# Transitional Care in Inborn Metabolic Diseases

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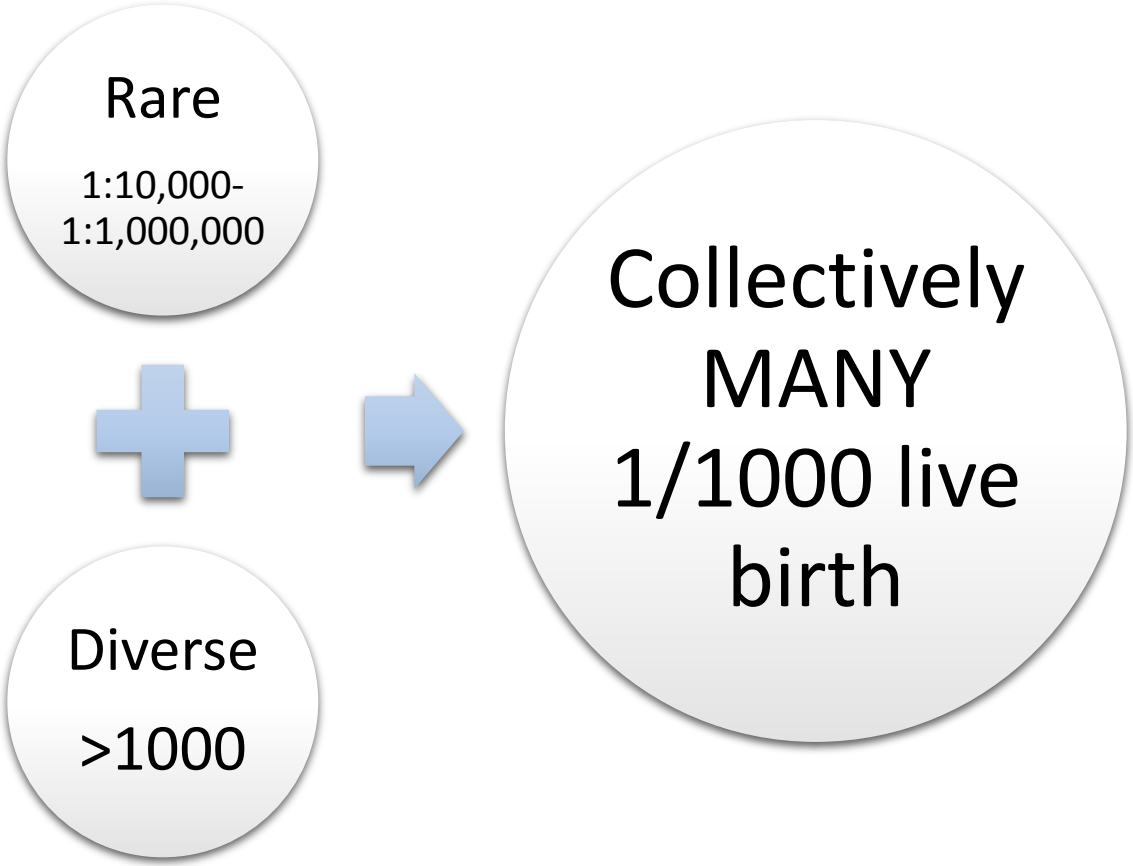
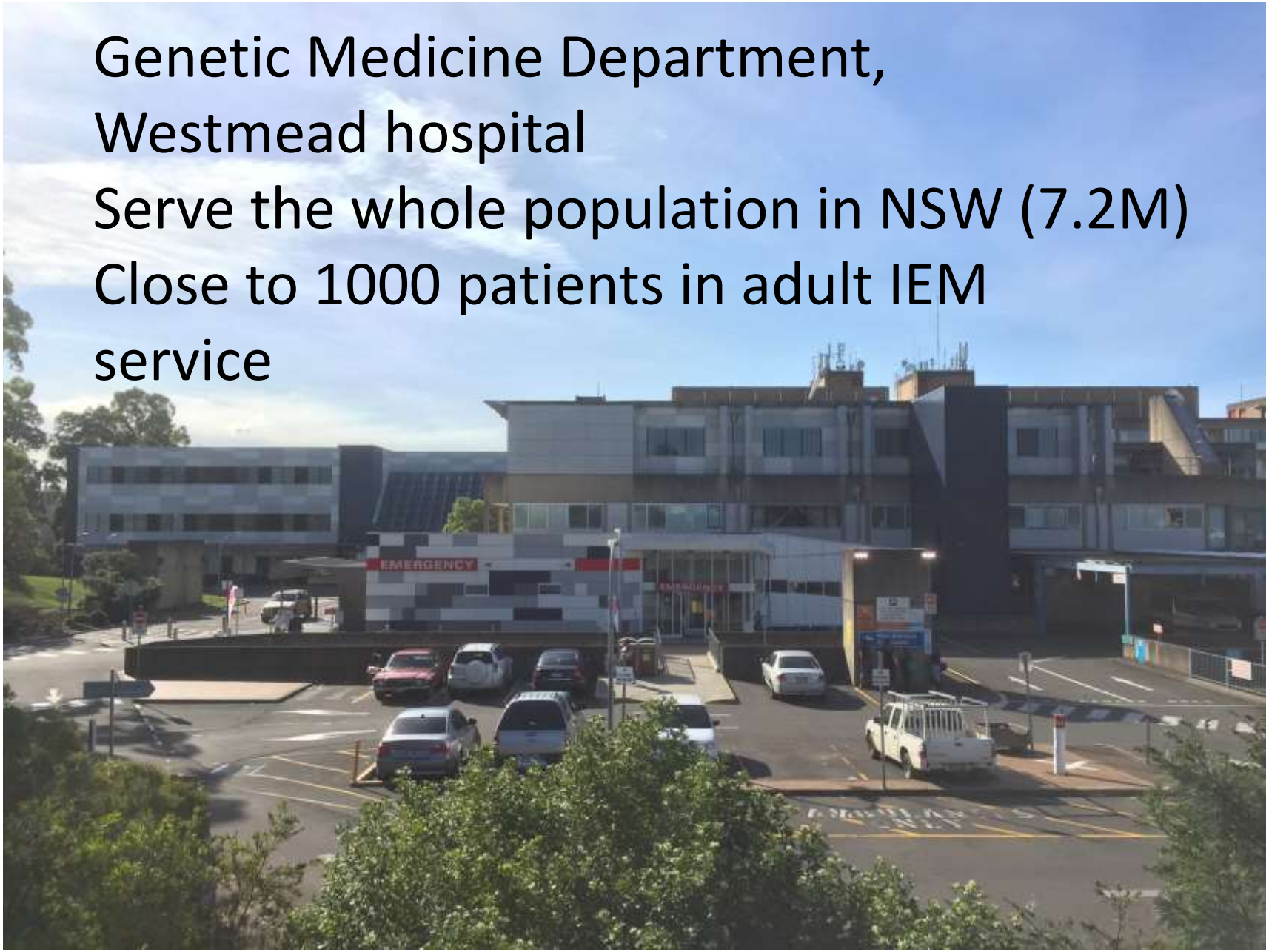
# Disclosure

- I am serving the principle investigator of the rare disease registry program and the MPS virtual advisory board, sponsored by Genzyme

# Inborn metabolic diseases






Genetic Medicine Department, Westmead hospital

Serve the whole population in NSW (7.2M)

Close to 1000 patients in adult IEM service

Question:
Do we have IEM patients around?

Question:
Where are the older IEM patients now

# Original article

Question: Do we have IEM patients around?

## Analysis of inborn errors of metabolism: disease spectrum for expanded newborn screening in Hong Kong

Han-Chih Hencher Lee, Chloe Miu Mak, Ching-Wan Lam, Yuet-Ping Yuen, Angel On-Kei Chan, Chi-Chung Shek, Tak-Shing Siu, Chi-Kong Lai, Chor-Kwan Ching, Wai-Kwan Siu, Sammy Pak-Lam Chen, Chun-Yiu Law, Morris Hok-Leung Tai, Sidney Tam and Albert Yan-Wo Chan

*Keywords:* *biochemical genetics; chemical pathology; expanded newborn screening; Hong Kong; inborn errors of metabolism; tandem mas*

- Difficult to know the exact incidence of IEM disease
- The estimation is around 1 in 4000 live birth for classical IEM

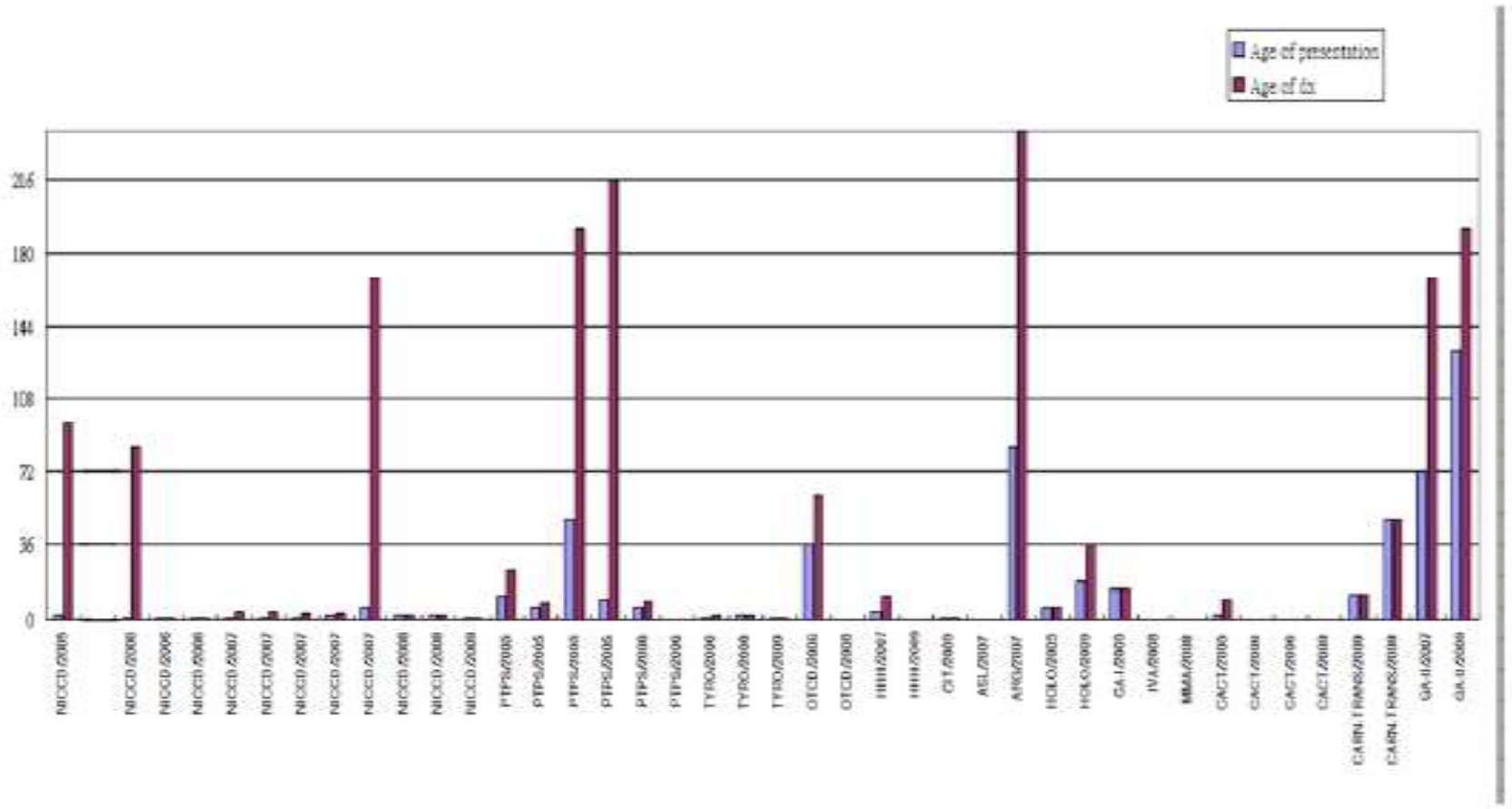
**Background** Data of classical inbo…dation are largely lacking in Hong Kong, wh…been initiated. The current study aimed to …ssical IEM in Hong Kong, which would be i…area.
**Methods** The laboratory records o… from year 2005 to 2009 inclusive in thi…enetic diagnostic services for IEM were retr…
**Results** Among the cohort, 43 p…emias (predominantly citrin deficiency, hyperphenylalan… pyruvoyl-tetrahydropterin synthase deficiency and tyrosinemia type I), 5 cases (12%) of organic acidemias (predominantly holocarboxylase synthetase deficiency) and 8 cases (19%) of fatty acid oxidation defects (predominantly carnitine-acylcarnitine translocase deficiency). The incidence of classical IEM in Hong Kong was roughly estimated to be at least 1 case per 4122 lives births, or 0.243 cases per 1000 live births. This incidence is similar to those reported worldwide, including the mainland of China. The estimated incidence of hyperphenylalaninemia was 1 in 29 542 live births.
**Conclusions** Our data indicate that it is indisputable for the introduction of expanded newborn screening program in Hong Kong. Since Hong Kong is a metropolitan city, a comprehensive expanded newborn screening program and referral system should be available to serve the neonates born in the area.

*Chin Med J 2011;124(7):983-989*

# Where are the older IEM patients now?

- A survey to paediatric units
  - Age 16 or above
  - Classical IEM
- PMH: 10 patients (age 1
- QMH: ?20-30 patients
- PWH: 1
- KWH: Nil
  - (15 IEM patients in their registry, oldest one in early teens)
- PYH: Nil

? A lost generation of IEM in adolescence

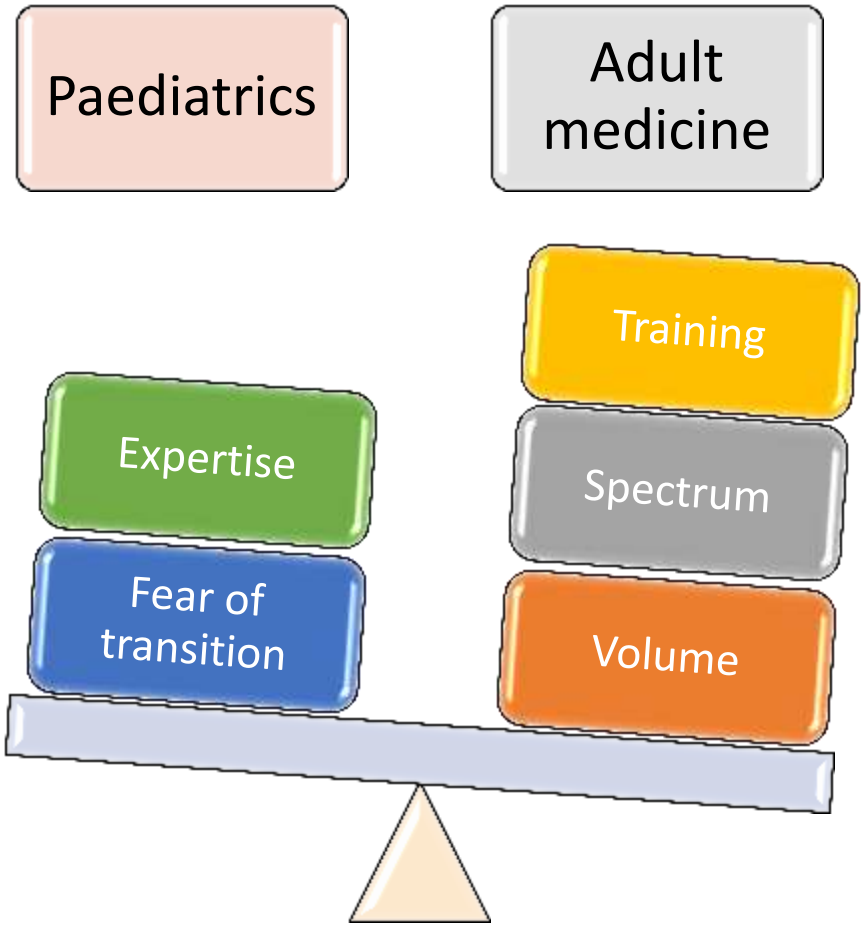



Mak M. Chemical pathology analysis of inborn errors of metabolism for expanded newborn screening in Hong Kong . The University of Hong Kong. 2012. http://hdl.handle.net/10722/180075

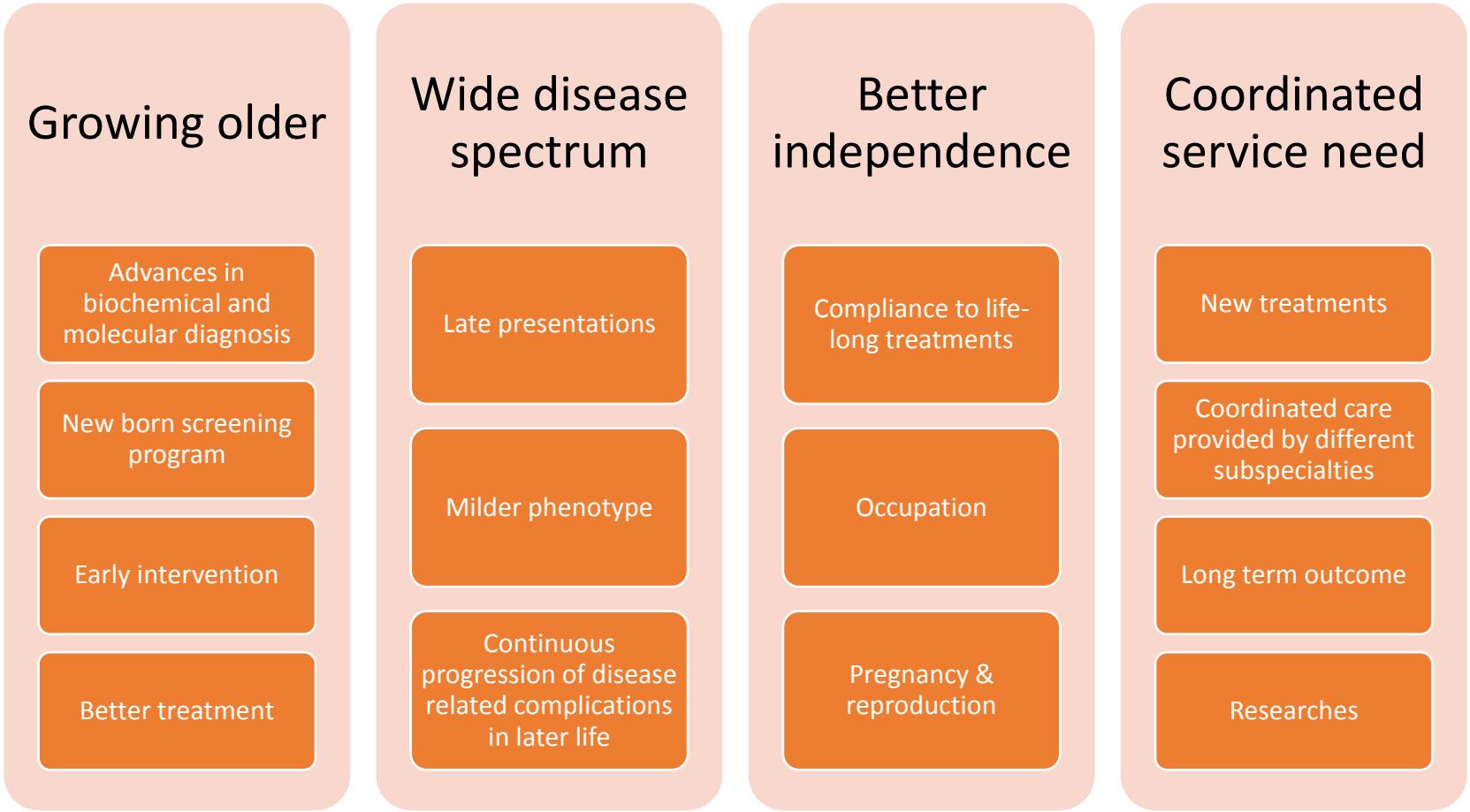
# The lost generation

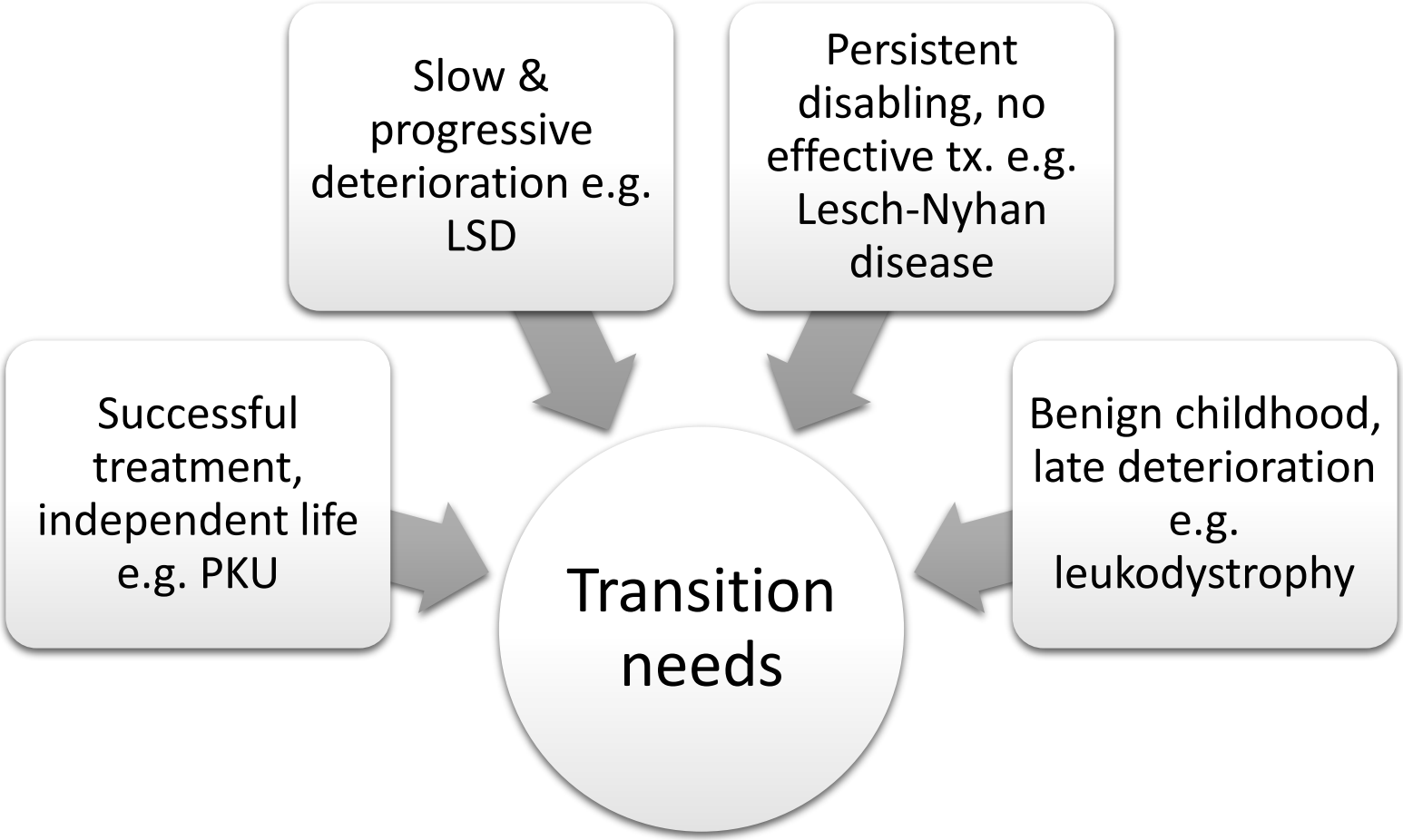
- Delay diagnosis / under- diagnosis / mis-diagnosis
  - Improving with better laboratory support and clinical awareness
  - High risk screening
- Newborn screening
  - TMS
  - Many disease at one go
  - NBS not just bring new young patients but new families with affected members in different age groups

# Who is looking after IEM patients

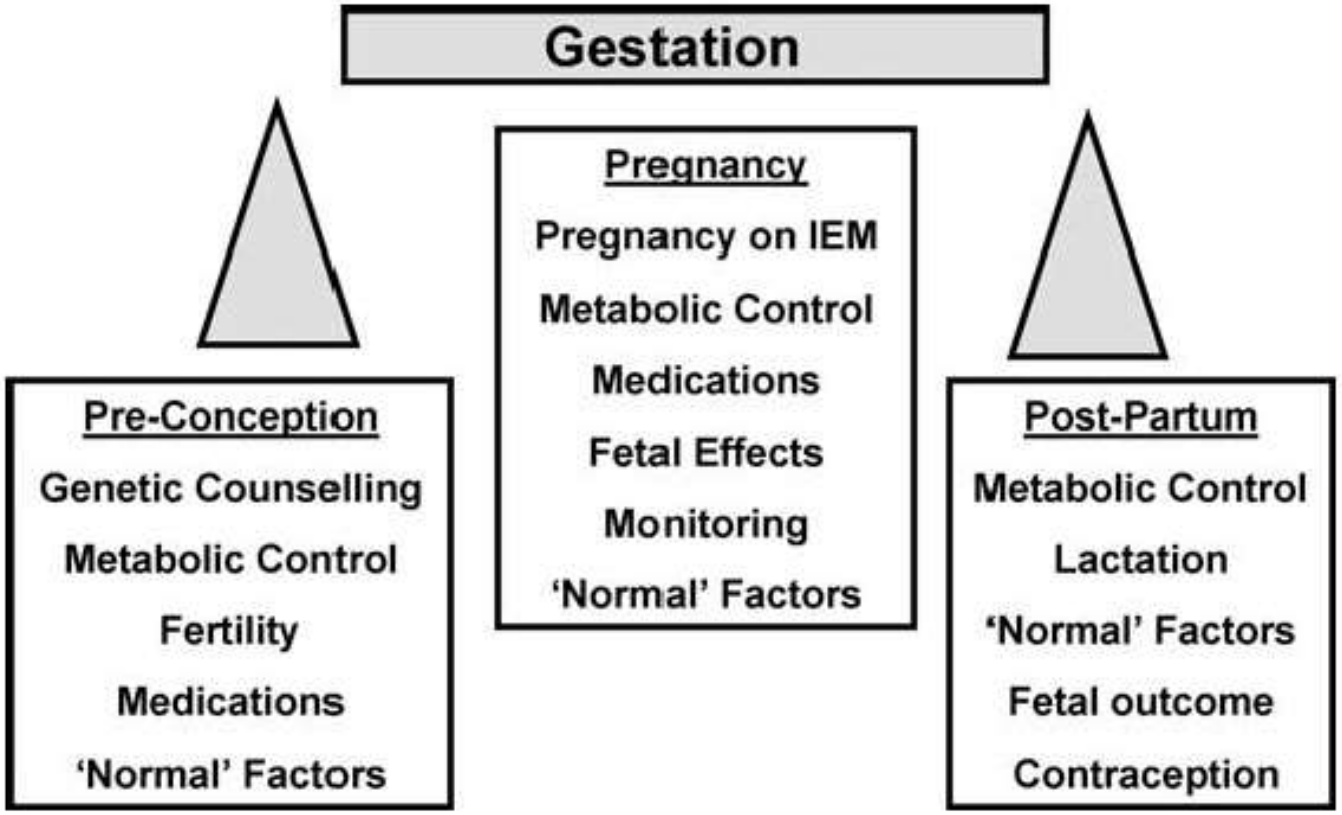


# Inborn metabolic diseases: trends in development



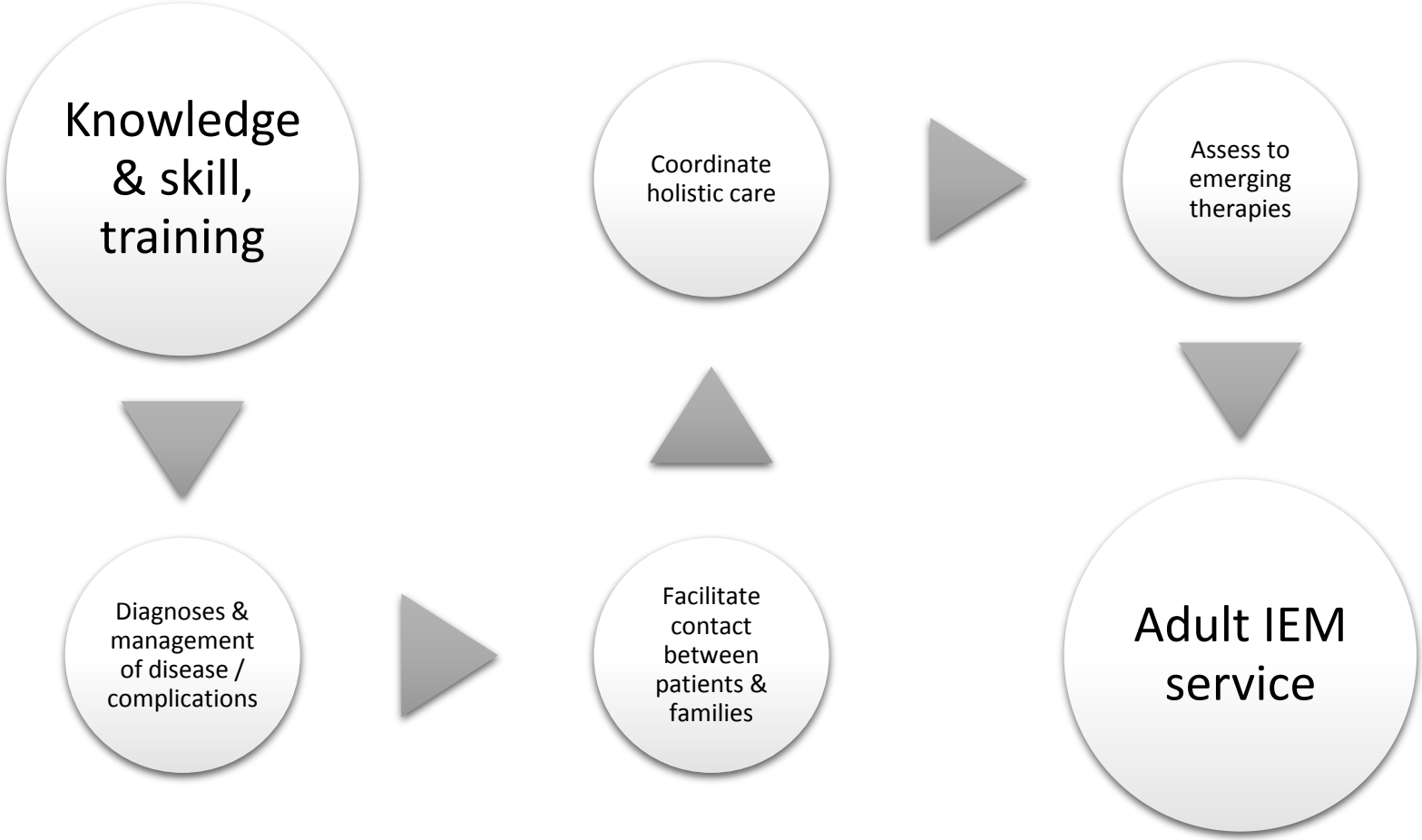

Slow & progressive deterioration e.g. LSD
Persistent disabling, no effective tx. e.g. Lesch-Nyhan disease
Successful treatment, independent life e.g. PKU
Benign childhood, late deterioration e.g. leukodystrophy
Transition needs

# Dealing with women with IEM disease undergoing pregnancy




J Inhert Metab Dis 2006;29:311-316

# Inborn metabolic diseases: trends in development



# Metabolic pathways: networks of care. A need assessment and review of services for people with inherited metabolic disease in the United Kingdom (2005)

- 24 IEM service providers in UK
  - 22 general IEM
  - 2 LSD only
- General IEM
  - 6 provides combined adult and paediatric service
  - 2 provides adult only service
  - 5 provides separate adult & paediatric service with some coordination
  - 4 provides paediatric service only
- 46 doctors or 22.6 WTE
- Estimated only 57% IEM patients under these service providers

J Inhert Metab Dis
2006;29:667-676

# Australia: designated adult IEM service only available in Sydney, Melbourne and Adelaide

- Victoria
  - Adult metabolic service Monash Medical Centre in mid 2009
- NSW
  - Adult metabolic service Westmead Hospital started in 2008, fully funded in 2010
- Queensland
  - No specific adult metabolic service
  - Adult patients requiring hospitalization admitted to an adult unit, metabolic clinician go around to provide consultations
- SA
  - Joint clinic in Royal Adelaide Hospital
- WA
  - No coordinated service

# Training in IEM clinical service

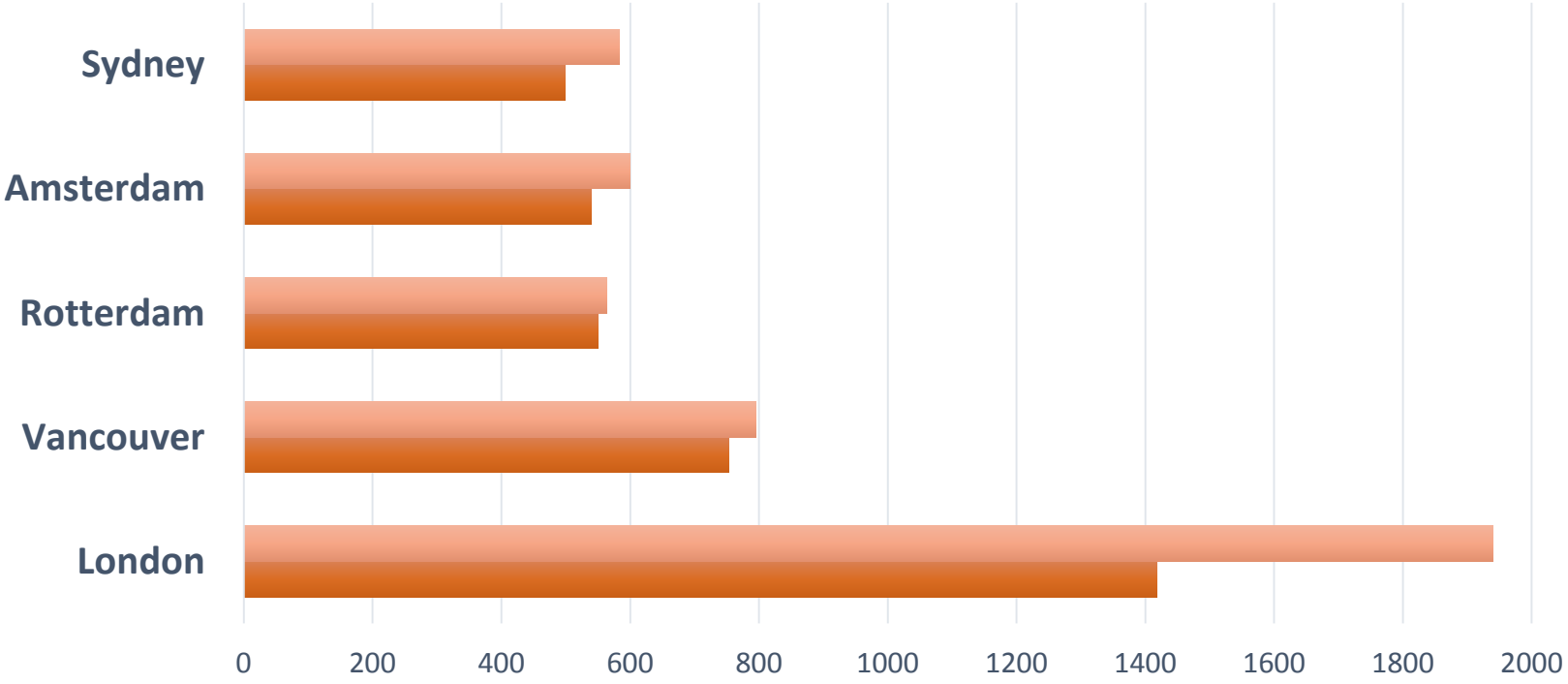
- UK
  - Higher training in IEM fell in subspecialty of Metabolic Medicine recognized by the Joint Royal College of Physicians Training Board
  - Trainees from Chemical pathology or General internal medicine
  - IEM is one of the five clinical domains in Metabolic Medicine curriculum (with DM, Lipid disorders, nutrition and bone disease)

# Training in IEM clinical service

- Australia
  - Advanced training in Clinical genetics under the Royal Australasian College of Physicians
  - Subspecialize in Metabolic Medicine in Clinical genetics

- Hong Kong
  - Proposed to incorporate IEM training in the coming Paediatric subspecialty Paediatric Endocrinology and Metabolic Medicine under Hong Kong College of Paediatricians

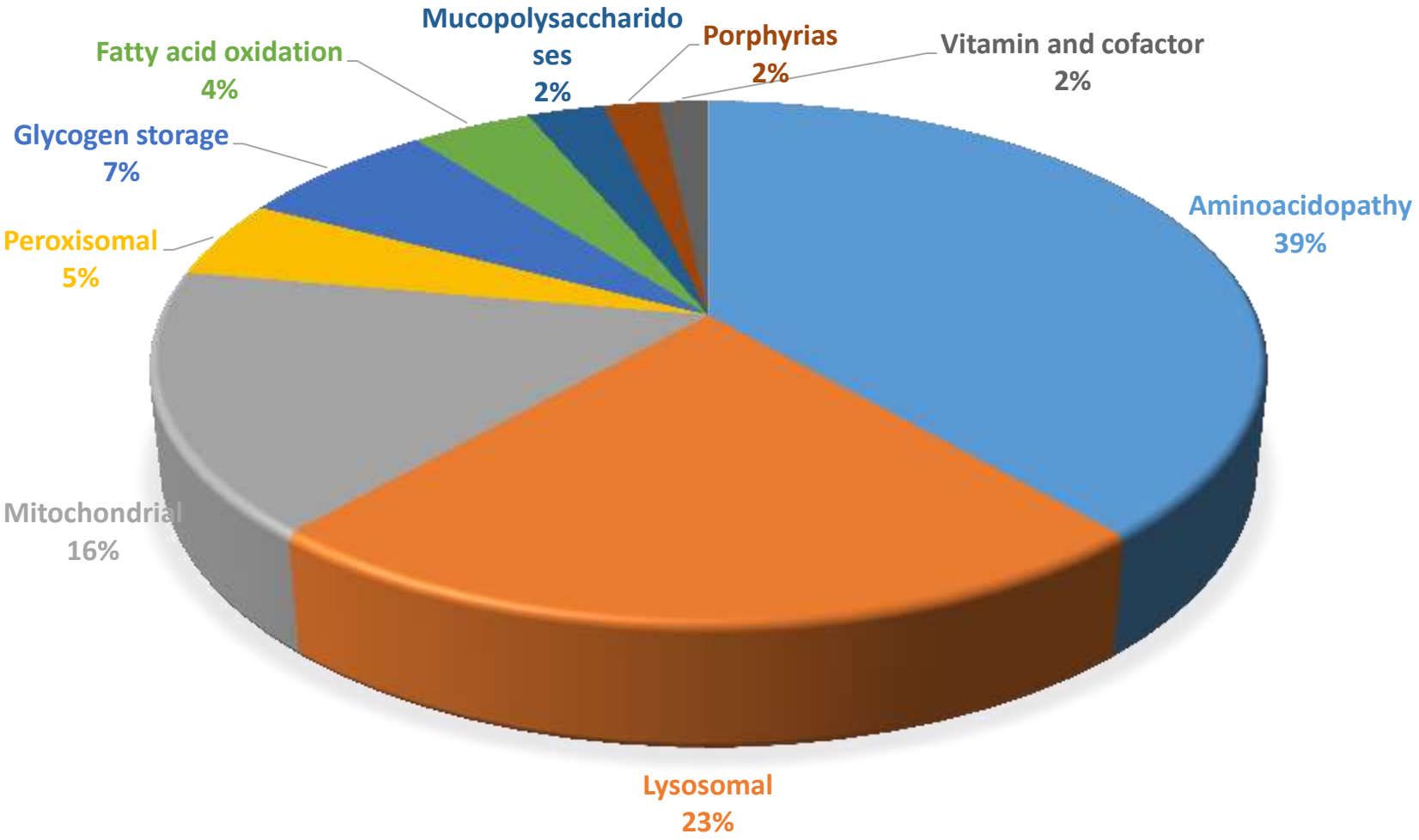
# Adult inborn metabolic disease services




| | London | Vancouver | Rotterdam | Amsterdam | Sydney |
|---|---|---|---|---|---|
| 2014 | 1940 | 795 | 564 | 600 | 583 |
| 2011 | 1418 | 753 | 551 | 540 | 499 |

JIMD Rep.2015 Oct 9

# Disorders seen in adult IEM services from an international multi-centre survey

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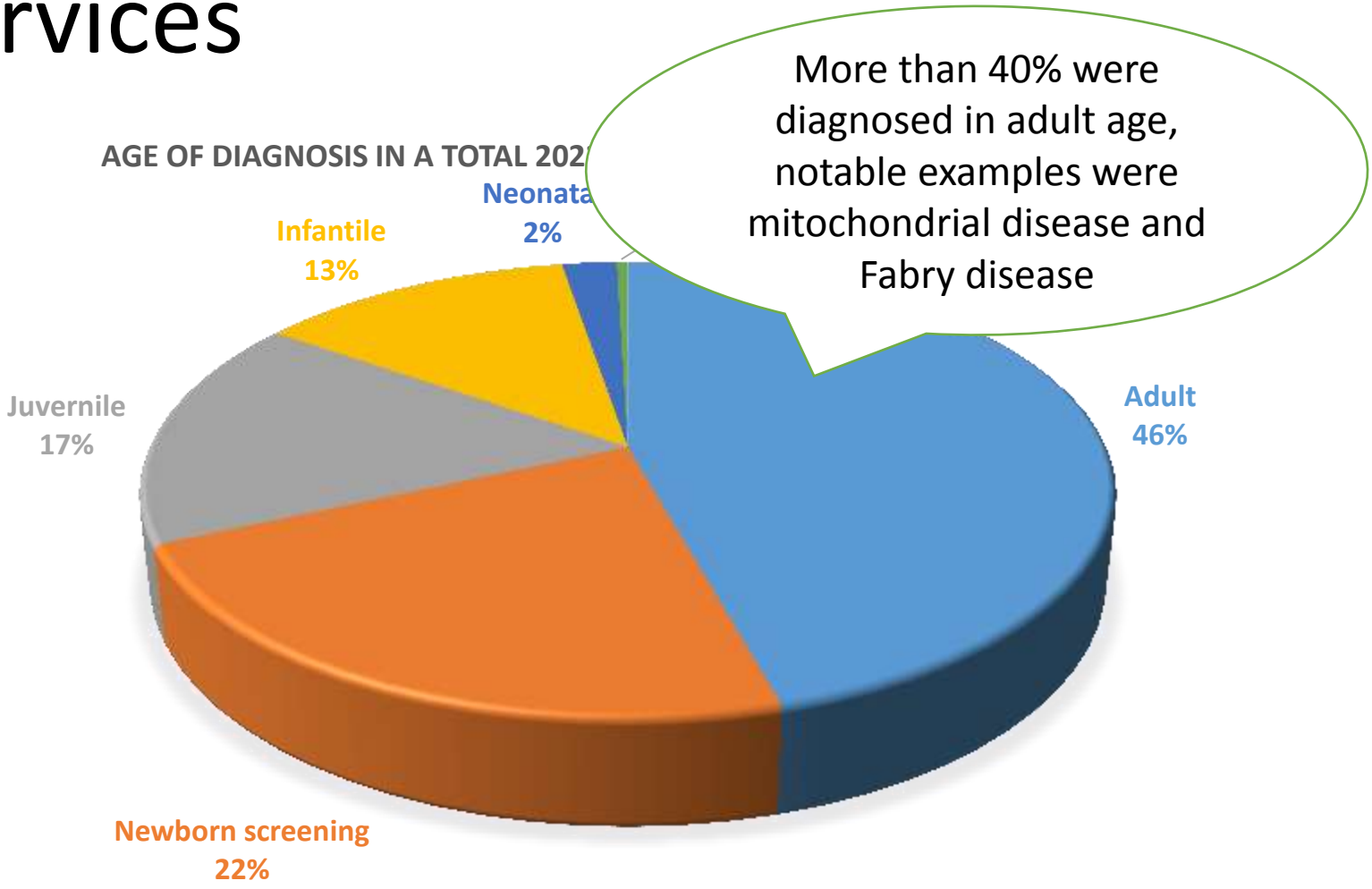


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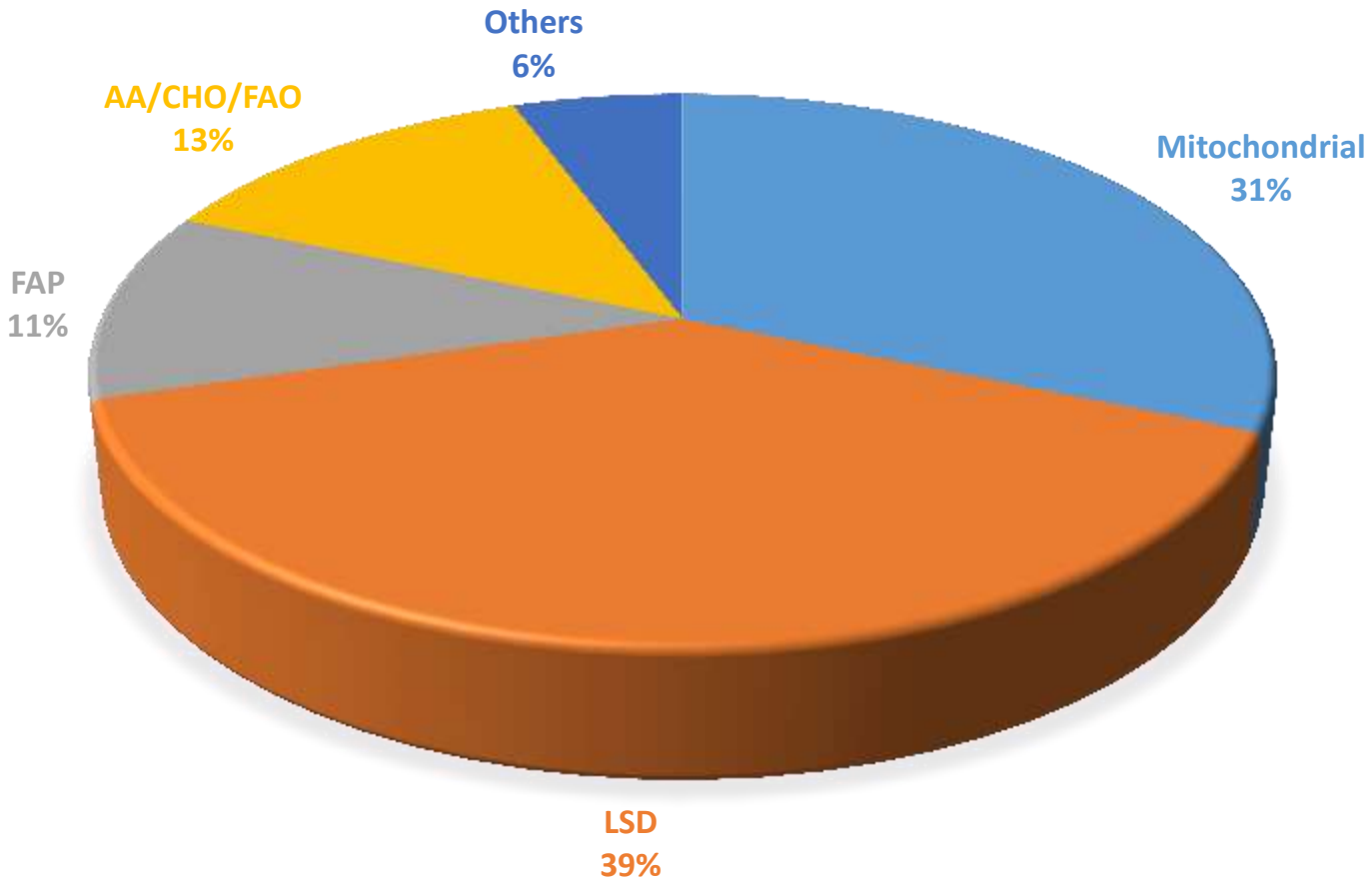



54 patients under PMH adult IEM registry

# PMH adult IEM registry

| | | | |
|---|---|---|---|
| Mitochondrial | MELAS | 10 | 1 |
| | MERRF/KSS/Leigh /unknown | 3 | 3 |
| LSD | Fabry | 6 | 1 |
| | LOPD | 6 | 3 |
| | MPS/ML/Gaucher | 0 | 5 |
| Classical IEM | AA | 1 | 2 |
| | CHO | 0 | 2 |
| | FAO | 0 | 2 |

# Adult inborn metabolic service in Princess Margaret Hospital

- July 2012, HAHO discussed on enzyme replacement therapy (ERT) arrangement for adult patients
- In the task force meeting, participating paediatricians and adult physicians all agreed that ERT only involved a few suitable patients, while the broader aspects of continuous medical care for other inborn metabolic diseases should not be overlooked.
- It was proposed to develop inborn metabolic service in adult medical units of QMH/PWH/QEH and PMH, taking care of both ERT and non-ERT related inborn metabolic diseases

# Adult inborn metabolic service in Princess Margaret Hospital

- Hospital management in Princess Margaret Hospital supported the establishment of adult IEM centre to serve KWC patients
- Started adult IEM clinic in Nov 2012
  - Initially a joint clinic with paediatrician -> adult physician 2015
  - Bimonthly -> Monthly 2016
- 2014 Princess Margaret Hospital became the only designated adult ERT treatment centre for LSD patients in HK
- Inborn metabolic disease service training
  - 2013 Charles Dent Metabolic Unit, Queen sq. London
  - 2015 Genetic medicine department, Westmead Hospital, Sydney

# Enzyme replacement therapy: a structured service driven by money concerns

- We started the first enzyme replacement therapy for a lady with late onset Pompe disease in 2011
- Since 2014, PMH started to assist ERT assessment and applications for patients from other clusters
- All newly started ERTs were managed in PMH

| | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |
|---|---|---|---|---|---|---|
| Late onset Pompe disease | 1 | 1 | 4 | 5 | 7 (1 UCH) | 7 (1 UCH) |
| Fabry disease | | | | 1 (QMH) | 4 (1 QMH, 1 QEH, 1 PWH) | 6 (1 QMH, 1 QEH, 1 PWH) |
| Gaucher disease | | | | | | 1 |
| MPS I | | | | | | 1 |

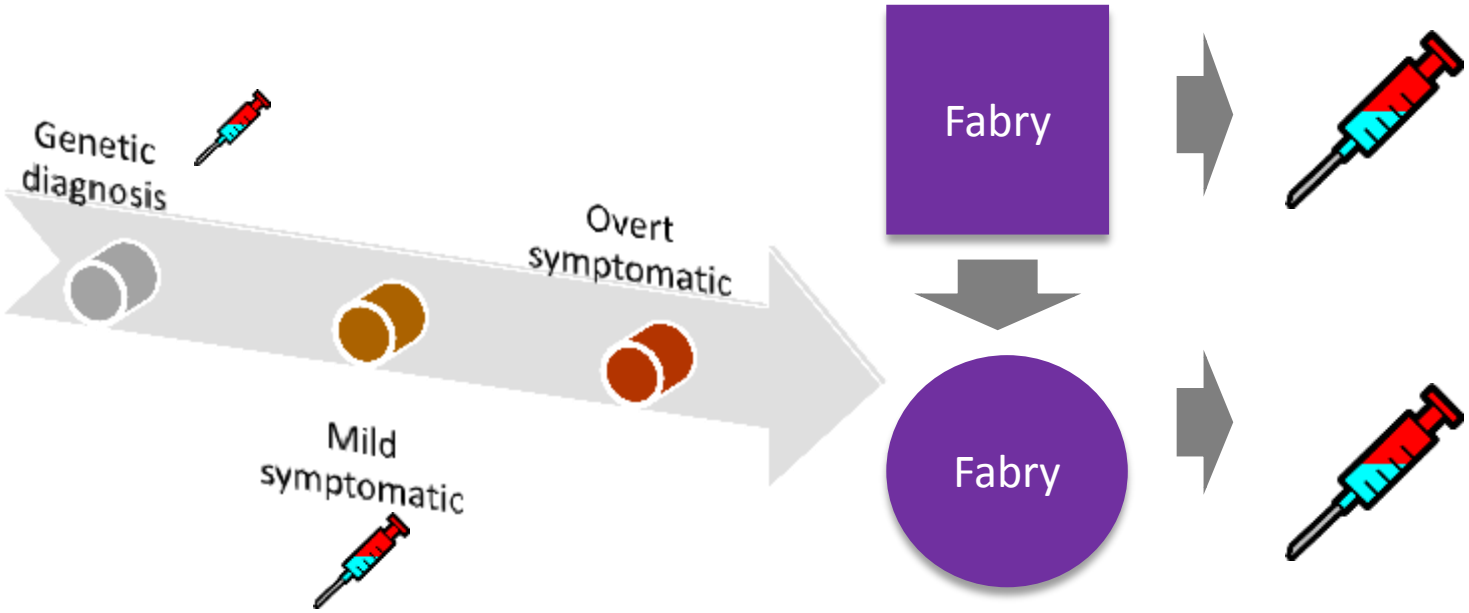
# Enzyme replacement therapy: a structured service driven by money concerns

- Enzyme therapy: un ultra-expensive therapy with modest benefit
  - Alglucosidase alfa (myozyme): $3.2M / y
  - Agalsidase beta (fabrazyme): $1.2M / y

for a 50kg person

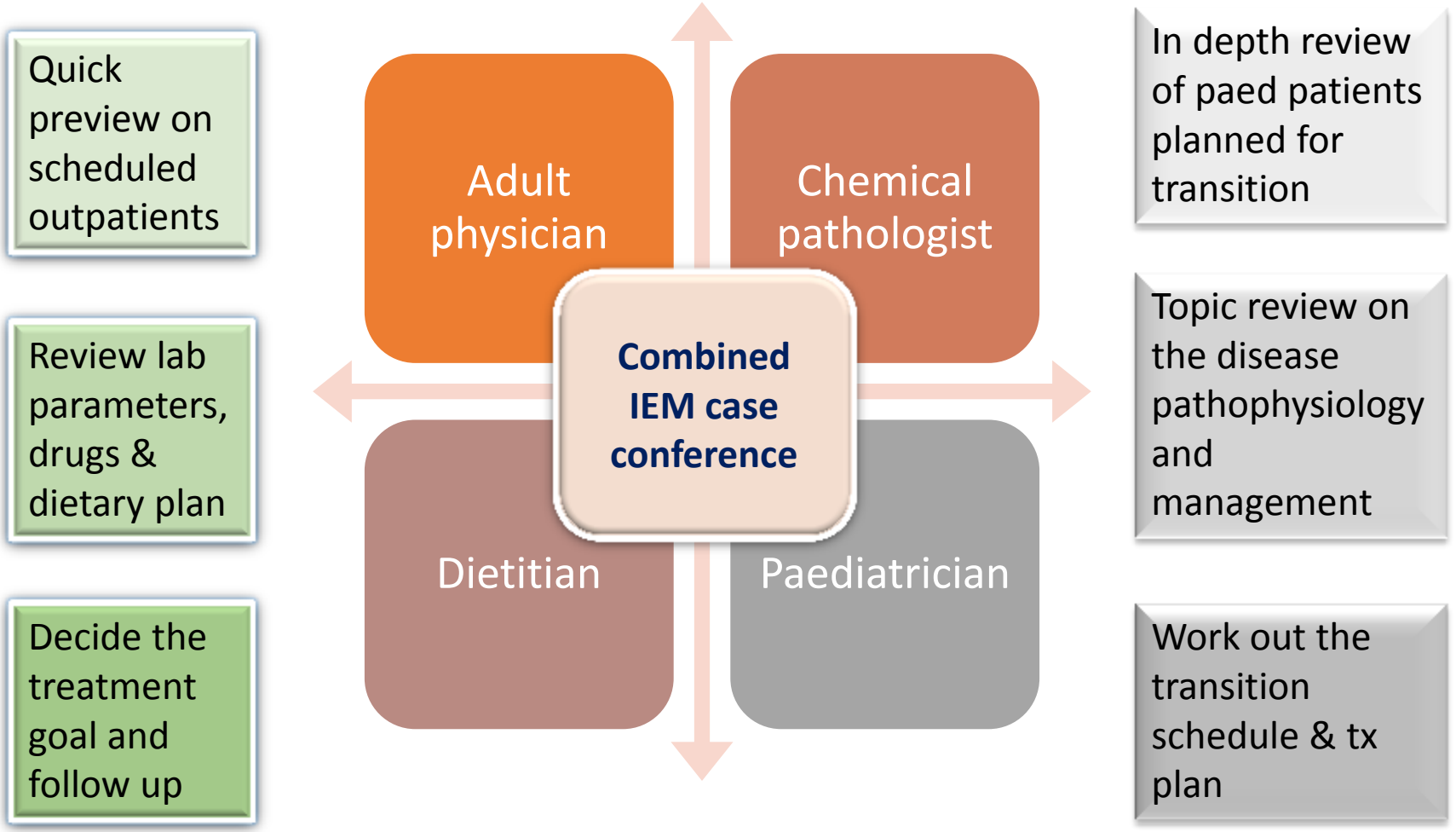
- Who & When to treat
  - ?International guidelines
    - Very similar guidelines from different countries
    - Many unanswered questions, lack of consensus with good scientific evidence to put down in guidelines to govern the clinical practice
  - ?Individualized
    - Genotype, prognosis

# Enzyme replacement therapy: longitudinal data is very important to optimize the use of ERT




Centralized management provides a window for longitudinal follow-up on asymptomatic and mild symptomatic patients and such information would be very helpful in deciding the best use of enzyme therapy

# An evolving transitional care model for inborn metabolic disease in Princess Margaret Hospital



# An evolving transitional care model for inborn metabolic disease in Princess Margaret Hospital

- International connections
- Under development
  - Individualized crisis management protocols to combat metabolic decompensation
  - Multidisciplinary expertise
- Future
  - New drug trials
  - Pregnancy registry
    - Coordinated management for IEM pregnancy, from pre-conception to post-partum

# Acknowledgements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- BioMarin

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- Dr Sammy Chen
- Dr Hencher Lee

From PMH dietetics

- Ms Judy Wong
- Mr Joseph Leung

From Westmead Hospital

- Dr Michel Tchen

HK MPS

HKSIEM Council members

Expert Panel on ERT for LSD

PMH Clinical Research Centre

PMH Ambulatory Care Centre