Developmental Delay & Neuroregression

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Content

- Development, delay & milestones
- Red-flags & neuro-regression
- Diagnostic approach
- Investigations & referrals
- Complex needs & MDT care
- Learning Points
- Resources

Developmental Delay

- Childhood Development
  - Functional skill acquisition (0-5years)
  - Sequence: physical, language, cognitive & emotional
- Delay = slow attainment/not reaching milestone
  - Common problem 5-10% children
- Global delay = significant in 2+ domains
  - 1-3% children
  - Inborn errors of metabolism - rare important cause 1-2%

Neurodevelopment

Gross motor

Fine motor & vision

Speech, language & hearing

Social, emotion, behavioural interaction

Milestones & Delay

Milestone = Median age skill acquisition (50% population)

Significant delay = Limit age (2SD)

Not achieved by Limit age →
Assesx + Invx + Intervention

Early recognition delay key !

Delay & Regression

- Single domain v. global ?
- Mild v. severe?
- Associated features
  - e.g. abnormal neurology?
- Limit ages?
- Plateau?
- Regression = loss milestones / skills?

Ref **Developmental problems and the child with special needs – Paediatrics**

Red Flags – Developmental Delay

Modality	Skill	Median age acquired	Limit Age
Gross Motor	**Sitting without support**	6-8 mo	**9 mo**
	Walking	12 mo	**18 mo**
	Run, jump	2.5 yrs	4 yrs
Fine Motor & Vision	**Fixing and following**	6-8 wks	**3 mo**
	Transferring toy	7mo	9mo
	Hand dominance	18 mo	**<12mo**
Hearing, Speech & Language	**Startles to loud noises**	newborn	**1-2 wks**
	Clear words/understanding	12mo	**18mo**
	2 words together	20-24 mo	**>2yrs**
Social, emotional, behaviour	**Shared enjoyment** (using eye contact or facial expression)	3-6mo	**9mo**
	Symbolic play (eg cuddle doll)	1.5-2 years	2-2.5 yrs
	Interactive, pretend play	2.5 years	**3 years**

Causes Developmental Delay

- **Chromosomal / Genetic**
- **Cerebral malformations / congenital**
- **Acquired**
  - Perinatal
  - Infection, injury, inflammation, tumour
- **Cerebral palsy**
- **Seizure disorder**
- **Metabolic**
  - Hypothyroidism
- **Neuromuscular disorders** (0.3:1000)
  - DMD, SMA, Congenital myopathy
  - Spinal cord lesions, e.g. spina bifida
- **Syndromes**
- **Progressive neurodegenerative conditions** (regression)
- **Social**
  - Neglect /adverse childhood experiences
- **Idiopathic**

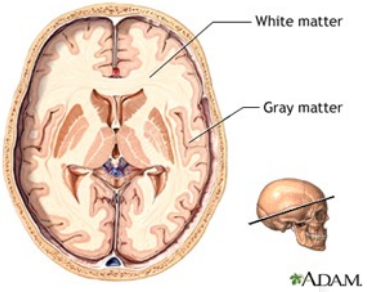
Neuroregression

Always:

Progressive neurologic deterioration

- Significant loss skills:
  - Motor, Speech, Sensory
- Responsiveness, Cognition, Behaviour
- Hypotonia, weakness
- Feeding, Swallow, Seizures

Causes Neurodevelopmental Regression



- **Without neurodegenerative process**:
- Seizure control
- Drug-related
- 2’ problem in static condition
  - e.g. mobility joint contractures
- Severe systemic illness
- Severe malnutrition

- Mental health & depression
- Neglect
- Autism Spectrum Disorder

- **With neurodegenerative or metabolic process**
  - **Inherited - Genetic**
  - **Metabolic**
  - **Storage disorders**: Lysosomal- eg MPS, Gaucher’s - enzyme replacement
  - **Mitochondrial:** Leigh’s, MELAS
  - **Grey matter** – Gaucher, MPS, Rett’s
  - **White Matter** – Leukodystrophies (Adrenoleukodystrophy, Canavan’s)
  - → Slow progressive
  - → Specific defects, some Rx
  - **Acquired** – MS (demyelinating), Wilson’s (BG)
  - Chronic viral (SSPE, HIV)

PIND Study - Progressive Intellectual & Neurological Deterioration in Childhood

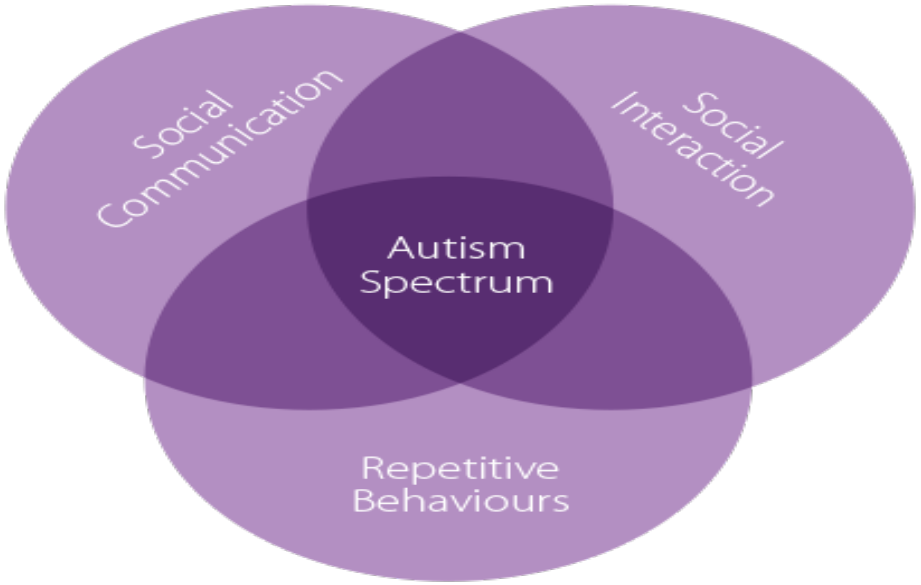
https://www.rcpch.ac.uk/work-we-do/bpsu/annual-reports

- BPSU - **Rare** neuro-degenerative disorders
  - Annual Report (1997 - 2021)
  - Cum. 2155 cases meet criteria
  - **80% <4 years old** (40% <1yr)

- **Majority** (>70%):
  - Mitochondiral cytopathies
  - Leukodystrophies (eg Krabbe's, Aicardi-Goutières)
  - Tay-Sach's
  - Rett's
  - Lysosomal

Autism Spectrum Disorder

- Common 1-2:100
- Triad impairments
- Features present <3 years old



- 10-20% Genetic
- Multifactorial
- Delay +/- regression

- Rett syndrome
  - 1:10,000, X-Linked
  - Loss language & motor, microcephaly (1yr)
  - Feeding, seizures, hand-wringing (2-3 yrs)
- Childhood disintegrative disorder
  - 1.7:100,000
  - N early devel
  - Abrupt later onset
  - Language, social, motor

Presentations to General Paediatrics

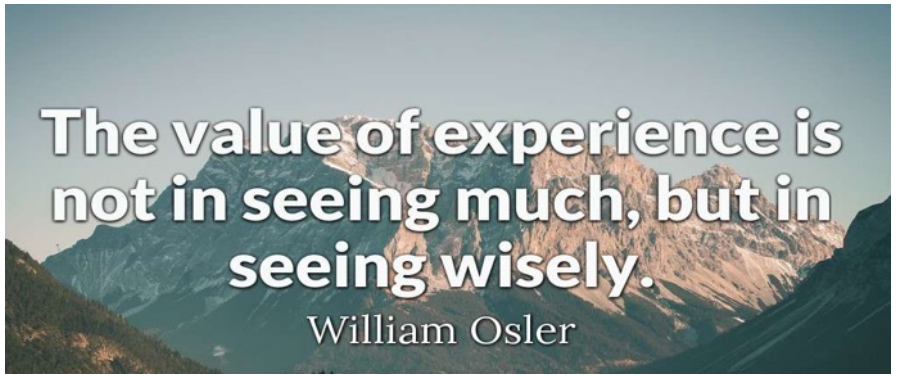
- Outpatients
- GP Referral
  - Growth, feeding
  - Floppy, low tone, stiff
  - Regression
- HV Referral

- Emergency Department
  - Seizures, encephalopathy
  - Swallow, choking
  - Motor problems, floppy
  - Behavioural change
  - Regression
- Incidental
  - Constellation problems

Assessment - Detailed History

Antenatal :	Growth, infections
Neonatal :	Prem, HIE, hypoglycaemia, bilirubin
Past Medical :	Infections, immunisations
	Growth, feeding, swallow
	Pain, seizures, sleep
Development Milestones:	Acquisition/ loss
Acquired brain injury:	Head injury, stroke
School:	Performance, cognition
Mental Health	
Family history:	3 generations, consanguinity, infant deaths
Social history:	CPPlan, LAC, adverse traumatic events

General Assessment



- **Observation & Play**
- **Examination:**
- Wt. Ht. & HC
- Dysmorphia
- Skin, eyes, muscle bulk, hand dominance
- Systemic – cardiac, organomegaly (HSM) , spine/ skeletal
- Neurological – hypotonia/ stiffness, power, reflexes, gait
- Devel abilities (motor, speech, lang, hearing, vision)
- Social Interaction

Neurodevelopment Assessment

Gross motor

- posture & movement

Fine motor

- vision & manipulation

Speech/ language & hearing

Social, emotion, behavioural interaction

Easy Questions – Telling Answers

- What is your child good at / find tricky?
- How does s/he move?
- Handle objects or toys?
- Talking / non-verbal & understanding you?
- Any concerns about seeing, hearing?
- What/ who does s/he play with?
- Does s/he have friends?
- Behaviour?
- Learning or gaining skills?
- Any loss of skills?
- https://mrcpch.paediatrics.co.uk/development/

Developmental Delay Investigations

Ref. Cleary (2005, ADC), Mithyantha (2017, ADC)

- Most common causes:
  - Chromosomal, cerebral malformation, idiopathic
- IEM rare cause isolated delay
  - Usually assoc. other clinical features
  - Specific treatment
- Signif Global Delay or Regression
  - Prompt urgent action
  - Manage future decompensation / decline
  - Early MDT

Baseline Investigations
Global Delay – with no assoc. findings

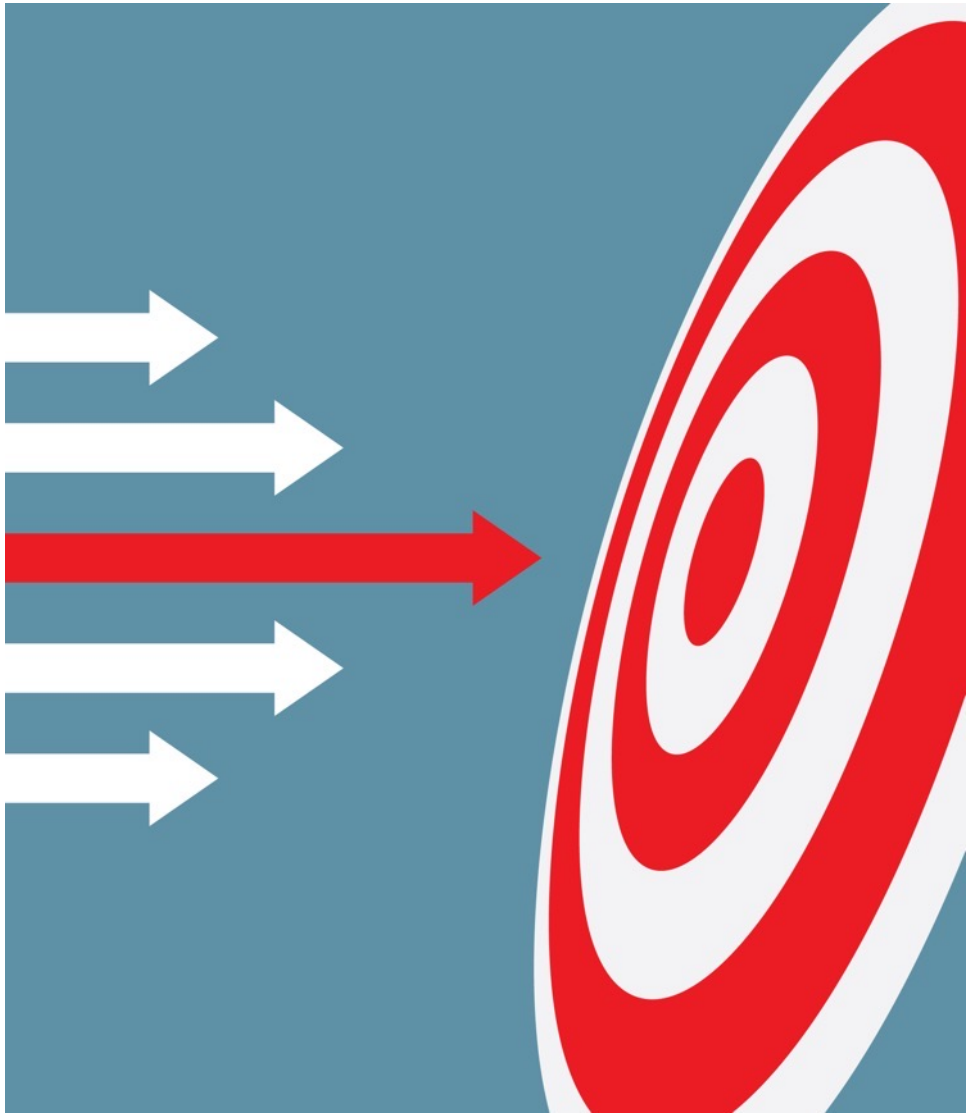
- Array CGH – chromosomes (10-20% yield)
  - +/- fragile X
- CK (DMD, myop)
- Thyroid function tests
- FBC, ferritin
- Urea, sodium, potassium, calcium, Vitamin D (nutrition)
- Liver function tests (metabolic)
- Check neonatal blood spot result
  - Congenital hypothyroid + metabolic (PKU, HCU)
- Vision & Hearing referrals
- Slight differences in papers/ guidelines

Global Delay + assoc. findings/red flags

- Baseline + :
- FHx, consanguinity, regression, congenital ataxia, seizures, organomegaly, coarse facial features
  - Blood gas
  - Glucose
  - Lactate, Ammonia
  - Urate
  - Biotinidase
  - Amino acids
  - Urine: Organic acids
- MRI brain
  - Signif micro/macroceph
  - Abnormal neurology
  - Seizures
  - Regression
- Neurology opinion
- Metabolic opinion

Referrals & Management

- **Referrals:**
- Single domain *not* limit age
  - →Therapist + review
- Single domain *at* limit age / Global delay
  - → Therapist + Community Paeds + baseline invx
- Any delay *with* abnormal neurology/seizures/signif. head size
  - → Urgent referral Neurology
  - →May need acute/ rapid access review
- Regression
  - →Acute/ rapid access review +Invx
  - →Urgent Neurology+ Metabolic



Medical Complexity + Complex Needs

- **Life Course Supportive MDT:**
  - Community Paediatrician, Medical & Surgical Specialties, Genetics, Palliative Care, AHPs, CCNT, School, Social Worker + Parents
- LTV + Recurrent chest infections
- Secretion mx
- Saliva mx
- Feeding PEG + constipation
- Tone Mx
- Posture, pain + hips
- **Good MDT / parent communication**

Complex Needs & MDT Care

- Care co-ordination & integrated care
- MDT & parent/ carer
  - Communication
  - Involvement – care planning/ decision making
  - Discharge planning
- Biopsychosocial approach
  - Health, Social & Mental health - Holistic care
  - Quality of life
  - Inclusivity
- Social Care, Respite, Community Supports
- Parents/ siblings needs

Learning Points

- Developmental delay is common
  - Understand development & milestones

- Early recognition delay or regression
  - Red flags & Serious causes – not to be missed

- Broad & focused history
- Focused observation, play & examination
- Early referrals

- Urgent response regression
- MDT care + parents

Summary Diagnostic Approach

Isolated Devel Delay - no assoc. features, no red flags (eg isolated speech delay)

- Refer to relevant Therapist
- Refer Vision & Hearing tests
- If approaching limit age→ refer Community Paediatrics

Global Delay – no other assoc features, no red flags

- Baseline bloods
- Vision, hearing tests
- Refer to Community Paediatrician + Therapists

Any delay **with** abnormal neurology/ seizures/ abnormal head size / red flags

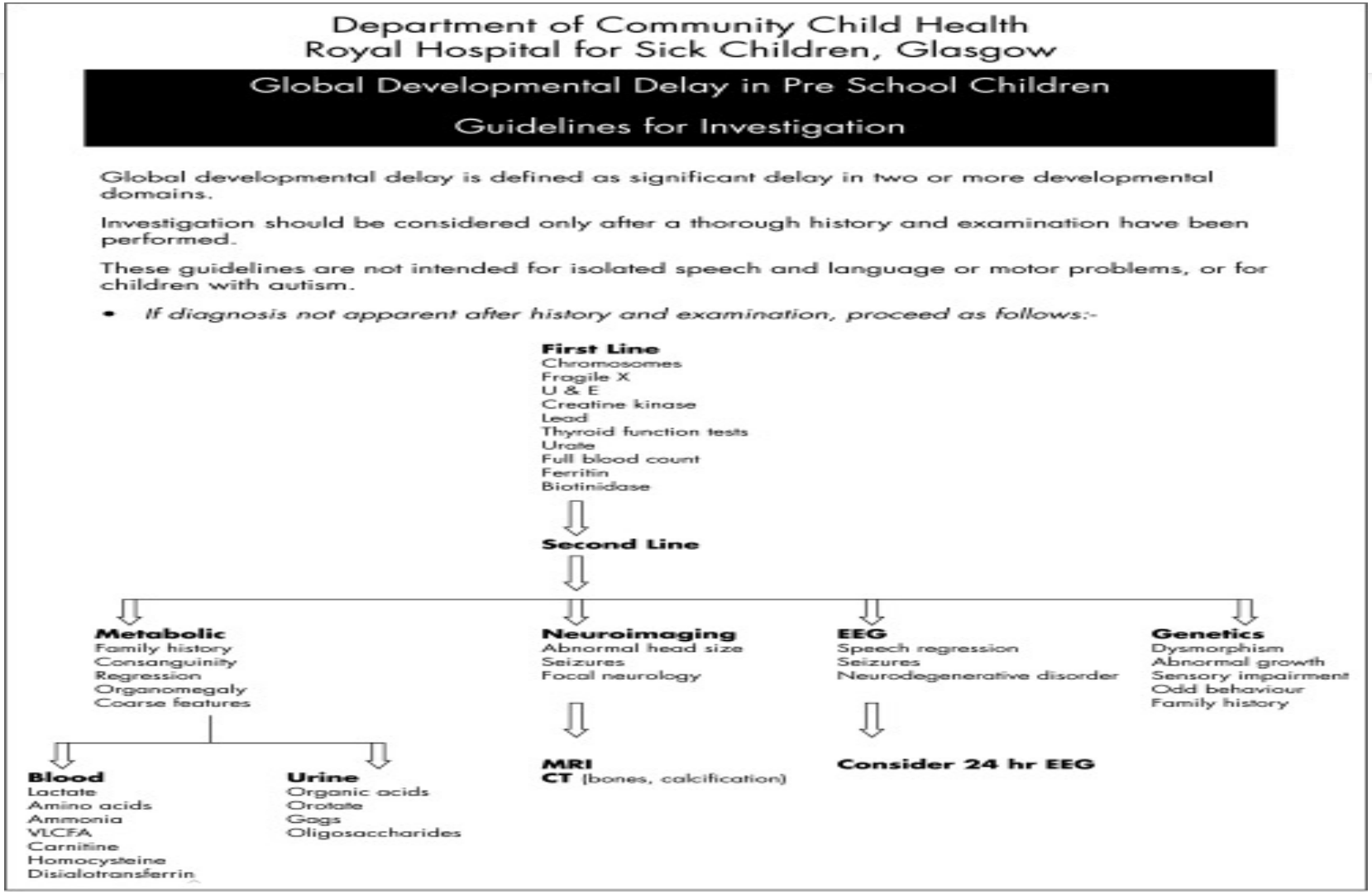
- Baseline bloods & tailored Invx
- → + MRI
- Refer urgently Neurology / Rapid access

Neuroregression

- Baseline bloods & tailored Invx
- → Urgent assessment
- Rapid access clinic
- Neurometabolic opinions
- → more extensive invx

Glasgow Sick Children Guideline

McDonald (2006, ADC)



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Global Developmental Delay in Pre School Children

Guidelines for Investigation

Global developmental delay is defined as significant delay in two or more developmental domains.

Investigation should be considered only after a thorough history and examination have been performed.

These guidelines are not intended for isolated speech and language or motor problems, or for children with autism.

- *If diagnosis not apparent after history and examination, proceed as follows:-*

First Line
Chromosomes
Fragile X
U & E
Creatine kinase
Lead
Thyroid function tests
Urate
Full blood count
Ferritin
Biotinidase

⇩

Second Line

⇩

Metabolic
Family history
Consanguinity
Regression
Organomegaly
Coarse features

⇩

Blood
Lactate
Amino acids
Ammonia
VLCFA
Carnitine
Homocysteine
Disialotransferrin

Urine
Organic acids
Orotate
Gags
Oligosaccharides

Neuroimaging
Abnormal head size
Seizures
Focal neurology

⇩

MRI
CT (bones, calcification)

EEG
Speech regression
Seizures
Neurodegenerative disorder

⇩

Consider 24 hr EEG

Genetics
Dysmorphism
Abnormal growth
Sensory impairment
Odd behaviour
Family history

Resources

- MRCPCH Developmental Station Guides
  - Development One Page Guide https://mrcpch.paediatrics.co.uk/development/
  - Common Conditions https://mrcpch.paediatrics.co.uk/development/developmental-common-conditions/
  - Videos https://mrcpch.paediatrics.co.uk/development/development-videos/
- Red Flags Early Identification Guide for Children (birth -five years)
  - https://www.childrens.health.qld.gov.au/wp-content/uploads/PDF/red-flags-a3.pdf
- Developmental Toys

Articles - ADC

- Cleary MA, Green A. Developmental delay: when to suspect and how to investigate for an inborn error of metabolism. *Arch Dis Child*. 2005 Nov;90(11):1128-32
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- Mithyantha R, Kneen R, McCann E, Gladstone M. Current evidence-based recommendations on investigating children with global developmental delay. *Arch Dis Child*. 2017 Nov;102(11):1071-1076.
- Hart AR, Sharma R, Atherton M, Alabed S, Simpson S, Barfield S, Cohen J, McGlashan N, Ravi A, Parker MJ, Connolly DJ. Aetiological investigations in early developmental impairment: are they worth it? *Arch Dis Child*. 2017 Nov;102(11):1004-1013.

Thanks. Questions?