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Comprehensive Care for Children with Trisomy 18 Across the Care Continuum: A Clinical Practice Guideline

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Speaker Disclosures

- None
- A huge THANK YOU to all the families who contributed to this presentation

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Learning Objectives

- Review the diagnosis/pathophysiology of Trisomy 18 and the progression in care of children with Trisomy 18 over the recent years.
- Discuss patient stories and the perspective of the caregiver of the child with Trisomy 18.
- Understand the process of creating a clinical practice guideline
- Understand use of the guideline when caring for children with Trisomy 18.

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How many people have cared for a child with Trisomy 18?

4

Of those who have cared for a child with Trisomy 18, how many have felt unsure making clinical decisions for this child because they were unfamiliar with the diagnosis?

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What is Trisomy 18?

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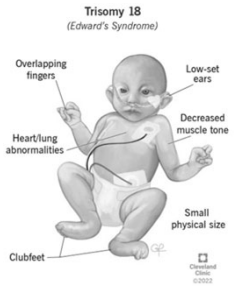
What is Trisomy 18?

Trisomy 18 (Edward's Syndrome) is a chromosomal abnormality in which there are three, rather than two, copies of the eighteenth chromosome



(Cleveland Clinic, 2022)

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Incidence & Survival

- Approximately 4.8 cases per 10,000 births
- Phenotype varies based on the presence of complete or incomplete trisomy.
- Five-year survival estimated to be 12.3%, although
- Survival rates are increasing

(Meyer et al., 2016; Springett et al., 2015)

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Have you cared for a child with Trisomy 18 that has had more modern medical interventions such as a tracheostomy or a cardiac surgery?

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The Idea

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The Idea

- The number of children with Trisomy 18 is increasing each year
- Families of children with Trisomy 18 tend to lean heavily on each other for support
- Support groups can cause lots of confusion which can make it difficult to make proper care decisions

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The Idea

- Children with Trisomy 18 would benefit from a care guideline to standardize care
- Modeled after the American Association of Pediatrics' (AAP) guideline for children with Trisomy 21
- This guideline was developed at Michigan Medicine

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Meet the Families

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Faith - 15 years old

- Geneticist referral after abnormalities seen on a routine ultrasound
- Initially treated at birth and offered full medical interventions, but medical recommendations changed when Trisomy 18 diagnosis was confirmed
- Able to walk with a walker and is able to do things such go on vacation and visit Santa

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Maristella – 14 years old

- Potential diagnosis through routine bloodwork
- Formal diagnosis "slowed down" care
- Ethics committee and CPS involved
- Can now respond to yes or no questions and loves to watch football

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Gianna – 16 months old

- Diagnosis found through NIPT at 10 weeks gestation
- Moved all care to Michigan Medicine prior to birth
- Off the ventilator during the day and can take some feeds by mouth
- Loves going to the park, family outings and playdates

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"Parents are robbed of hope because the doctors don't have any hope."

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Creating the Guideline

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Literature Review & Synthesis

- Trisomy 18
  - The literature was searched for recent Trisomy 18 literature
  - Kepple et al. (2021) was identified as a starting point
  - The Support Organization for Trisomy (Trisomy.org)
    - Pyle et al. (2018)
- Clinical Practice Guidelines (CPGs)
  - The literature was searched to find evidence for the use of clinical practice guidelines

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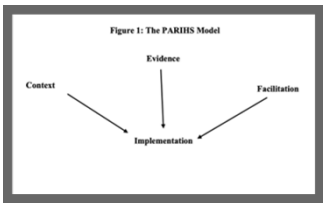
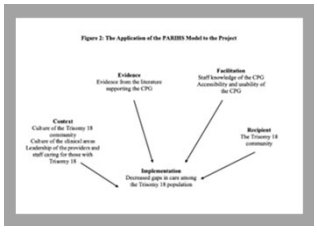
Theoretical Framework/Model





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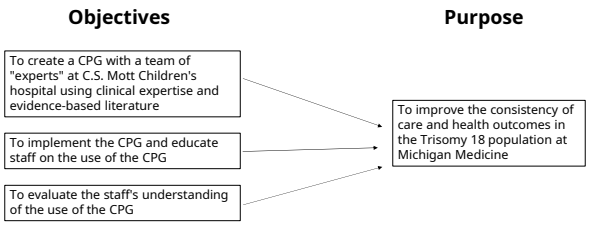
Project Purpose and Objectives



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Project Description

- Identify key literature
- Create the team
- Write the guideline
- Publish guideline
- Educate staff on the guideline
- Evaluate the guideline

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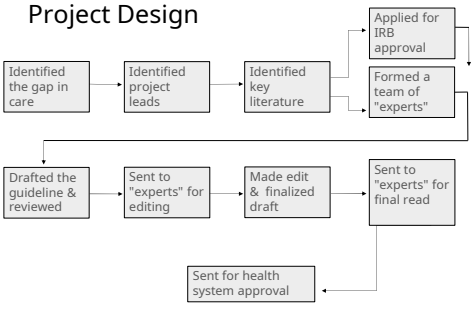
Project Design



Project Leads

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The Trisomy 18 Care Guideline

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The Results

The CPG

- Statement, purpose, scope, definition and introduction
- Recommendations for cardiology, pulmonology/sleep, neurology, ophthalmology, genitourinary, nutrition and gastrointestinal abnormalities, hematology and oncology, musculoskeletal, obstetrics and gynecology, otolaryngology (including airway and audiology), physical and occupational therapy, and general
- A checklist that can be given to primary care providers and families to help ensure that children with Trisomy 18 are getting the proper recommendations

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Care of the Child with Trisomy 18 According to the Guideline

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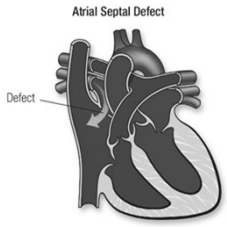
Cardiology

- Between 45% and 95% have congenital cardiovascular malformations
- Ventricular septal defects, patent ductus arteriosus and atrial septal defects are the most common



[1]American Heart Association, 2024; Imataka et al., 2016; Pont et al., 2006; Springett et al., 2015)

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Cardiology Standard of Care

- Initial echocardiogram in the first few days of life.
  - If the echocardiogram is normal, then repeat at 1 month.
  - If the echocardiogram is abnormal, consult pediatric cardiology.
- If child had fetal echocardiogram, refer to the maternal medical record for the cardiac assessment and plan

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Pulmonary

- Approximately 80% have pulmonary involvement.
  - Central sleep apnea,
  - Obstructive sleep apnea (OSA),
  - Hypoventilation,
  - Chronic pulmonary aspiration,
  - Pulmonary hypertension,
  - Laryngotracheobronchial defects
- Respiratory disorders are among the most common cause of death
- Sleep disordered breathing occurs in approximately 45%

(Brummer, 2021; Bruns, & Campbell 2014; Kettler et al., 2020)

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Pulmonary Standard of Care

- Consultation with a Pediatric Pulmonologist if symptoms of hypoxia, suspected central or obstructive apnea or postoperative pulmonary complications.
- Palivizumab (Synagis) or nirsevimab (Beyfortus)
- Screen for sleep apnea (central and obstructive) at every primary care visit.
- Consider Polysomnogram if
  - stridor, unexplained hypoxia, hypercarbia, or pulmonary hypertension.
  - 3 months after any airway surgery
  - Blood gas in NICU pCO2 is > 50mmHg
- By age 4 if not previously done.
- Consider consultation with Otolaryngologist for unexplained or prolonged hypoxia.
- Infants should undergo a car seat study prior to discharge.

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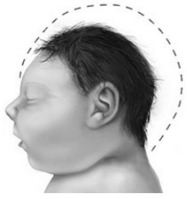
Neurology

- Congenital nervous system anomalies choroid plexus cysts (most common), cerebellar hypoplasia,
  - Enlarged cisterna magna
  - Neural tube defects
  - Anencephaly
  - Hydrocephalus
  - Dandy-Walker malformation
  - Microcephaly
- Seizures reported in approx. 64% and are often medication-resistant in those with structural brain malformations
- Cognitive disabilities are common



(Centers for Disease Control and Prevention, n.d.; Cereda & Carey, 2012; Kumada et al., 2013; Matricardi et al., 2016)

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Neurology Standard of Care

- A postnatal cranial ultrasound and/or head magnetic resonance imaging should be performed and concerning findings should be addressed in consultation with a Pediatric Neurosurgeon.
- Given the high rate of seizures in trisomy 18, a Pediatric Neurologist should be consulted if there any concerns for seizures such as abnormal movements or staring episodes.

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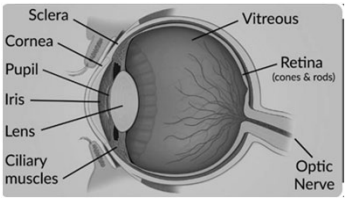
Ophthalmology

- Anophthalmus,
- Bilateral retinal dysplasia
- Optic nerve hypoplasia
- Congenital glaucoma
- Congenital cataracts



(Correia et al., 2017; Shavell, 2020)

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Ophthalmology Standard of Care

- Ophthalmologic exam at birth by a Pediatric Ophthalmologist and yearly thereafter.
- Consider offering sunglasses to older children with photophobia or unexplained irritability.

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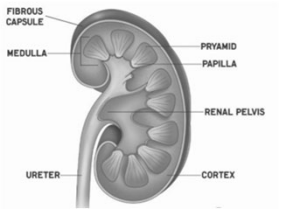
Genitourinary

- Approximately 18% have genitourinary abnormalities
  - Renal agenesis,
  - Duplication of urinary tract
  - Horseshoe kidney,
  - Cystic kidney disease
  - Congenital hydronephrosis
  - Ectopic kidney
  - Renal dysplasia
  - Obstructive genitourinary defects
  - Hypospadias/epispadias



(Anatomy Stuff, 2020; Springett et al., 2015)

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Genitourinary Standard of Care

- Newborns should have an abdominal ultrasound done at 48-72 hours after birth to evaluate for renal/urologic abnormalities.
- If abnormalities are found on the prenatal ultrasound but not the postnatal ultrasound, repeat the renal ultrasound at 4-6 weeks of life.
- Congenital genitourinary abnormalities should be addressed in consultation with a Pediatric Nephrologist and/or Urologist.
- Consideration should be made for additional imaging and prophylactic antibiotics.

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Nutrition & Gastrointestinal

- Decreased muscle tone and coordination, and
- Low gastric motility
- Meckel's diverticulum
- Esophageal atresia
- Diaphragmatic hernia
- Tracheoesophageal fistula
- Intestinal malrotation
- Pyloric stenosis
- Ano-rectal atresia/stenosis
- Abdominal gas, and constipation

(Kepple et al., 2021)

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Nutrition & GI Standards of Care

- Involve speech and OT for infants with feeding difficulty or poor weight gain.
- Video swallow study for infants demonstrating signs of dysphagia.
- Consider an enteral feeding tube for children with dysphagia and poor weight gain
- Growth measured using a Trisomy 18 growth chart
- Nutrition should be managed by a pediatric dietician with experience with Trisomy 18.
- Consult Pediatric Surgery to manage congenital gastrointestinal malformations and/or tumors .
- Consult Pediatric GI for refractory constipation and feeding intolerance.

(Baty, 1994a; Baty 1994b)

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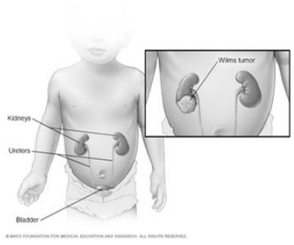
Hematology and Oncology

- At risk for neoplastic disorders
  - Hepatoblastoma
  - Wilms tumor
- At risk for hematological abnormalities
  - Thrombocytopenia
  - Neutrophilia
  - Anemia
  - Hypogammaglobinemia



(Farmakis et al, 2019; Kosho et al., 2006; Mayo Clinic, 2023; Wiedmeier et al., 2008)

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Hematology and Oncology Standard of Care

- Screen for hepatoblastoma via abdominal ultrasounds and serum alpha-fetoprotein (AFP) every three months, starting at birth until age 4
- If the AFP >50-100 ng/ml, repeat level in 6 weeks and the most recent ultrasound re-examined.
- Renal ultrasounds to screen for Wilm's tumor every 3 months from birth until age 7 and every 6 months from ages 7 to 12
- Complete blood count with differential obtained within the first 48 hours after birth.

(Farmakis, 2018; Kepple, 2021)

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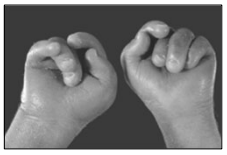
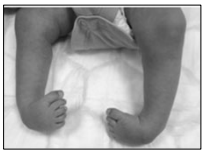
Musculoskeletal

- Radial aplasia
- Joint contractures
- Vertical talus
- Clubbed feet
- Scoliosis
- Overriding fingers
- Hypotonia





(Barts Orthopedics, 2014; Cereda & Carey, 2012; Root & Carey, 1994; WebPath, n.d.)

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Musculoskeletal-Standards of Care

- Yearly orthopedic exams with a low clinical threshold to obtain hip and spinal x-rays.
- Spinal x-ray every year starting after 2 years of age.
- Refer children with scoliosis to Pediatric Orthopedic Surgery.
- Physical Medicine and Rehabilitation (PMR) referral by by 3 months of age and annually for therapy, developmental assessments, securing adaptive equipment and bracing/orthotic needs.

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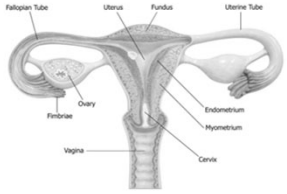
Gynecology

- Little information on puberty is know due to historically short lifespan
- Delayed puberty
- Amenorrhea
- Premature ovarian failure



(Alshami et al., 2020; Krotzer et al., 2020; Smith et al., 1989; Suwin, 2020)

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Gynecology Standard of Care

- Primary care providers should carefully monitor growth and pubertal progression.
- Consider a referral to a pediatric endocrinologist for children with decreased growth velocity.
- Consider a referral to a gynecologist for females with primary or secondary amenorrhea.

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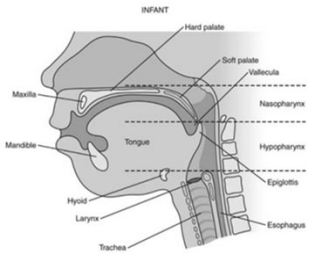
Otolaryngology

- Cleft lip and palate
- Ear abnormalities including structural defects and hearing loss
- Airway Obstruction
- Palate
- Large tonsils & adenoids
- Obstruction from base of tongue
- Small mandible
- Malacia of larynx, trachea, and bronchi



(Anesthesia Key, 2016)

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Otolaryngology Standard of Care

- Pediatric Otolaryngology referral for craniofacial abnormalities, stertor, stridor, gasping, retractions or for a child undergoing general anesthesia.
- General anesthesia should be performed in a center with a Pediatric Anesthesiologist and Pediatric Otolaryngologist
- Consultation with a Pediatric Anesthesiologist or Pediatric Otolaryngologist prior to elective intubation.
- Narcotics should be used with caution particularly if there are signs of upper airway obstruction.
- Routine audiologic evaluation at birth and within six months then yearly

(Birmingham, 2021)

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Therapy Standards

- All children should have occupational and physical therapy consultation prior to initial discharge from the hospital.
- Routine follow up with Early On for longitudinal social, educational, and developmental services.
- Regular outpatient assessments in physical and occupational therapy for developmental evaluations, range of motion assessments, and orthotic evaluation.

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Primary Care

Track

- Growth, nutrition, and swallowing
- Psychomotor and cognitive development
- Vision and hearing
- Emotional status of patient and family and infrafamilial relationships

Provide

- Routine childhood immunizations and RSV prophylaxis
- Referrals for an individualized Education Program for children starting at age 3.
- Referrals for speech, physical, and occupational therapy.

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Screen for

- Seizures or other neurological concerns.
- Ophthalmological problems.
- Orthopedic concerns including scoliosis.
- Pulmonary symptoms and frequency of illnesses.
- Sleep concerns including snoring and excessive daytime sleepiness.
- Pubertal development

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Schedule and track routine testing

- Abdominal Ultrasound and AFP every 3 months until age 4 then every 6 months until age 12
- Renal ultrasound every 3 months from age 4-7
- Audiologic evaluation age 6 months and then annually
- Vision evaluation at age 12 months then annually
- Orthopedic exam age 2 then annually
- Polysomnogram by age 4

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Exhibit A

Staying on Track with Trisomy 18

Trisomy 18 is a chromosomal abnormality that causes multiple medical morbidities. While some abnormalities will be present at birth, or apparent with a thorough history and physical exam, others might require careful monitoring and surveillance. Below is a checklist of surveillance tests to ensure that medical issues are identified and treated promptly.

Birth
- ☐ Cranial ultrasound or MRI
- ☐ Echocardiogram
- ☐ Ophthalmologic exam
- ☐ Abdominal ultrasound
- ☐ Serum alpha-fetoprotein (AFP)
- ☐ Complete blood count with differential
- ☐ Audiologic examination
- ☐ Occupation and physical therapy consultation
- ☐ Early On referral
- ☐ Polysomnogram
  - If any clinical concerns for obstructive or central apnea
  - If patient in NICU AND blood gas shows PCO2 > 50mm/Hg

1 mo
- ☐ Abdominal ultrasound to assess for renal abnormalities
  - Only done at 1mo if abnormalities seen on prenatal, but not postnatal ultrasound

3mos
- ☐ Abdominal ultrasound
- ☐ Serum AFP
- ☐ Physical Medicine and Rehabilitation (PMR) evaluation

6 mos
- ☐ Abdominal ultrasound
- ☐ Serum AFP
- ☐ Audiologic evaluation

9 mos
- ☐ Abdominal ultrasound
- ☐ Serum AFP

12 mos
- ☐ Abdominal ultrasound
- ☐ Serum AFP
- ☐ Ophthalmologic exam
- ☐ Dental exam

Starting at age 1
- ☐ Abdominal ultrasounds every 3 months
  - Until age 4
- ☐ Serum AFPs every 3 months
  - Until age 4
- ☐ Annual orthopedic exam and spinal x-rays
  - Starting at age 2
- ☐ Annual ophthalmologic evaluations
- ☐ Renal ultrasounds every 3 months
  - Between ages 4 and 7
- ☐ Abdominal ultrasounds every 6 months
  - From age 7-12
- ☐ Baseline polysomnogram by age 4 or sooner if concerns for obstructive or central sleep apnea

Puberty
- ☐ Monitor growth and pubertal development.

In addition, all well-child visits for children with Trisomy 18 should include the following:
- ☐ Assessment of growth, nutrition, and swallowing
- ☐ Growth should be measured using a Trisomy 18 growth chart
- ☐ Assessment of psychomotor motor, social, verbal and cognitive development
  - Referral to Early Oscylloscal therapy/occupational therapy/speech therapy
- ☐ Development of seizures or other neurological or ophthalmological concerns
- ☐ Assessment for scoliosis, hand or foot deformities
- ☐ Assessment of respiratory illnesses, airway clearance, and noisy breathing
- ☐ Assessment of sleep disturbances including snoring and excessive daytime sleepiness
- ☐ Dental assessment every 6 months
- ☐ Routine vaccinations as well as Palivizumab and 23-valent pneumococcal vaccine
- ☐ Assessment of psychological, social, educational, and emotional needs of the child and family

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Next Steps

- Implement the CPG
- Educate staff on the use of the CPG.
  - Education video
  - In-services
  - A presentation for nurse practitioners and residents
- Evaluate the staff's understanding of the use of the CPG
- Edit the guideline as needed
- Update periodically with new literature and recommendations

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Family Opinions

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Family Opinions

- All positive responses
  - "**Only beneficial**"
- A more organized way to keep track of things
- Helpful in the primary care setting because all subspecialities are not easily accessible
- Families appreciate anything that can help move their children forward

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Questions?

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