for GMDS to better map referrals in order to facilitate appropriate billing. Despite a period of extreme difficulty with staff movements, revenue has increased by 50% compared to 2 years ago. This has occurred by utilising appropriate billing codes and using the multi-disciplinary team more effectively for billing purposes.



Periodic Revenue Actual $ per FY

Period	1-Jul	2-Aug	3-Sep	4-Oct	5-Nov	6-Dec	7-Jan	8-Feb	9-Mar	10-Apr	11-May	12-Jun	Total
Actual $ FY 2014/2015	-10,833	-4,699	-4,619	-9,772	-2,672	-2,664	-9,020	-6,178	-14,868	-4,190	-5,574	-52,681	**-127,770**
Actual $ FY 2015/2016	-15,645	-25,966	-14,607	-6,571	-11,738	-7,941	-4,404	-8,629	-10,361	-7,229	-11,194	-15,356	**-139,642**
Actual $ FY 2016/2017	-11,539	-7,548	-16,889	-8,495	-23,421	-14,303	-8,977	-14,054	-18,236	-18,637	-17,154	-37,477	**-196,730**

Figure 3 Revenue for GMDS- Westmead. (Source CHIMP)

Future Model of Care

The mode of operation and models of care of GMDS include extensive medical management, specialised dietary manipulation, acute in-patient management, acute out-patient management, chronic disease complex care and extensive therapeutic input.

Staffing

Worldwide, best outcomes are achieved by flexible acute care being delivered directly by trained multi-disciplinary staff. It is not possible to provide the same model of care at both SCH and CHW without resource duplication; hence a combined service model utilising the same staff at both sites is preferable and more cost effective. SCHN-GMDS will provide a NSW and ACT state-wide service. A summary of the staffing required to form and sustain an 'SCHN GMDS' service outlined in table 10.

Ambulatory Service

The outpatient service at SCH is planned to be increased to 3 days per week (from 1 day) when the full complement of staff is practicing to allow consultation target timelines to be reached. The aim is to also have a dedicated 1.0FTE nurse practitioner, on site at SCH as well as periodic attendance of the remainder of the SCHN GMDS workforce. At CHW where the state-wide high risk metabolic clinical service is located, during standard working hours, there would be Consultant, senior nurse, fellow, and dietetic cover for acute admissions.

Admissions

Admissions at SCH continue to be under general paediatric care. At CHW for primary metabolic therapy, GMDS will continue to be AMO1, but when there is no specific metabolic therapy other teams are primarily involved. The range of conditions with a major metabolic component are vast. Conditions such as mitochondrial respiratory chain disorders which currently have no specific therapy and are likely **not** to have GMDS AMO1. GMDS will consult when referred non-AMO1 patients. The approach to inpatient care is carefully examined on a case by case basis, for the less complex cases the SCH-based metabolic patients who are under a shared-care model is appropriate, but if complex with specific metabolic investigation and therapy, GMDS should be AMO1 and the patient transferred to CHW.

Consultations

New consults are to be seen as quickly as possible, based on the perceived urgency, including in CICU at SCH and the NICU at RHW (general requirement is that non-urgent consults are seen within 24 hrs. of receiving the request for a consult, and urgent consults (PICU/NIU) seen within 4 hrs, (usually handled, at least by phone, within the hour).

On-call

The GMDS consultants have provided first on-call cover for many years in the absence of dedicated and funded training positions. In 2016 0.5 FTE fellow assisted but could only provide 1 in 4 cover for GMDS. On-call is unstainable in the short-term with the current consultant staff.

Currently of the 3.8 FTE staff specialists, 1.0 FTE Staff has not contributed to the clinical service since July 2017 and 1.0 FTE is being filled by a general paediatrician who has been working with the GMDS since August 2017. This person requires supervision by the other 2 specialists. Hence there are only 1.8 FTE staff specialists in metabolic medicine in NSW.

1.0 FTE Staff Specialist urgently needs to be employed.

A further 1.0 FTE staff specialist will be required to accommodate future expansion of GMDS as outlined within 3 years. Alternative arrangements utilising the support of clinical geneticists from Randwick has not been successful; hence recruitment of 1.0 FTE dedicated metabolic specialist is required. A training post supporting the acute service is also required. Moving in the long-term to a network model across both sites, this would best be served by 2 people on-call, which should require 6 people to staff. This should comprise a minimum of 3.8 FTE consultants and 2 metabolic fellows across the network to provide a legally safe on-call structure.

Outpatient services

Current outpatient services will continue. The waiting time at CHW currently runs at 4 – 6 months for the senior consultants. Hence there should be further opportunity for expansion of services, particularly for transitional patients in the Bright Alliance Building and proposed new spaces at CHW. Phenylketonuria has hitherto only be managed at CHW but patients can be seen at SCH and some patients may be transferred with appropriate dietetic support.

Outreach Services

GMDS Westmead has provided out-reach services to Hunter Clinical Genetics service, but this was withheld in 2016 due to staffing shortages. When there is a full complement of staff, this will be renewed and further regional out-reach clinics can potentially be sourced by mutual LHD agreement.

Transition Services

The paediatric and adult genetic metabolic services have not been able to engage effectively in transition services, with the adult metabolic consultant seldom being able to meet families prior to transition. This has occurred due to the time constraints of the one adult metabolic consultant and two paediatric metabolic consultants. With improved funding of both services, transition is planned utilising the commissioned Bright Alliance clinical area and the proposed Westmead clinical area.

Training and development

GMDS practices an acute and chronic model of care in medicine and has been of interest to trainees trying to understand biochemical and physiological principles. The service engages in education at all levels – under-graduate, allied health, across paediatric sub-specialities and post graduate research. The interface with biochemical, newborn screening and genetics laboratories allows trainees to understand modern diagnostic and therapeutic methodologies. The difference between clinical and research therapeutics is also seen. Hence training in GMDS can leave non-vocational trainees with transferable skills applied to other areas of medicine. In particular, the design and conduct of clinical trials can be taught in GMDS, improving clinicians knowledge of clinical research in practice.

Interdisciplinary care

Traditionally staff specialists provide diagnosis, however ideally for all diagnoses, a multi-disciplinary team (MDT) should be present when staff specialist first “break the bad news” of a diagnosis. The high morbidity and mortality rate, complexity of care, rare nature, multi-cultural clientele and lack of community resources for this group of patients put them at higher risk for psycho-social stressors than many other disorders. TRIM REF SCHN 16-2269 provided temporary funding leading to a change in the model of care. An interdisciplinary team working together is more likely to identify psycho-social stressors which could lead to misunderstanding or poor compliance from patients.

New patients should ideally be admitted as a day only patient (if clinically stable) to allow the team to get to know and educate the family. This would also reflect actual activity incurred by such patients. The PKU model requires a 24-hour admission for a medical procedure to further investigate if treatment is primarily dietary or requires specific medications. A model similar to the Diabetes Day program would be appropriate for this patient cohort allowing families’ time to adjust to diagnosis and ask questions – but the psycho-social assessment can be more complex, without community resources and clear treatment paradigms and varied decision-making processes.

Dietetic

Current metabolic management plans designed for use by families have been significantly simplified over recent years. This supports management at home but has only been possible because of the

depth of clinical dietetic expertise available at SCHN. Metabolic dieticians therefore, often act in isolation of other dietetic services without the security of international evidence or practice guidelines. Hence a well-trained pro-active independent dietetic workforce is required. For many conditions, dietary management is life-saving treatment. Staff are functioning at a high level often autonomous of senior dietetic supervision as the knowledge of the extreme dietary differences of rare metabolic disorders is not widely known. Hence the recommendation for appropriate grades for practice is being made with senior dieticians training junior ones.

In an attempt to address the need for practical food education of patients and their families to facilitate compliance with management of their metabolic condition, a 0.5FTE Nutrition Education assistant has been employed, funded from pharmaceutical company donation. This role significantly enhances patient compliance through practical application of diet management taught to the families by the dietician's. This was funded temporarily in TRIM SCHN 16-2269 and should be permanent.

Nursing

The combined 1.4 FTE clinical role of the nurses at CHW encompasses complex patient case management (education of patients, families and staff, co-ordinating and planning admissions, discharges, transfers and investigations, management of central venous access lines, pre-emptive identification of problems and liaison with local, state and national services and implementation of evidence-based nursing. The service provides the department an early warning system. New therapies over the last 20 years has meant extensive support for patients who would not have survived in the past. In particular, there are a range of hospital and federal systems where the CNCs coordinate assessment programmes and assist in the collation and submission of data required annually. For example, patients with lysosomal storage disorders requiring enzyme replacement therapy (ERT's). When the additional CNC 0.4 FTE was created, only 2 patients were receiving treatment with ERT, now however 40 patients have been through the programme, 9 of whom had stem cell transplants. There are currently 28 patients with lysosomal storage disorders being treated with ERT by GMDS. For these high cost drugs regulated by the Federal Government's Life Saving Drugs Program, regular clinical review and annual assessments by multiple medical teams and reports to the Federal Government are required. Continuity in co-ordination of assessments and data submission is imperative. The treatment landscape to continues to change as the number of clinical trials in progress into development of new treatments for children with metabolic conditions.

Last year, the second CNC role at Westmead was enhanced temporarily per TRIM SCHN-17-935. This has helped nursing continuity and support tremendously with greater capacity for transitional support and case management.

Creation of a nurse practitioner (NP) role at SCH allows continuity of service when metabolic staff specialists are off site. A NP can work independently within a defined Scope of Practice which is important when there is no medical support on site. The NP will prescribe medications, intravenous fluids, order routine investigations, liaise with other sub-speciality teams, and review patients. These are tasks which are essential for the daily functioning of the metabolic service and cannot be performed by a CNC. With the recent commencement of enzyme replacement therapy (ERT) at SCH, Randwick it has become essential for someone to be present 1.0 FTE to coordinate and manage the infusions. There will be particular opportunity to expand outpatient clinics led by the NP.

Social Work

The high morbidity and mortality rate, complexity of case mix, rare nature, multi-cultural clientele and lack of community resources for this group of patients put them at higher risk for psycho-social stressors than many other disorders. Effective community support structures do not as yet exist for patients with rare diseases and it is challenging to have referrals to accepted closer to home. By contrast there are established systems for patients with autism, cancers or cerebral palsy.

Some patients are at risk of acute decompensation as the demographics have shifted with several non-English speaking families so education from a dietetics, nursing, medical and social work is not simple. These patients are fragile and complex with tailor-made treatments which are difficult to convey to families with limited skills. In some cases the carers are illiterate and innumerate in their own language. If there is ongoing noncompliance with the treatment plan including dietary restriction it is considered medical neglect and reportable to Family and Community Services in the interests of the child. GMDS makes several such notifications every year. *GMDS is resourced to identify these crises but not to prevent them.*

Ideally (like diabetes and CF), new patients should be admitted to allow the team to get to know and educate family. This would also reflect actual activity incurred by such patients. The PKU model, for a non-acute disorder, actually works well with a 24 hour admission allowing families' time to adjust to diagnosis and ask questions – the admission occurs for a medical procedure but the psycho-social assessment is much more complete. Further investigation is required to identify if a model similar to the Diabetes Day program would be appropriate for this patient cohort where the patient is admitted a week and have a multidisciplinary approach to managing. Currently GMDS is not staffed or has the facilities to undertake such a program.

If GMDS 0.4 FTE is compared to areas within the Social Work Department such as Diabetes 2.0 FTE social workers attached to the service with a patient cohort of 850. GMDS has approximately has approximately the same cohort. Spina bifida have 350 patients and 1.0 FTE social worker.

Genetic Counsellor

Genetics services across the world are dealing with huge amounts of data generated by novel methodologies in genomic testing, most particularly whole genome sequencing. Historically, GMDS did not perform extensive genetic testing, relying primarily on biochemistry but the availability of novel testing has made this prevalent in the clinical arena. Testing of several genes can lead to variant of unknown significance (VUS) and sometimes produce unexpected genetic changes in other non-targeted genes. GMDS staff are finding that more of their time is spent counselling for these issues prior to testing and dealing with results when available. GMDS has several staff including staff specialists who are not clinical geneticists and hence need the assistance of an experienced genetic counsellor. Furthermore, mitochondrial respiratory chain disorders have non-Mendelian inheritance patterns requiring more intricate counselling. Given the intensity of the management of patients and the range of inheritance patterns and variants being dealt with, similar to other roles in GMDS a genetic counsellor level 3 would be appropriate.

Research

GMDS SCHN and Westmead Adult Hospital remain the only dedicated therapeutic genetic services in NSW. All GMDS related clinical trial activity has occurred at the Westmead sites. Clinical trial procurement and management is a laborious exercise and requires personnel with time and experience to manage. Subsequent to a series of liver transplants due to life threatening metabolic disorders, Professor Ian Alexander has developed novel gene therapy for one urea cycle disorder, OTC deficiency with the potential for further development. Clinical trials are envisaged overseas using Professor Alexander's technology, but SCHN GMDS does not have the human resources to commit to such trials. With the advent of whole genome sequencing, a range of novel disorders have been described by genetics services at both SCH, Randwick and CHW, Westmead. If there is a therapeutic element these patients are referred to GMDS meaning that the service has to ascertain therapeutic viability. This is best conducted within a human research ethics framework. GMDS has experience of investigator led clinical trials having brought products to the market with commercial partnership. Clinical trials for gene therapy in metabolic conditions have commenced in South Australia with patients referred from our service. Hence NSW has fallen behind in ground-breaking research. GMDS has recognised for several years the advent of the new genetic therapeutic environment and in 2017 has raised over $150,000 to provide seed funding for research infrastructure. This coupled with previous donated funds and trial surplus monies can be used to employ a research fellow and research administrator. Once research capability is established competitive and commercial grant procurement will be sought. This will bring income to SCHN.

Governance

GMDS is under the governance of WSGP at Westmead. The primary governance lies within the Diagnostic Division. Accountability will still need to occur to the Medical Programme at Randwick.

5 Year Plan

GMDS is at the forefront of genomic investigation and translational medicine. Conditions considered untreatable 20 to 50 years ago now seem reasonable candidates for definitive treatment. Staff required to manage these and participate in ground breaking interventional trials need to be employed in the next 5 years in order that NSW is able to deliver novel treatments and thrive in the novel therapeutic arena. Hence a comprehensive clinical service is required in order for new treatments to be integrated into a therapeutic regimen.

In order to realise potential, the paediatric and adult metabolic services should be designated state-wide services, which allow the services to operate across the state delivering local personalised care. The interface with the state-wide biochemical genetics laboratory and state-wide newborn screening service mean that these services should continue to be co-located.

NSW has the potential to lead other states in Australia in attracting ground breaking research to our shores. Implementation will allow NSW to demonstrate leaderships within the National Genomics Framework. At a federal level, that the specialty be recognised independently as metabolic medicine (genetic), which has been supported by the Peak Body – Australasian Society of Inborn of Metabolism. This would allow appropriate billing for the field.

Integration of new treatments into the theraputic sphere requires meticulous ethical consideration of the efficacy of such interventions. Some treatments may have biological plausibility but yet be an onerous imposition into a familiy's life without real clinical gains. Hence all treatments need to be

evaluated judiciously. Research treatments utilise objective measures such as 6 minute walk tests or neurosychometric tests to gauge efficacy. Hence in five years, the systematic use of occupational therapists, physiotherapists and psychologists within GMDS should be mainstream. Funding for these should be considered as they are already part of international gold standard services in Germany, The Netherlands and UK.

This business plan allows the springboard to deliver effective care in the paeditric setting, allowing interface with adult services and attract investment in NSW for clinical trials. It allows training and development for future metabolic and non metabolic trainees interested in delivering the NSW healths genomic strategy. Investment now in the clinical service would mean that in 5 years, a succession plan for current consultants could be implemented and investment in clinical trials will have been realised with a more comprehensive multi-disciplinary team under the stewardship of the five metabolic specialists acroos the state.

Summary Recommendations (GMDS services at both Randwick and Westmead)

1. 1.0 FTE staff specialist to be recruited nationally / internationally.
2. 1 FTE Metabolic Fellow working across SCHN - Provisional Fellow Level 4.
3. Dietician permanent 1.0 FTE level 3 (current 0.5 FTE permanent and 0.4 FTE level 2 temp)
4. Training grade dietician 1.0 FTE level 1 / 2 (per award) – new post.
5. Social Worker 0.3 FTE permanent level 3 and 0.7 FTE temp level 2 – to become permanent 1.5 FTE level 3 in 2018
6. Nutrition Education assistant-0.5 FTE- to become permanent 0.6 FTE in 2018
7. Admin support currently 1.0 FTE level 3 to become 2.0 FTE – 1.0 FTE level 3 enhancement.
8. Creation of 1.0 FTE nurse practitioner for SCHN Randwick.
9. Permanent funding of 0.6 FTE CNC (temp enhancement 2017/18 with established 1.4 FTE).
10. Creation of 1.0 FTE Genetic Counsellor level 3 for GMDS-SCHN.
11. Creation of research coordinator (Level 9 registered nurse) and 1.0 FTE research fellow temporary 1 yr from donated funds.

TABLE 10:	**Current SCH**	**Current CHW**	Enhancement Required	Comments TRIM REF SCHN 16-2269 provided temporary funding leading to a change in the model of care.
Medical- Staff Specialist FTE	0.2 FTE	3.6 FTE	Staff Specialist FTE enhancement of 1.0FTE immediately.	Currently of the 3.8 FTE staff, only 1.8 FTE recognised metabolic paediatricians are providing services. 1.0 FTE Staff specialist has not contributed to the clinical service since July 2017. 1.0 FTE is being filled by a general paediatrician who been working with GMDS since August 2018. This person requires supervision by the other 2 specialists. Alternative arrangements utilising the support of clinical geneticists from Randwick has not been successful; In the next 3 years if service growth and complexity continues, with continued new implementation of newborn screening, genomic diagnostics and novel therapeutics, a 5th staff specialist is envisaged.
Medical – JMO FTE		0.5 FTE	Enhancement of 1.0 FTE Provisional fellow to sustain workload and on-call at both sites. Complete funding deficit of STP programme for 0.5 FTE fellow.	In 2016 1.0 FTE fellow was appointed to cover both the paediatric and adult metabolic services at CHW and Westmead with 0.5 FTE dedicated to SCHN. The service has now supervised 3 fellows with feedback that the workload covering both adult and paediatric metabolic services is incredibly onerous. The model of 0.5 FTE fellow covering the entirety of GMDS across SCHN is not sufficient and will not be compliant with junior doctor working hours.
Social Work		0.3 (L3) Perm 0.7 (L2) Temp	1.2 level 3 permanent due to complex case mix and group work.	The enhanced staffing level has enabled better management of crises with social workers assisting with notification of risks of significant harm. Prevention and group work is feasible with current temporary staffing
Dietetics	O. 4 FTE level 3	0.46 FTE Level 6 0.4 FTE Level 5 1.0 FTE level 4 0. 4 FTE level 2 (temporary)	Enhance SCH, Randwick by 0.1 FTE level 3 Enhance CHW, Westmead to 0.5 FTE level 3 (from 0.4 FTE level 2) and made permanent. New post level 1 / 2 1.0 FTE dietician – training post.	Cover arrangements on a temporary basis at CHW and suitable staff have been appointed to the roles The service would operate across the network however primary sites will remain unchanged.
Nutrition Education Assistant		0.5 FTE Nutrition Education Assistant (temporary)	0.1 FTE enhancement for a Nutrition Education assistant Health Education officer – current temporary – made permanent. From 0.5 FTE temp to 0.6 permanent.	

Nursing	SCH, Randwick No FTE funded -	CHW, Westmead 1.4 FTE CNC – Permanent funding; CNC 0.6 FTE temporary	CNC 0.6 FTE made permanent 1.0 FTE nurse practioner	GMDS-SCHNursing support currently provided by CNC aligned to Clinical Genetics Department
Genetic Counsellor	Current Ad-hoc support from clinical genetics services	Current Ad-hoc support from clinical genetics services	1.0 FTE (level 4 – yr 2)	GMDS has several staff including staff specialists who are not clinical geneticists and hence need the assistance of an experienced genetic counsellor. Furthermore, mitochondrial respiratory chain disorders have non-Mendelian inheritance patterns requiring more intricate counselling. Given the intensity of the management of patients and the range of inheritance patterns and variants being dealt with, similar to other roles in GMDS a genetic counsellor level 3 would be appropriate.
Administration	SCH, Randwick all administrative services are provided by the Clinical Genetics administrative support	1.0 FTE level 3 admin officer (1.0 also paid for by biochemical genetics lab)	SCHN – 1.0 FTE level 3 admin officer.	1.0 FTE admin support level 3 was formally allocated to Professor Christodoulou who was substantially employed as a GMDS consultant but had wider roles particularly as Director, Western Sydney Genetics Program. Similarly 1.0 FTE level 3 admin support had historically been allocated to Professor Bridget Wilcken whose substantive employment was in GMDS but was also head of The Newborn Screening and Biochemical Genetics laboratories.
Research administrator and Fellow			Recommendation 1.0 FTE Provisional fellow and 1.0 FTE registered nurse level 9 (from donated funds) provisional 1 year	NSW has fallen behind in ground-breaking research. GMDS has recognised for several years the advent of the new genetic therapeutic environment and in 2017 has raised over $150,000 to provide seed funding for research infrastructure. This coupled with previous donated funds and trial surplus monies can be used to employ a research fellow and research administrator. Once research capability is established competitive and commercial grant procurement will be sought. This will bring income to SCHN.

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Appendix: Costing

GENERAL FUND

SUMMARY BUDGET BUILD UP FOR:

Description	Total current SCHN**	Total proposed SCHN	Enhancement required
Direct Costs to Department			
Salary and Wages incl annual leave, long service leave, shift penalties and allowances*	32,889	1,182,707	1,149,817
Overtime			0
TESL		33,000	33,000
Workers Comp	810	29,235	28,425
Superannuation	3,040	110,080	107,040
ERE On-cost 7.5%	2,755	71,394	68,638
Sub-total - ERE	39,495	1,426,416	1,386,921
Total Enhancement Allocation and Funding Source			1,386,921
Total Costing	39,495	1,426,416	
Total FTE's	- 0.32	9.64	9.32

* inclusive of shift penalties, management allowance and other allowances where applicable
***Oncall allowance and call backs have not been included in these calculations due to the lower material impact and predicted infrequency.

** Does not include CPI or award increases.

Proposed Structure

Roles	Position description	Salaries & Wages	Super	Workers Comp.	Impact	TESL	Sub Total	FTE
1.0 FTE Provisional fellow	Registrar, Fourth Year	135,097	12,487	3,327	11,318	-	162,229	1.08
Social Work level 3 1 FTE	Social Worker Level 3, Year 2	109,631	10,133	2,700	9,185	-	131,649	1.08
Randwick to 0.5 FTE level 3	Dietitian Level 3 Year 2	10,147	936	250	850	-	12,182	0.10
Enhance CHW, Westmead to 0.5 FTE level 3 (from 0.4 FTE level 2)	Dietitian Level 3 Year 2	53,406	4,925	1,314	4,473	-	64,118	0.53
New post level 1 / 2 1.0 FTE dietician	Dietitian Level 1 Year 2	65,380	6,030	1,608	5,476	-	78,494	1.00
Nutrition Education assistant 0.6 FTE	Hlth Educat Officer-Non Gradua, Fourth Year	37,513	3,460	923	3,142	-	45,037	0.60
0.6 CNC2	Clinical Nurse Specialist G2	61,214	5,645	1,506	5,127	-	73,492	0.60
1.0 FTE GMDS Clinical Nurse Practitioner	Nurse Practitioner, Thereafter	130,434	12,029	3,208	10,925	-	156,596	1.00
Genetic Counsellor 1 FTE	Genetics Counsellor Level 4, Year 2	117,995	10,906	2,906	9,886	-	141,692	1.08
Administrative Support 1 FTE	Administrative Officer Level 3, Second Year	60,335	5,564	1,484	5,054	-	72,437	1.00
JMO 1 FTE (GMDS)- 50% in CHW	Registrar, Fourth Year	71,104	6,572	1,751	5,957		85,384	0.57
Staff specialist	Staff Specialist	330,450	31,393	8,261		33,000	403,104	1.00
Total		**1,182,707**	**110,080**	**29,235**	**71,394**	**33,000**	**1,426,416**	**9.64**

Current Position Offsets

Position Titles	Position description	Salaries & Wages	Super	WC	Impact	TESL	Sub Total	FTE
Social Work level 3 (0.3FTE perm)	Social Worker Level 3, Year 2	- 32,889	- 3,040	(810)	(2,755)	-	- 39,495	- 0.32
Enhancement Request		1,149,817	107,040	28,425	68,638	33,000	1,386,921	9.32

facility_identifier	calendar_year	urgency_on_admission_description	Unique MRN	Count of stay_number	Average of nwau_final	Max of nwau_final	Max of length_of_stay_total2	Average of length_of_stay_total2	Sum of length_of_stay_total	Sum of episode_cost
A207	2016	Emergency	57	119	3.074513	51.41196	50	4.462185	531	$ 1,772,197.70
	2017	Emergency	66	145	3.955001	92.16013	238	7.103448	1030	$ 1,161,931.35
C238	2016	Emergency	12	19	3.89659	46.55586	55	6.842105	130	$ 572,239.07
	2017	Emergency	13	14	2.037547	16.95156	18	4.857143	68	$ 52,709.67
A207	2016	Non-Emergency	82	541	0.731939	44.50223	55	1.578558	854	$ 2,369,927.75
	2017	Non-Emergency	89	497	0.925216	57.26233	141	2.299799	1143	$ 2,245,508.06
C238	2016	Non-Emergency	20	40	1.10517	7.2435	22	2.325	93	$ 457,518.81
	2017	Non-Emergency	19	77	0.898299	8.424154	8	1.558442	120	$ 175,825.88

Appendix: State-wide Service Activity: PKU

Prior to 2000, the predominant diagnosis was Phenylketonuria (PKU), however with advances in genetic testing, the number of new disorders and treatments have been discovered in the last 20 – 30 years meaning that whilst the absolute numbers of PKU patients has not changed, they now comprise 20% of the total GMDE cohort in 2017

Table 4: Demographic Profile of PKU Patients accessing GMDS services in February 2018

	PKU
Active Patients (n)	144
Average Age (Yrs)	10.5
• Metro LHDs	96
• Rural and Regional LHDs	37
• ACT	4
• OS	`1

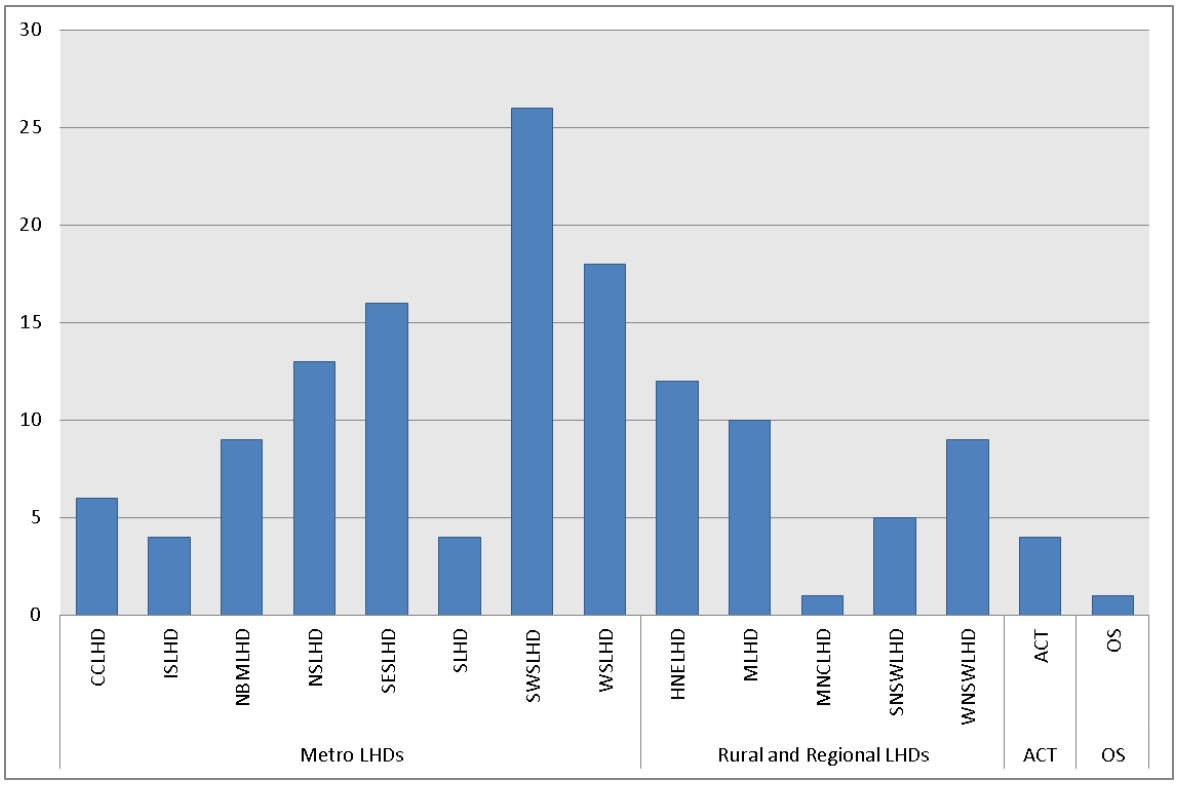

Figure 7: Geographical Profile for GMDS PKU Patient Cohort SCHN

Treatment of classical PKU is managed in an outpatient setting following initial diagnosis with admissions limited to surgical or dental interventions in the past 2 years. Requires a very low protein diet with prescription formula and food products . Interdisciplinary care from a team including nursing, medical, dietetics and social work is required to work with the family and provide support as he grows up and progresses through the stages of his life.

Table : Inpatient data for PKU patients 2016-2017

Year	Unique MRN	Episodes	NWAU Average	LOS Average	Max NWAU	Max LOS
2017	5	7	1.1	1	1.2	1
2016	7	9	1.4	1.4	4	5

Table: Active patients by disorder, by site, as of 29 March 2018

DISORDER	CHW	SCH	SCHN
Abetalipoproteunaemia		1	1
Acid lipase deficiency	2		2
Adenylosuccinate lyase deficiency, ADSL	1		1
Adrenoleukodystrophy, ALD	4		4
Alpha-mannosidosis		1	1
Argininosuccinic aciduria, ASA	8		8
Aspartylglucosaminuria, AGU	2		2
Barth syndrome	2		2
Beta-Ketohiolase Deficiency	3	3	6
Biotinidase def		2	2
Canavan disease	1		1
Carbamoyl-phosphate synthase deficiency	5		5
Carnitine uptake defect, CUD	12	2	14
Carnitine-acylcarnitine translocase deficiency, CACT	1		1
Citrin deficiency	1		1
Citrullinaemia	4	4	8
Cobalamin C deficiency	12	1	13
Congenital Glycosylation Disorder	4	3	7
Creatine Transporter Deficiency	2	1	3
Differential Diagnosis	4	5	9
Dihydropteridine reductase deficiency	2		2
Fabry disease, Fabry	10	1	11
Fatty acid transporter defect	1		1
Fructose bisphosphatase deficiency	4		4
Fucosidosis	1		1
Fumarase deficiency,	2		2
Galactokinase deficiency	5		5
Galactosaemia	22	2	24
Gaucher disease, Gaucher	2		2
GLRX5 deficiency	2		2
GLUT 1 deficiency	3		3
Glutaric aciduria	22		22

Glutathione synthetase deficiency	1		1
Glycerol Kinase deficiency	1		1
Glycogen Storage Disease	27	5	32
GM1 Gangliosidosis,	1		1
HFI		1	1
HMG CoA Lyase Deficiency	3		3
HMG CoA synthase deficiency	2	2	4
Homocystinuria, HCU	12	3	15
Hydroxyglutaric aciduria	3		3
HyperPHE	40		40
Isobutyryl CoA dehydrogenase deficiency, IBG	1		1
IVA	3	1	4
Kearns-Sayre syndrome	2	1	3
Ketotic Hypoglycaemia	6	2	8
LCHAD	3		3
Leigh Disease	1	4	5
Lipoprotein lipase deficiency	1		1
LPIN1 deficiency	2		2
Lysinuric protein Intolerance, LPI	2		2
Malonic Acidemia	2		2
Maple syrup urine disease, MSUD	15		15
MCAD	85	21	106
MCCC	9	4	13
MELAS	5	2	7
Metachromatic leukodystrophy	1		1
Methylene tetrahydrofolate reductase deficiency, MTHFR	2		2
Methylglutaconic aciduria	1		1
Miller Synd DHOD def		1	1
Mitocondrial Condition	21	8	29
MMA	5	1	6
MPS	37	1	38
Mucolipidosis	2		2
Multiple carboxylase deficiency, MCD	1		1
Multiple respiratory chain disorder	2		2
NARP		1	1
NCL -Batten		1	1
Niemann Pick Disease	4		4
NonKetotic Hyperglycaemia	1	1	2
OTC	18	1	19
PCD deficiency	1		1
PDHC	5	1	6
Peroxisomal disorder - unknown	2		2

Phenylketonuria, PKU	144		144
Pitt-Hopkin's syndrome	3		3
Pompe	4	3	7
Pontocerebellar hypoplasia	1		1
Propionic acidemia, PA	5		5
Pyruvoyl-Tetrahydro Biopterin Synthethase deficiency	6		6
Rett syndrome	100		100
Rhizomelic chondrodysplasia punctata	1		1
Riboflavin transporter deficiency		1	1
Sialidosis		1	1
Sialuria		1	1
SLO	3	2	5
Succinic semialdehyde dehydrogenase deficiency, SSADH	1		1
Transcobalamin II deficiency, TC II deficiency	1		1
Trifunctional protein deficiency, TFP	1		1
Trimethylaminuria, TMAU	9		9
Tyrosinaemia	3	5	8
VLCAD	24	6	30
X-linked creatine deficiency	1		1
Hartnup disorder	1		1
Lathosterolosis	1		1
Grand Total	**783**	**107**	**890**

PAEDIATRICS

A NATIONAL MODEL OF CARE FOR PAEDIATRIC HEALTHCARE SERVICES IN IRELAND

CHAPTER 31: PAEDIATRIC METABOLIC MEDICINE

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Clinical Strategy and Programmes Division

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

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31.0 INTRODUCTION

Inherited Metabolic Disorders (IMDs) cover a group of over 530 individual conditions, each caused by defective activity in a single enzyme or transport protein (Blau et al., 2014). Although individually metabolic conditions are rare, the incidence being <1.5 – 4 per 10,000 births, collectively they are a considerable cause of morbidity and mortality early in life (Applegarth et al., 2000).

A diagnosis of an IMD has a profound impact on patients and their families, their communities and the health system. Many of these conditions present in the newborn period or during the first few years of life, but some may also present in adolescence or later in life. The overall public health burden of these disorders is therefore cumulative. The diverse range of conditions varies widely in presentation and management according to which body systems are affected and the severity of the underlying defect. Without early identification and/or introduction of specialist diet or drug treatments, patients face severe disruption of metabolic processes in the body such as energy production, manufacture or breakdown of proteins, and management and storage of fats/ fatty acids, carbohydrates or complex molecules. The result is that patients have either a severe deficiency of products essential to health or an accumulation of toxic products. Without treatment, many conditions can lead to neurological symptoms, severe learning or physical disability, or overwhelming illness and even death at an early age. The rarity and complex nature of IMDs requires integrated specialised clinical and laboratory services to provide satisfactory diagnosis and acute/ long-term management.

Current and proposed expanded newborn bloodspot screening programmes identify some inborn metabolic diseases, and new technologies for diagnosis and more effective treatments promote improved survival rates and quality of life for children and adolescents with IMDs. Expansion of the newborn screening programme to include other treatable metabolic conditions (in line with other developed countries) is urgently required to avoid preventable morbidity and mortality amongst affected children. With major advances in new treatments and advanced technology along with improved diagnostic efficiency (Walter, 2009), there are therapies emerging for many conditions that were previously considered to be untreatable, e.g. Lysosomal Storage Disorders. Within this context, there is increasing awareness of the urgent need to improve patient access to treatments for rare metabolic diseases across Europe. Paediatricians generally have higher exposure than many other physicians to rare disease patients (Knerr and Treacy, 2014).

The challenges of the transition from paediatric- to adult-based services, which are at an early stage of development for adult patients with IMDs in Ireland as opposed to the United Kingdom (UK) and many continental European countries, has been identified as an important area to be addressed (Knerr and Treacy, 2014).

A study in the UK itemised the demand for adult patients with IMDs, including a multidisciplinary approach, with the clinician and dietitian as the core of the team, but with the collaboration of clinical nurse specialists, social workers and other specialist services including laboratory (Martín-Hernández et al., 2009). An international study that evaluated the situation of adult and adolescent patients with metabolic diseases in Germany revealed that expertise for metabolic medicine was mainly provided by metabolic paediatricians (26 paediatric metabolic departments compared to three specialised internal medical departments in this country) but that the need for independent adult metabolic services is increasing as patients with IMDs survive longer (Hoffmann et al., 2005). Management of IMDs requires a coordinated approach from the core IMD multidisciplinary team with access to IMD laboratory expertise as well as support from many different medical specialties (Rare Disease Centres Proposal, 2012/13). An IHSAB review (2006) identified the National Centre for Inherited Metabolic Disorders (NCIMD) at Children's University Hospital, Temple Street (Temple Street) as a Centre of Excellence (CoE) for paediatric metabolic medicine.

31.1 CURRENT SERVICE PROVISION

The commencement of newborn screening in the 1960s contributed considerably to the development of paediatric metabolic services at Temple Street. There has been substantial expansion of the service since then to encompass entirely metabolic functions and delivery of care as a Centre of Expertise (CoE) for metabolic diseases. The identification of new IMDs due to advanced technology, improved diagnostics and treatment strategies, and better clinical outcomes have all contributed to the expansion of workload. There are currently 1830 metabolic patients in the NCIMD Temple Street service, of which approximately one quarter are now adults and their care needs to be addressed separately; 482 adult patients continue to receive dietetic services from Temple Street.

The large paediatric cohort require a high standard of multidisciplinary care, with integration of medical and psychosocial aspects, education and access to patient organisations and clinical trials, as recommended by the European Union Committee of Experts on Rare Diseases (EUCERD) in 2011 and 2013. The National Screening and Metabolic Laboratories are based at Temple Street ensuring that metabolic patients receive a continuum of diagnostic, care and support services according to their needs. Temple Street metabolic consultants also provide a service in Our Lady's Children's Hospital Crumlin (Crumlin) and in (limited) outreach clinics providing equitable and safe access for children with IMDs. As many IMDs can be fatal early in life, there are close links with Laura Lynn House and with the liaison nurse for children with life-limiting conditions. These IMDs include severe forms of mitochondrial conditions that present with liver failure or encephalopathy for example, neuro-metabolic degenerative diseases and many others.

NCIMD is a designated CoE since 2006 and has been a national centre since 1986. As a CoE, the department provides expertise for the management and care of patients with rare metabolic diseases at national level, and at international level where necessary. Our scope is to cover all metabolic patients' needs, and to bring together and coordinate multidisciplinary competences and skills (including health and social care professionals) to serve the specific medical, rehabilitation and palliation needs of these vulnerable paediatric patients. The research component of the NCIMD at Temple Street is also very strong. We contribute to research aimed at optimising diagnosis, care and treatment, including the clinical evaluation of long-term effects of new treatments.

31.1.1 Staffing

Current staffing levels are outlined below:

Medical	**Consultant**	**Registrar**	**SHO**	
	3.9WTE	3-4WTE	1-2WTE	
Nursing	**CNM3**	**Enzyme Coordinator**	**Research Nurse**	
	1WTE	1WTE (funded by industry)	1WTE (funded by grants & industry)	
	CNS	CNM2	HCA	
	1.4WTE	1WTE	1WTE	
	St. Brigid's Ward			
	CNM2	Clinical Education Facilitator	Staff Nurses	HCA
	1WTE	1WTE	10.27WTE	1WTE

Dietetics	4.4WTE funded by Temple Street (including 0.6WTE Dietitian Manager; 3.8WTE clinical posts) 1WTE funded by industry (research & clinical) 1WTE:245 paediatric patients requiring dietetic input, service provided 365 days per year with weekend/public holiday on call		
Psychology	2WTE	Social Worker	1.5WTE
Play Specialist	0.5WTE		
Physiotherapist	0.5WTE (funded by industry)		
Genetics Counsellor	0.5WTE previously funded by industry, post expired February 2014		
Administration	4.6WTE (including 0.6WTE dietetic administrative support)		

31.1.2 New Referrals

There were 374 new paediatric referrals to the service in 2014, 330 in 2013 and 362 in 2012. New paediatric referrals are received from:

- National Newborn Screening Programme (NNSP) for IMDs – Phenylketonuria (PKU), Galactosaemia, Homocystinuria, Maple Syrup Urine Disease (MSUD). Newborns with a positive blood screening result are usually seen within 24 hours for admission to Temple Street. Babies with classical galactosaemia or MSUD will be either admitted directly to Temple Street or locally for assessment by a paediatrician and initiation of therapy. Newborns are often very sick at the time of diagnosis and need specific emergency therapy. Stabilisation at peripheral units is preferable prior to transfer to Temple Street.
- Consultant paediatrician referrals, e.g. developmental and general paediatrics, neurology, cardiology, and gastroenterology. Referral letters are screened by paediatric metabolic consultants, and are either seen in outpatients in Temple Street or are admitted directly for further investigations - this cuts out unnecessary OPD visits and reduces time to diagnosis.
- Inpatient consultation referrals within Temple Street (approx. 120 per year)
- Inpatient consultation referrals from Crumlin (approx. 180-190 per year)
- Telephone consultations from paediatric and neonatal units, ICU/HDU in Dublin and nationwide
- GP referrals – suspected metabolic disorder, and known paediatric metabolic patients moving to the Republic of Ireland.

There are close working relationships between the multidisciplinary metabolic team, the metabolic laboratories, and the national newborn screening laboratory in Temple Street. The primary purpose of the NNSP is to provide early treatment for IMDs detected by screening in order to prevent severe disability or death. The incidence of selected IMDs diagnosed on newborn screening in Ireland is:

Newborn Screening Introduced	IMD	Irish Incidence
1966	Phenylketonuria	1:4,500
1971	Homocystinuria	1:68,000
1972	Classical Galactosaemia	1:16,476
1972	Maple Syrup Urine Disease	1:125,000

The annual reports of the NNSP show actual numbers of cases diagnosed in recent years, highlighting that the majority of paediatric metabolic patients attending the metabolic service in Temple Street are not diagnosed through newborn screening:

IMD	2007	2008	2009	2010	2011	2012	2013	2014
Phenylketonuria	19	26	13	16	12	13	18	19
Classical Galactosaemia Homocystinuria	2	5	10	6	2	7	9	7
Homocystinuria	1	0	1	1	2	0	0	2
Maple Syrup Urine Disease	2	0	0	0	1	0	0	0
TOTAL	24	31	24	23	17	20	27	28

The 'top ten' metabolic diseases seen in NCIMD Temple Street are:

- PKU
- Respiratory chain defects/ mitochondrial disorders
- Classical galactosaemia
- Homocystinuria
- Fatty acid oxidation defects (all types)
- Mucopolysaccharidoses (all types)
- Glutaric aciduria (GA1)
- Urea cycle defects
- Glycogen storage disorder (all types)
- MSUD

Mucopolysaccharidosis Type 1H (MPS1H) is more common in Ireland than any other country (1:26,000 incidence) and patients with Hurler Syndrome (severe phenotype) require haematopoietic stem cell transplantation. The retirement of Dr. Anne O'Meara, consultant oncologist in Crumlin who had performed approximately 50 MPS1H transplants, has led to significant problems in the provision of care to the MPS1H patient group as there is no local transplant service currently offered to these children. Since March 2013, six children have been referred to Manchester for transplantation at an agreed cost of €200,000 per transplant. These patients require specialised haematology expertise pre-, during and post-transplant and the metabolic unit at Temple Street is unable to take on the transplant-related care of these patients. Their care pathway is complex, involving metabolic medicine and haematology teams at Crumlin and Royal Manchester Children's Hospital, as well as many other disciplines including ear, nose and throat (ENT), ophthalmology and orthopaedics split between the two main children's hospitals. A local transplant service is urgently needed, and will have the potential to reduce costs given that on average three babies are diagnosed with MPS1H annually.

31.1.3 Clinical Activity

In principle, children with IMDs who present early in life (i.e. as neonates or during infancy) suffer from a more severe form than patients with a later onset. It is therefore estimated that the management of neonatal or infant cases is much more complex than the management of patients with late onset or intermittent form. There are metabolic diseases that present as overwhelming illness in young children, e.g. Leigh's disease, urea cycle defects, organic acidurias, LARS defect (Casey et al., 2012), and patients who survive into adulthood usually have a milder phenotype. Other conditions, such as PKU, are much less detrimental in adult males and females beyond their child-bearing years than in vulnerable children and babies.

Another feature of the clinical workload is the relatively large proportion of children from the Travelling community, who are over-represented, as children from this population have a 15-fold increased prevalence of IMDs in comparison to children not from the Travelling community (Lam et al., 2013).

Current caseloads are as follows (data correct as of July 2015):

Total No. of Children	Total No. of Adults	TOTAL	New Paediatric Referrals Pending (waiting list)	No. Requiring Dietitian Input
1348 (<18 years)	482 (18 years +)	1830	107	1153 (63%)

Inpatient and outpatient activity is summarised as follows:

	2012	2013	2014
Admissions to St. Brigid's Ward Temple Street	381	449	564
Total Number of Bed Days	1217	1118	1590
OPD Clinics (Temple Street only)	2246	2100	2502

The total number of admissions is higher than reported here as sick neonates are usually admitted to Michael's B ward or ICU, or admissions may be to a general paediatric ward (e.g. for muscle biopsies) or to the day ward (e.g. for MRI or lumbar puncture). The average length of stay is three days (2014 data).

The metabolic ward has gradually been reduced from a full time ward to a five-day ward (four nights/five days, Monday to Friday). This has adversely affected the ability to admit children for planned investigations, e.g. fasting studies. The number of admissions was 500 in 2008 compared with 564 in 2014. Despite an increase in workload, available resources are being used more efficiently, through better outpatient and community services for patients with IMDs, e.g. vaccines administered locally with telephone contact and vaccine protocols, and the transfer of patients on enzyme replacement therapy (ERT) to home therapy. St. Brigid's ward was open for 228 days in 2014, and the significant rate of transfer of metabolic patients to other wards within the hospital can affect continuity of a child's ongoing treatment and care. In addition to approximately 120 inpatient consultation referrals within Temple Street, there are 180-190 in-house metabolic consultations in Crumlin each year which is an under-resourced service provided by the metabolic consultants with no secretarial or nursing support and minimal non-consultant hospital doctor support. There are seven to nine metabolic clinics held each week in Temple Street, with seven to 12 patients attending each clinic, 48 weeks per year.

All clinics are consultant-led with the exception of the PKU clinic, which is nurse- dietitian-led under the supervision of a paediatric metabolic consultant. A two-day multidisciplinary mucopolysaccharidoses clinic is held annually with a metabolic consultant and representatives from neurosurgery, dentistry, ophthalmology. There are also six dietetic-led carers clinics held each year. Outpatient clinics in Crumlin are led by the consultants from Temple Street (Dr. Ellen Crushell and Dr. Joanne Hughes) with minimal non-consultant hospital doctor support (4 hours SHO time per week). There are approximately 100-110 metabolic patient attendances in Crumlin each year.

Outreach clinics have been established to provide a better service for children with IMDs. Limerick is at the forefront (four clinics / year since January 2012) with Dr. Anne Marie Murphy acting as the local paediatrician with an interest in paediatric metabolic medicine. Eighteen children with IMDs were reviewed locally in 2014 at a consultant-led clinic with specialist nurse and dietitian support. An outreach service is also planned for Cork

and Galway. A concern for service planning is the long-term sustainability taking into account yearly increases in patient numbers and the complexity of care required. In line with international best practice, patients want to have shared care portfolios with local paediatricians and GPs where possible.

31.1.4 Education and Training

The Temple Street metabolic team provides education and training to healthcare professionals of all disciplines, as well as other groups such as teachers and personal/homecare facilitators, in Dublin and elsewhere whenever possible. However, there is a lack of paediatric specialist registrar (SpR) trainees which has been highlighted for a number of years, and enhanced education of future paediatricians and trainees in paediatric metabolic diseases is strongly recommended. A national survey of paediatricians and neonatologists undertaken in 2008 by the Health Service Executive (HSE) found that only 26% of respondents (18/70) had some training in paediatric metabolic medicine.

The nursing component of the metabolic unit is very strong, with the development of a metabolic education FETAC Level 8 course affiliated with Dublin City University run over seven non-consecutive days. This course has been adapted to include inviting other health and social care professionals to undertake the module. While the unit has clinical nurse specialists, it does not have advanced nurse practitioners, who would have a greater emphasis on research and audit.

Online access to patient/parent information and education as well as research activities is provided through the new NCIMD website (http://metabolic.ie). We launched our new website on 15 October 2015. It was accessed by over 3,000 users so far.

31.1.5 National Rare Disease Plan

The national rare disease plan was launched in July 2014 with a view to improving care of patients with rare diseases, and has gained momentum in raising awareness of rare diseases and the need to improve patient access to treatments for rare diseases. It will provide a framework for recognition of rare diseases and sharing of knowledge and expertise.

31.2 PROPOSED MODEL OF CARE

In the future, the national paediatric IMD centre will:

- Accept 24/7 referrals for paediatric patients with suspected IMDs
- Provide access to inpatient/ neonatal/ critical care facilities where appropriate
- Provide dedicated IMD inpatient and outpatient facilities
- Provide timely diagnosis with appropriate counselling and psychological support for the patient and their family/carers
- Work closely with general paediatricians and neonatologists to ensure the best holistic medical care for patients, particularly in the inpatient setting
- Provide access to other specialised paediatric services, e.g. hepatology, cardiology, etc. as appropriate
- Perform regular patient reviews as per national guidelines or clinical practice, with written or electronic records of current treatment and patient response
- Provide high quality clinical expertise in accordance with national policy and guidance where available, or in accordance with accepted clinical practice

- Provide 24/7 access to clinical advice in conjunction with other paediatric and adult centres in a formally agreed service provider network
- Provide appropriate pharmaceutical drug treatment, dietary therapy and care
- Perform regular laboratory and other diagnostic tests as appropriate to monitor patient response to dietary therapy and/or medication
- Provide patient-centred services, sensitive to the individual's physical, psychological and emotional needs and supported through the provision of patient-appropriate information
- Develop and implement protocols for appropriate transition of metabolic patients at Temple Street
- Initiate appropriate and safe transfer of adult IMD patients to the adult metabolic service under formal arrangements between both hospitals
- Perform a minimum annual multidisciplinary review of all patients of core IMDs
- Agree care pathways and treatment protocols, and monitor compliance
- Provide access to appropriate and agreed shared care arrangements with other primary and/or secondary care providers, 'hub-and-spoke model of care'
- Provide options for home therapy where appropriate, supported by regular clinical monitoring, e.g. for children with lysosomal storage disorders
- Provide a telephone helpline for patients' families and carers, healthcare professionals, and non-healthcare and voluntary sector professionals. Online access to patient/parent information and education as well as research activities is provided through the new NCIMD website (http://metabolic.ie).

The fundamental requirements at NCIMD Temple Street comprise increased multidisciplinary staffing levels at NCIMD Temple Street in order to provide safe, accessible, and efficient services for our expanding cohort of children and adolescents with complex IMDs. This is of particular importance for the development and implementation of an appropriate, safe and effective transition process and transfer of (adult) metabolic patients to the appropriate adult services, and for future care standards, including expanded outreach clinics in line with the 'hub-and-spoke model of care'.

31.2.1 Outreach Services

Clinicians will work together to promote appropriate outreach facilities and local support structures (for children and adolescents with general IMDs and PKU patients). Outreach clinics should be extended to encompass Cork, Limerick, Galway and others. Support is provided to the Northern Ireland metabolic service through monthly cross border meetings at the National Centre for Inherited Metabolic Disorders in Temple Street with the Belfast-based metabolic paediatrician and clinical pathologist, to discuss complex cases, diagnostic pathways and clinical management.

31.2.2 Transition from Paediatric to Adult Services

Paediatric and adult IMD centres will develop appropriate working relationships under formal arrangements at hospital level, with the centres working together to ensure smooth and efficient transition of adult patients to appropriate facilities in line with best practice. In the proposed Model of Care the paediatric IMD centre will:

- offer adult patients and their families/carers an agreed period of assessment by the joint paediatric/adult team to ensure seamless transfer to adult services
- agree and provide a formalised operational transition policy at hospital level
- provide a clinical transfer record with all relevant clinical information
- provide age-appropriate written and/or electronic information to patients and their families/carers
- Develop and implement protocols for appropriate transition of metabolic patients at Temple Street

- Initiate appropriate and safe transfer of adult IMD patients to the adult metabolic service under formal arrangements between both hospitals. Transfer/transition of metabolic patients from NCIMD to the Adult Metabolic Service at The Mater has to incorporate the complex needs of these patients and their risk of acute metabolic decompensations.

31.2.3 Patient Education Programmes

Patient and parent education programmes, development of patient/family information material, active involvement and close collaboration with parent support groups are essential and well-established components of the metabolic service at Temple Street. A range of educational material has been developed by multidisciplinary team members including clinical nurse specialists, dietitians, psychologists and play specialists. Education plays an integral role at each outpatient attendance and inpatient admission. The NCIMD has established links with patient and parent support groups both at a national and at an international level. Online access to patient/parent information and education is provided through our new NCIMD website (http://metabolic.ie).

31.2.4 Clinical Care Standards, Guidelines and Care Pathways

Guidelines for the emergency management of patients with IMDs have been developed since 1993 at the NCIMD, and are currently updated every six months using expert opinion and focused literature reviews. Details of a range of guidelines, information leaflets, policies and procedures are contained within Appendices 1-3.

31.3 REQUIREMENTS FOR SUCCESSFUL IMPLEMENTATION OF MODEL OF CARE

The fundamental requirements for future delivery of the service at the NCIMD are strongly related to:

i. consolidation of current standards of care for paediatric patients with IMDs
ii. expansion of the clinical spectrum of new diagnoses and new therapies.
iii. ability to provide emerging treatment options for the paediatric IMD cohort
iv. challenges for future management and future care standards, including expanded day care services and greater need for outreach clinics (hub-and-spoke model of care)
v. challenges for appropriate, effective and safe transition and transfer of (adult) metabolic patients to the Adult Metabolic Service.

The fundamental requirements at NCIMD Temple Street comprise increased multidisciplinary staffing levels at NCIMD Temple Street in order to provide safe, accessible, efficient services for our expanding cohort of children with complex IMDs.

Future demands and strategies at the NCIMD also include sustainable development of clinical studies, including new enzyme therapies and hepatocyte transplantation, and coordinating services to provide eligible paediatric patients with IMDs access to therapeutic trials as well as further development of audits and quality initiatives.

31.3.1 Staffing

The metabolic ward in Temple Street was reduced to a five-day service (Monday-Friday), however a Monday-Sunday service would be more appropriate for this patient cohort. Greater involvement of general paediatrics, in particular with inpatients, is recommended. A combined metabolic-general paediatric admission would be

best positioned to ensure safe delivery of holistic care and also serve to further educate paediatric trainees in the area of IMDs. A multidisciplinary team approach is also essential for the management of patients with IMDs. Multidisciplinary staffing requirements to deliver this model of care are summarised below:

Staff Category	Previously Agreed (WTE)	Current (WTE)	Proposed (WTE)
Consultant Metabolic Paediatrician	4	3.9	6
Specialist Registrar/ Registrar	4	3	4
SHO	1	1-2	1
Nursing (Total)	26	17.67	26 (including 1 research nurse and 1 ERT coordinator)
Dietitian (Temple Street funded)	8	4.4	8 (including 0.5 research dietitian)
Physiotherapist	0	0.5	1
Psychologist	3	2	3 (or 2 clinical psychologists +3 trainees)
Social Worker	2	1.5	2
Play Specialist	1	0.5	1
Genetic Counsellor	0	0	1
Speech and Language Therapist	0	0	1
Occupational Therapist	0	0	1
Administration	6	4.6	6

31.3.2 Education and Training

Medical students from University College Dublin (UCD), Trinity College Dublin (TCD) and the Royal College of Surgeons in Ireland (RCSI), and occasionally from international universities, are accepted on the metabolic team and are integrated into the teaching schedule for their attachments. Student electives are accommodated and encouraged, and a number of successful medical student projects have been completed. Formal teaching programmes are provided through affiliations with UCD, TCD and RCSI, and training of paediatric non-consultant hospital doctors (NCHD) with the Royal College of Physicians in Ireland (RCPI). Postgraduate medical education is an integral part of the metabolic unit, with formal teaching rounds each week for NCHDs as well as a weekly journal club and clinical-laboratory meeting.

The first week of each six-month NCHD term is dedicated to teaching to provide the knowledge base required for caring for children with IMDs. National metabolic study days are also held almost annually. Neuro-metabolic and multidisciplinary cross border meetings are conducted on a regular basis, i.e. monthly.

31.3.3 Governance

Current governance structures comprise the Temple Street Chief Executive Officer, Temple Street Board of Directors and (paediatric) Clinical Director at Temple Street, and the NCIMD Clinical Director Dr. A.A. Monavari. There are close links to the HSE National Clinical Programmes. There are established collaborations with a variety of international societies and working groups with a view to improving patient outcomes, and developing international guidelines and consensus procedures. Multidisciplinary team members have been involved with high level presentations at scientific meetings on the latest clinical innovations, networking and collaborating with colleagues from a range of disciplines all working to improve the care of individuals with IMDs. An external review of the metabolic department at Temple Street by Walter and Levy (2005) recommended that all primary managerial responsibilities were centralised under the authority of the Clinical Director with named individuals in particular disciplines having some managerial responsibility for their area of work. Subsequently a dietitian manager and clinical nurse manager III were appointed.

Strong clinical governance is also evidenced by:

- NCIMD Temple Street is a CoE designation for paediatric metabolic care since 2006 and a National Centre since 1986.
- Nurse- and dietetic-led clinics were recognised as an excellent development by the external review in 2005
- Large multidisciplinary team have developed clinical practice guidelines for a range of conditions
- Established newborn screening programme, with proposals under consideration to expand the national newborn bloodspot screening programme to include two additional inborn metabolic disorders (medium chain acyl-CoA dehydrogenase deficiency and glutaric aciduria type 1)
- Established collaboration with international working groups, i.e., European Galactosaemia Network (EGN); Homocystinuria (E-HOD); Niemann Pick Diseases (INPDR); Mucopolysaccharidoses- International Consensus Procedures; Tyrosinaemia Type 1 Surveillance Programme; Liver cell therapy: Urea cycle defects – SELICA-clinical trial program.
- Established collaboration with national and international societies and metabolic working groups and high-level presentations at international scientific meetings (e.g. IPA, SSIEM, SIMD, BIMDG and others) to ensure the highest possible level of patient care and medical knowledge. Members of our team are serving at the committee of the Irish Society of Inherited Metabolic Disorders (ISIMD), including the president, treasurer, and board.

The issue of 'ring fencing' the budget for the NCIMD is complex, and has been further exacerbated by financial cuts which adversely affect services, e.g. delayed admissions for diagnostic investigations, waiting times are now 6 months to first appointments for new patients (excluding newborns and emergencies). The budget for the NCIMD should be ring fenced, as well as that for new treatments such as enzyme replacement therapy.

31.4 PROGRAMME METRICS AND EVALUATION

The introduction of national initiatives will include:

- A national patient register for children with IMDs at NCIMD Temple Street
- A national database of paediatric research trials and clinical outcome studies
- Annual audit and governance report

A database of patients with IMDs is currently held in NCIMD Temple Street. With support from Temple Street ICT team, this database is kept at the highest possible standard and is eligible for anonymized patient-oriented clinical research. Key performance indicators have been identified to measure and evaluate performance of the service, and clinical audits are conducted regularly.

31.5 KEY RECOMMENDATIONS

- Increase multidisciplinary staffing levels at NCIMD Temple Street in order to provide safe, accessible, efficient services for children with IMDs.
- Develop and implement protocols for appropriate transition of metabolic patients in Temple Street to enable appropriate and safe transfer of adult IMD patients to the adult metabolic service under formal arrangements between both hospitals (proposed: + 1 WTE Consultant Metabolic Paediatrician at NCIMD). This has to incorporate the complex needs of this high-risk cohort, including their risk of acute metabolic decompensations. Transfer and transition from paediatric to adult metabolic services are at an early stage of development for these patients in Ireland as opposed to the UK and many continental European countries.
- Develop and implement protocols for future care standards, including expanded day care services, outreach clinics ('hub-and-spoke model of care') to improve paediatric care providers' ability to arrange for care within a reasonable driving distance for patients/families and to provide specialty care in patients' own communities where possible (proposed: + 1 WTE Consultant Metabolic Paediatrician at NCIMD). In addition, more effective treatments for IMDs in children along with improved survival rates is leading to a higher requirements for specialised clinical service to provide satisfactory acute and long-term management. The overall aim is to improve quality of care and outcome and to reduce avoidable risk for this vulnerable cohort.
- Increase the metabolic service in Temple Street from five to seven days. Move to combined metabolic / general paediatrics admissions for metabolic patients where possible.
- An Irish MPS1H transplant service is required.

31.6 ABBREVIATIONS AND ACRONYMS

CoE	Centre of Expertise
EUCERD	European Union Committee of Experts on Rare Diseases HSE Health Service Executive
IMD	Inherited Metabolic Disorders
MPS1H	Mucopolysaccharidosis Type 1H
MSUD	Maple Syrup Urine Disease
NCIMD	National Centre for Inherited Metabolic Disorders
NCHD	Non consultant hospital doctor
NNSP	National Newborn Screening Programme
PKU	Phenylketonuria
RCPI	Royal College of Physicians in Ireland RCSI Royal College of Surgeons in Ireland
SHO	Senior House Officer
SpR	Specialist Registrar
UCD	University College Dublin
UK	United Kingdom
WTE	Whole Time Equivalent
ISIMD	Irish Society of Inherited Metabolic Disorders

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31.8 APPENDICES

31.8.1 Appendix 1: Examples of Protocols, Policies, Procedures, Guidelines and Care Pathways in NCIMD

Protocols
• Fasting study
• Hypoglycaemia work-up
• 24 hours Glucose and lactate profile
• Oral glucose load
• Lactate / pyruvate ratio studies
• Oral protein load
• Protocol for post-heparin lipoprotein lipase test in children
• Protocol for enzyme replacement infusion reaction
• Allopurinol test
• Phenylalanine load

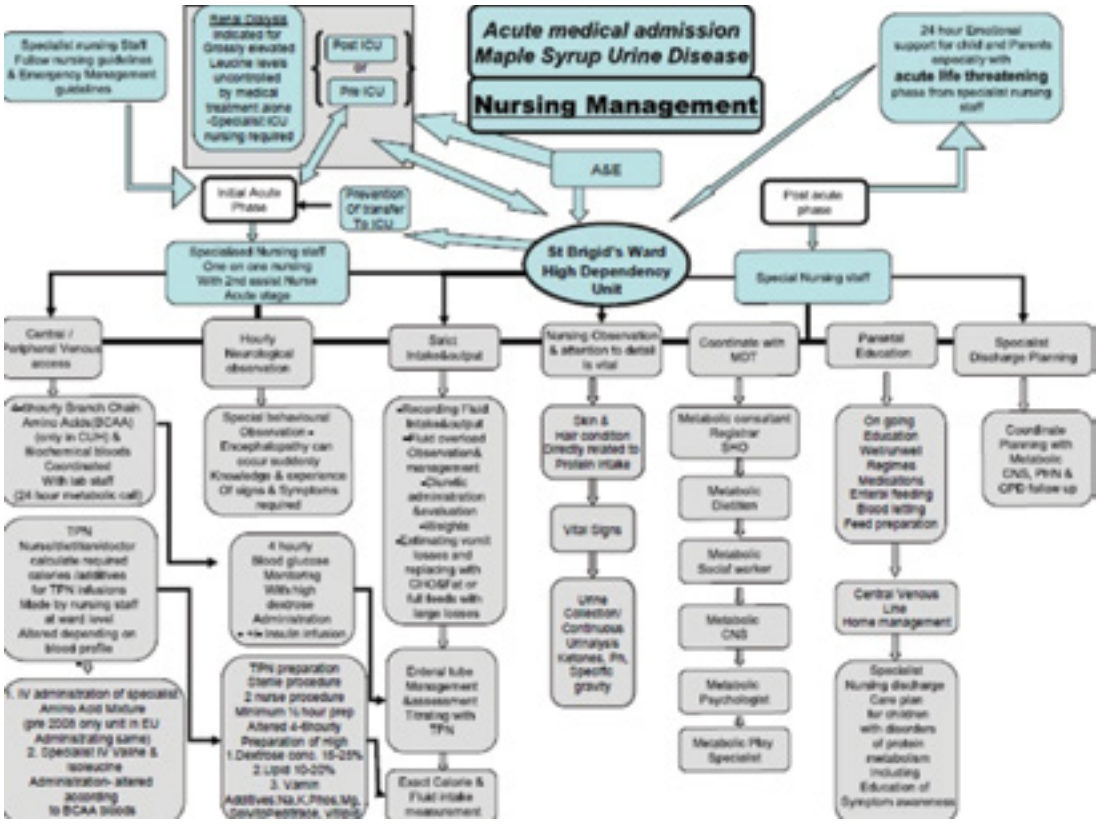
Policies and Guidelines for Dietary Management of IMDs
• Guidelines on the dietary treatment of a newly diagnosed infant with classical galactosaemia and on-going dietary management throughout the life cycle • Policy on treatment of newly diagnosed PKU baby • Hyperphenylaninaemia level reporting guidelines • Guidelines for the management of hyperphenylalaninaemia throughout the life cycle • Guidelines for protein exchange identification • Guidelines for dietary management of Smith Lemli Opitz Syndrome
Care Plans
• Metabolic investigation care plan • Protein load care plan • Altered nutritional requirements: Glutaric Aciduria Type 1 care plan • Urea Cycle Defects (new diagnosis) care plan • Potential / Actual Altered Neurological function secondary to Maple Syrup Urine Disease (MSUD) • Galactosaemia (new diagnosis) care plan • PKU (new diagnosis) care plan • HCU (new diagnosis) care plan • Potential / Actual Altered Neurological Function secondary to Hyperammonaemia Care plan • Enzyme replacement for Lysosomal Storage Disorders care plan • Glycogen storage disease care plan. • Hypoglycaemia care plan • Altered Nutritional Requirements: Methylmalonic aciduria (MMA) / Propionic aciduria (PA) Care Plan • Applying credit card sized emergency cards for patients (e.g. MSUD, GA1) that outline a simplified six-step acute management plan, based on international best practice (Hawkes & Crushell et al., 2011). Each of these cards is disease specific, and contact details of the patient's physician, nurse and on call metabolic service are listed on the alternate side. This was well received by physicians and patients. • Standard therapeutic pathways, emergency regimes and diagnostic flow-charts for the management of patients with disorders of branched-chain amino acids have recently been published in a medical textbook for reference by a member of our group (Knerr et al., 2014)

31.8.2 Appendix 2 Examples of Patient Information Leaflets in NCIMD

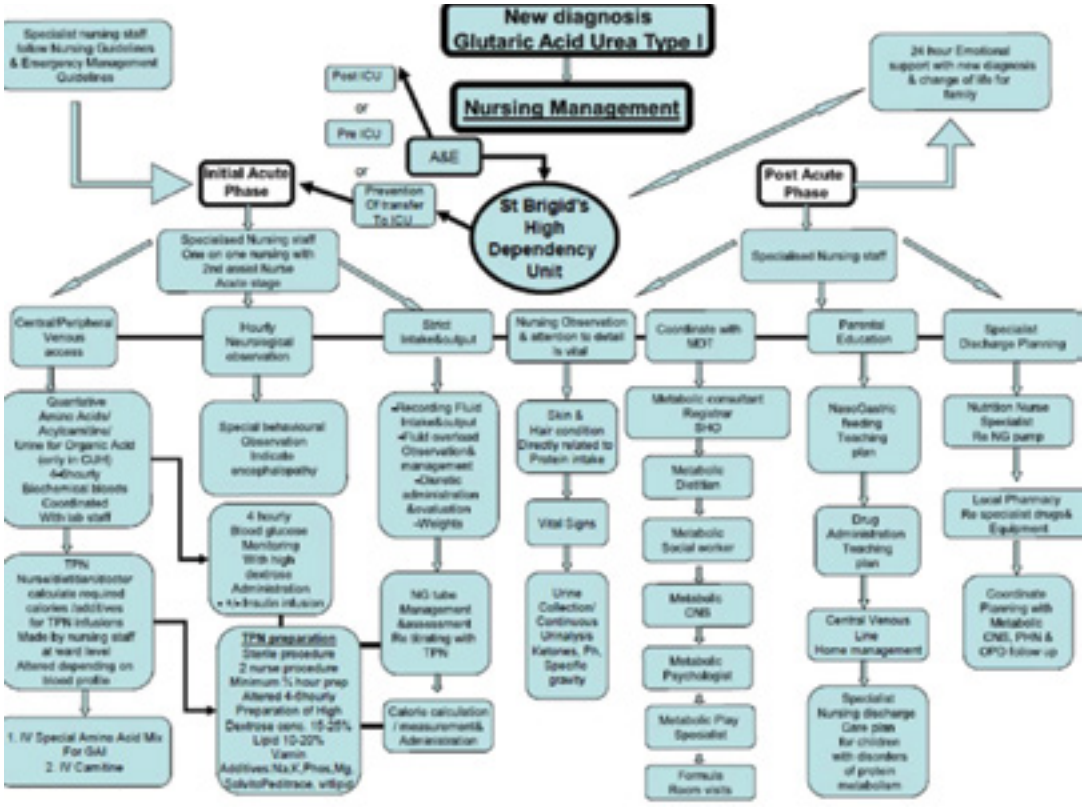
- Muscle biopsy
- Skin biopsy (parent)
- Skin biopsy (adult)
- Fasting study
- Glucose and lactate profile
- Oral glucose load
- Lactate / pyruvate ratio
- 'Welcome to St Brigid's Ward' – inpatient unit information
- Recessive Inheritance – an information leaflet for parents and families
- Mitochondrial illness
- New diagnosis handbooks for babies diagnosed with PKU, MSUD, MMA, PA, HCU, GA1
- Diet sheet for newly diagnosed Galactosaemia baby
- Weaning booklets for Galactosaemia and all protein disorders
- MCAD with information appropriate for babies through to adulthood.

31.8.3 Appendix 3 Patient Pathways / Algorithms

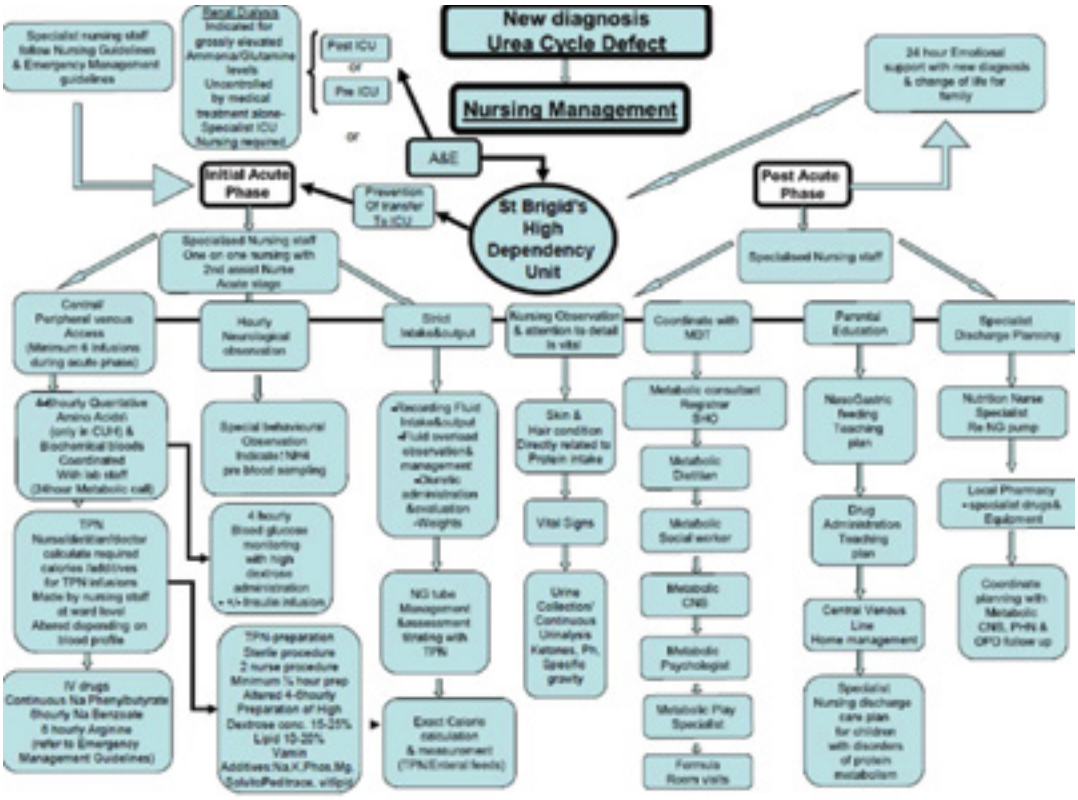
Pathway for Nursing Management of Maple Syrup Urine Disease (MSUD)



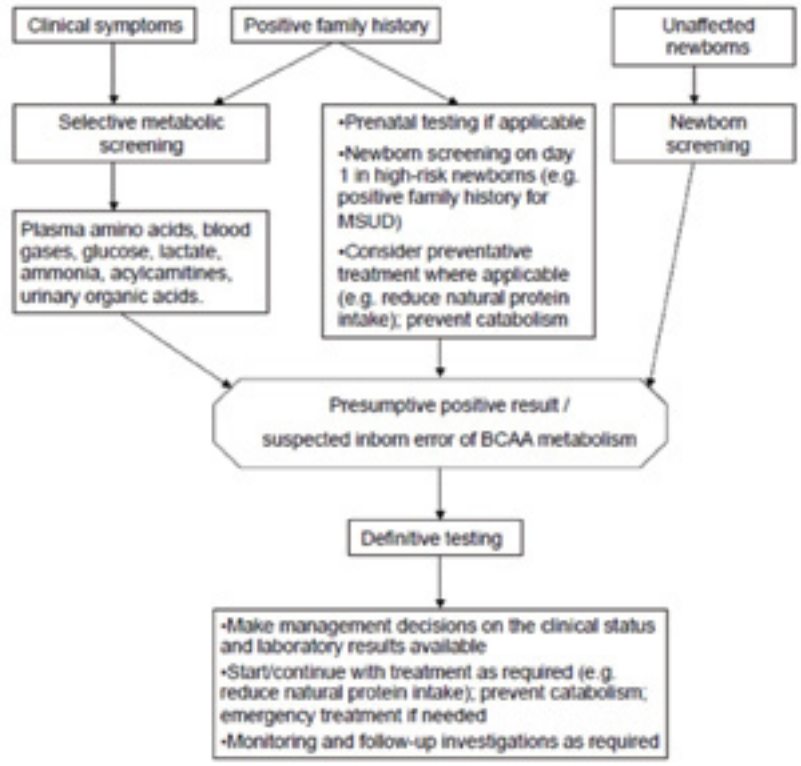
Pathway for Nursing Management of Glutaric Aciduria (GA1)



Pathway for Nursing Management of Urea Cycle Defect



Diagnostic Flowchart for Newborns with Suspected IMD



Standard Therapy and Emergency Flowchart for Children with IMDs