

**Supplementary Table 2. TLR eligibility criteria**

<b>Search Term Group</b>	<b>Inclusion Criteria</b>	<b>Exclusion Criteria</b>
<b>Population</b>	<ul style="list-style-type: none"> <li>• Patients with CTX</li> <li>• Any individual undergoing testing for CTX</li> </ul>	<ul style="list-style-type: none"> <li>• Patients without CTX</li> <li>• Individuals not undergoing testing for CTX</li> </ul>
<b>Interventions</b>	<ul style="list-style-type: none"> <li>• Any or none</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Any or none</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
<i>Outcomes: Screening, diagnosis and confirmation of CTX</i>		
<b>Outcomes</b>	<p>Articles reporting outcomes related to CTX testing (in a diagnostic or confirmatory setting) including but not limited to:</p> <ul style="list-style-type: none"> <li>• Biochemical testing</li> <li>• Molecular genetic testing for <i>CYP27A1</i> pathogenic variants</li> <li>• Pharmacokinetic (PK)/pharmacodynamic (PD) methods and other laboratory findings</li> <li>• Brain MRI or computerized tomography (CT) showing atrophy or lesions</li> <li>• Magnetic resonance (MR) spectroscopy showing increased brain lactate concentration</li> <li>• Other symptom-based diagnoses, including:               <ul style="list-style-type: none"> <li>• Infantile-onset diarrhoea</li> <li>• Childhood-onset cataract</li> <li>• Young adult-onset tendon xanthomas</li> <li>• Adult-onset progression neurologic dysfunction, such as dementia or seizures</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Articles not reporting any eligible outcomes related to the screening, diagnosis or confirmation of CTX</li> </ul>

Search Term Group	Inclusion Criteria	Exclusion Criteria
<i>Outcomes: Treatment</i>		
<p>Articles reporting at least one of the following outcomes when assessing an established or potential treatment for CTX:</p> <ul style="list-style-type: none"> <li>• Prophylactic CTX treatment, early CTX treatment or treatment to manage CTX</li> <li>• Clinical outcomes (efficacy, safety and tolerability)</li> <li>• Quality of life outcomes (utility values and quality of life)</li> </ul>	<p>Articles not reporting any eligible outcomes relating to the treatment of CTX</p>	
<i>Outcomes: Monitoring</i>		
<p>Articles reporting on outcomes related to monitoring of patients with CTX, including:</p> <ul style="list-style-type: none"> <li>• Neurologic and neuropsychological evaluation</li> <li>• Brain MRI</li> <li>• Echocardiogram</li> <li>• Total body density</li> <li>• Genetic counselling</li> <li>• Follow-up appointments</li> </ul>	<ul style="list-style-type: none"> <li>• Articles not reporting any eligible outcomes related to monitoring of patients with CTX</li> </ul>	
<i>Outcomes: Multidisciplinary care</i>		
<p>Articles reporting on multiple care settings or multidisciplinary teams (MDTs) caring for CTX patients, including:</p> <ul style="list-style-type: none"> <li>• Healthcare professionals in MDTs</li> <li>• Care received by MDTs</li> <li>• CTX departments or clinics</li> </ul>	<ul style="list-style-type: none"> <li>• Articles not reporting any eligible outcomes related to multidisciplinary care for patients with CTX</li> </ul>	

Search Term Group	Inclusion Criteria	Exclusion Criteria
	<i>Outcomes: Prognosis</i>	
	Articles reporting on outcomes related to prognosis of patients with CTX, including: <ul style="list-style-type: none"> <li>• Worsening/stability of symptoms</li> <li>• Patients who have not responded to treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Articles not reporting any eligible outcomes related to prognosis of patients with CTX</li> </ul>
<b>Study design</b>	<ul style="list-style-type: none"> <li>• Randomised controlled trials</li> <li>• Non-randomised interventional studies</li> <li>• Observational studies (including registries and surveys)</li> <li>• Case reports or series (included separately at abstract stage but not taken forward to full-text stage)</li> <li>• Cross-sectional studies</li> <li>• Narrative reviews</li> </ul>	<ul style="list-style-type: none"> <li>• Congress abstracts or congress reviews</li> <li>• Commentaries or letters</li> <li>• Editorials</li> <li>• Economic evaluations</li> </ul>
<b>Date</b>	<ul style="list-style-type: none"> <li>• Database inception to present</li> </ul>	<ul style="list-style-type: none"> <li>• N/A</li> </ul>
<b>Other considerations</b>	<ul style="list-style-type: none"> <li>• Only abstracts or full-texts in the English language will be included</li> <li>• Studies conducted in humans</li> </ul>	<ul style="list-style-type: none"> <li>• Abstracts or full-texts not in the English language</li> <li>• <i>In vitro</i> or animal studies</li> </ul>

Each title and abstract were reviewed against the inclusion/exclusion criteria by one reviewer, with a second independent reviewer validating 10% of full-text articles deemed suitable for inclusion. CT: computed tomography; CTX: cerebrotendinous xanthomatosis; MDT: multidisciplinary team; MR: magnetic resonance; MRI: magnetic resonance imaging; N/A: not applicable; PK/PD: pharmacokinetics/pharmacodynamics.