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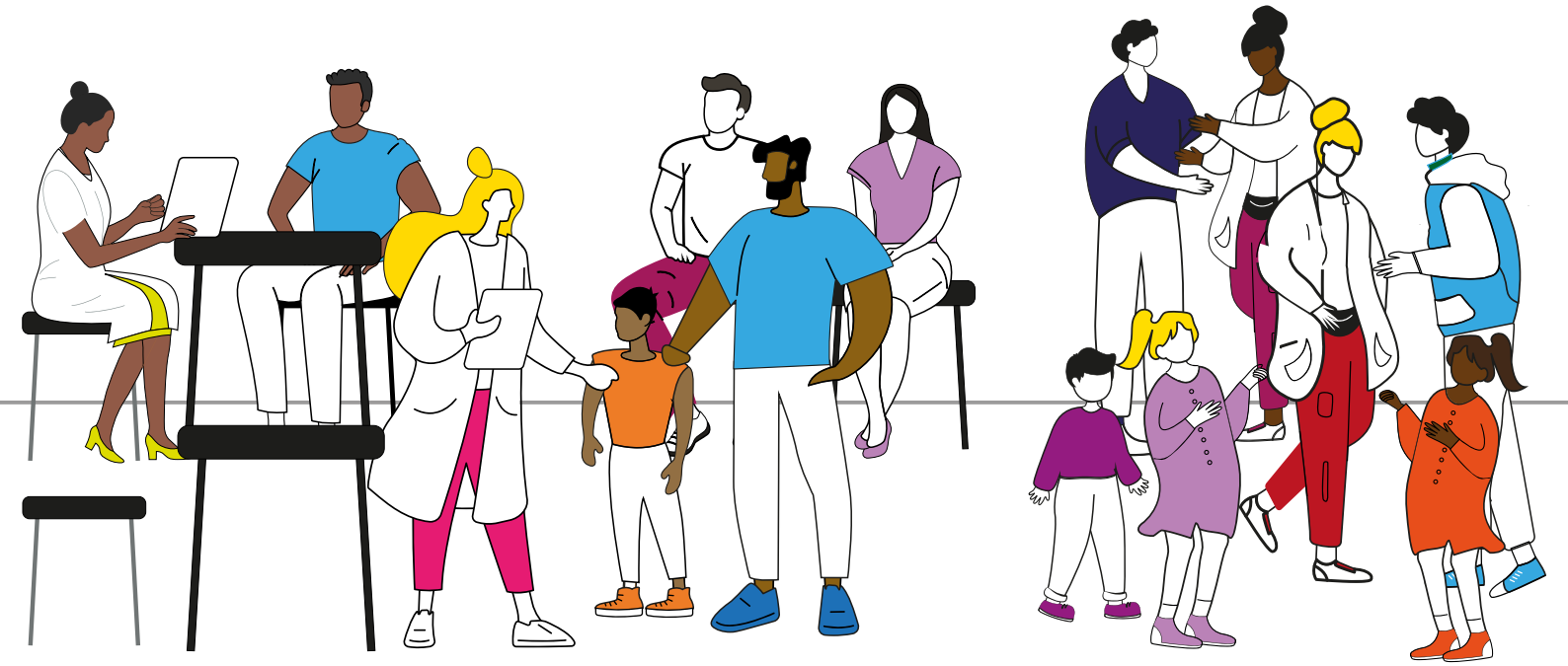
The Glyde Clinical Trial Summary for Healthcare Professionals



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What is the Glyde trial?

Glyde is an international, multi-centre randomised double-blind crossover clinical trial comparing **Glycosade®** and **Uncooked Cornstarch (UCCS)** for the dietary management of Hepatic Glycogen Storage Diseases (HGSD). The trial was conducted between 2016 and 2020.

What is Glycosade®?

Glycosade is a food for special medical purposes (FSMP) for the dietary management of HGSD. It is a hydrothermally processed high amylopectin waxy maize starch, to be used under medical supervision.

Study aim:

To establish whether Glycosade improves outcomes for participants with HGSD compared to UCCS.

Study objectives:

- To compare the duration of normal blood glucose, lactate and ketone levels of participants with HGSD (Types I, III, VI and IX) post equivalent intakes of UCCS and Glycosade.

After participants consumed equivalent intakes of Glycosade and UCCS, their blood glucose levels were measured over a 12 hour period with an endpoint of ≤3.6mmol/L.

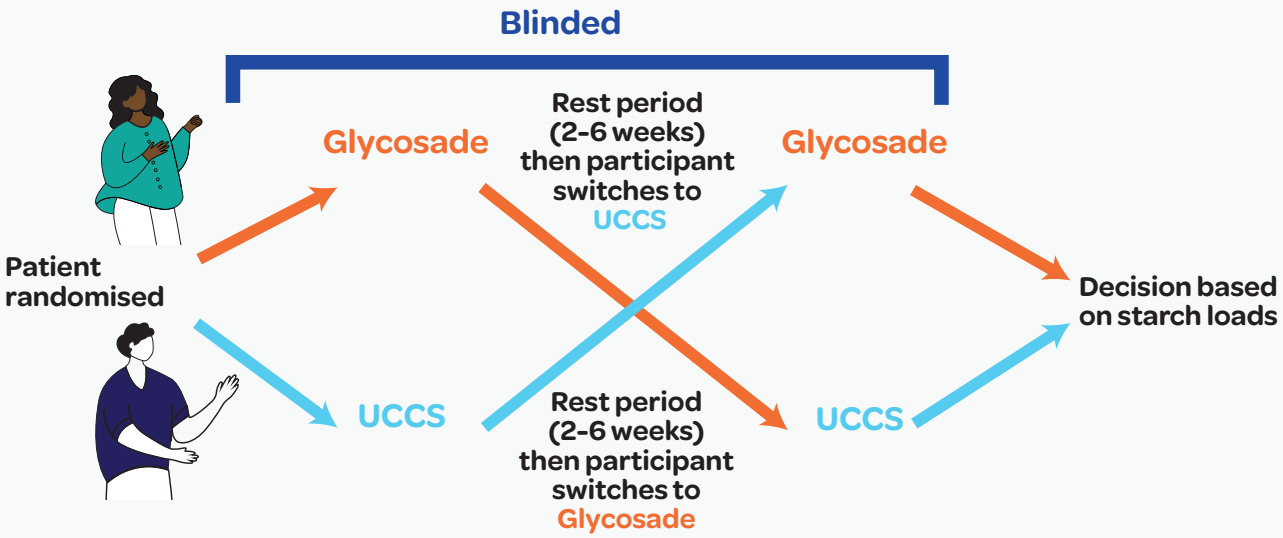
For those with GSD Type I, lactate levels were also measured.

For those with the ketotic types of GSD (III, VI and IX), β-hydroxybutyrate (BOHB) was also assessed (ketosis defined by : BOHB ≥ 1.0 mmol/L (participants < 14 years) BOHB ≥ 0.4 mmol/L (participants ≥ 14 years)).

- To assess the tolerance and acceptability of Glycosade compared to UCCS.

Study design:

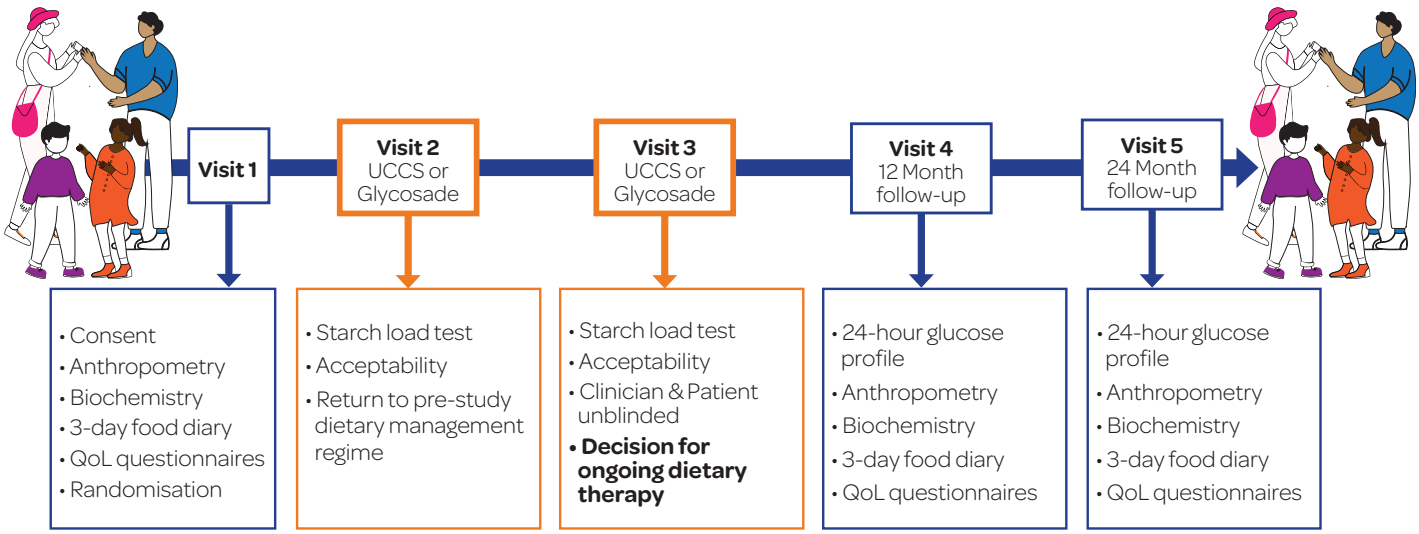
Randomised, double-blind, crossover fasting study. Two 12 hour starch load tests (Glycosade and UCCS) were given randomly within a 6 week period and tolerance and efficacy were assessed.



Clinicians and participants jointly considered the biochemistry and the acceptability of Glycosade and UCCS. From this, the participant and the clinician jointly decided whether the participant would continue on Glycosade or UCCS. **This decision was made while the clinicians and participants were still blinded to the two study products.**

Part two of the trial

Whilst continuing with the chosen starch, participants entered a 24 month follow-up phase. During this time metabolic control, biochemistry, food intake, growth for children and weight for adults, as well as Quality of Life (QoL) were monitored.



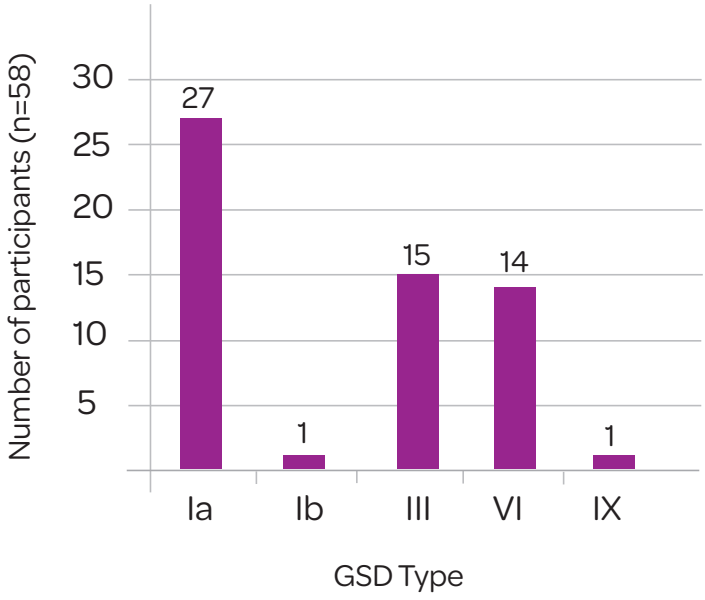
Where was the trial held?

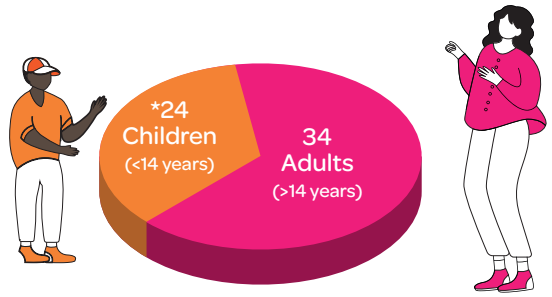
The trial was held at 6 internationally recognised GSD centres:

- Evelina Children's hospital, London, UK
- Great Ormond Street Hospital, London, UK
- National Hospital for Neurology and Neurosurgery, London, UK
- University Medical Center Groningen, Netherlands
- Hopital Antoine Beclere, Paris, France
- Connecticut Children's Hopsital, USA

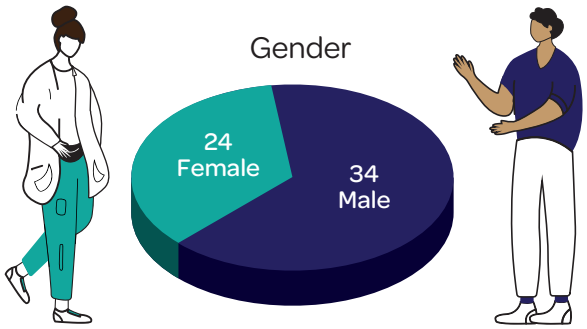
Participants:

58 participants completed the study.





*3 of the 24 children were under the age of 5 years.



Results:

1) Blood glucose levels

- Glycosade, when compared to UCCS, **prolonged fasting across all age groups and HGSD types** (Ia, III, VI & IX) without impacting metabolic control.

- All participants, when on Glycosade, tolerated fasts of at least 6 hours, and **82% (41/50) of participants were able to fast for more than 8 hours.**

GSD Type Ia

- The results observed were **most significant for those with GSD Type Ia**, who were able to maintain their blood glucose levels for 6 hours or more on Glycosade.

- Mean **blood glucose levels were maintained at a higher level when using Glycosade** compared to UCCS in those with GSD Type Ia towards the end of the starch loads. This could provide a safety benefit as it may delay hypoglycaemia.

Ketotic types of HGSD

- **Ketotic GSD participants blood glucose levels did not fall below 3.6mmol/L** with mean blood glucose levels always higher in the Glycosade group compared to UCCS group.

- The use of Glycosade for the dietary management of HGSD **offers the opportunity for participants to sleep through the night without needing to wake for a snack or additional starch dose.**

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2) Ketone levels

-There was a **significant delay in ketosis** in the **Glycosade group** (9.4 hours compared to 8 hours in the UCCS group).

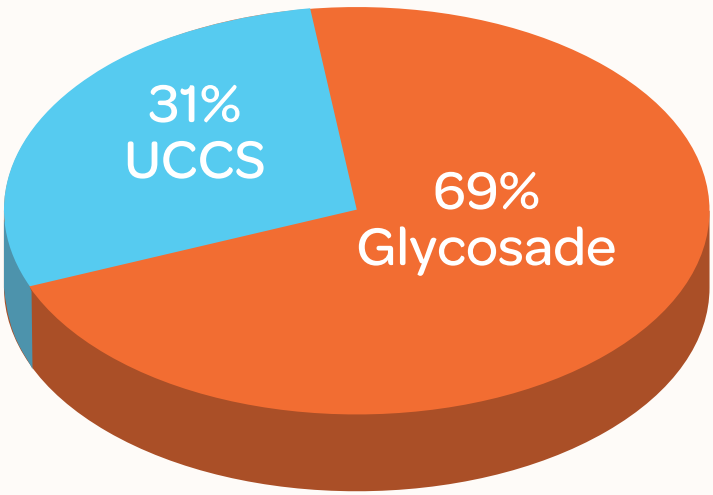
- Participants were found to have a **20% increase in fasting tolerance prior to development of ketones when they took Glycosade.**

Extended fasting potentially allows **less frequent intakes of starch** during the day and **longer periods of sleep overnight**.

Prevention of ketosis may help prevent ketone induced vomiting and metabolic crises in this population. In addition, chronic ketosis can lead to long term complications, but the duration of this study and relatively small sample studies did not allow these to be assessed.

3) Choice of ongoing management

Whilst still blinded, clinicians and participants jointly considered the participant's biochemistry results and the acceptability of the starch. **69% (38/55) chose to stay on Glycosade compared to 31% (17/55) on UCCS.**



4) Number of doses

All participants who chose Glycosade required **fewer intakes** over 24 hours, without impacting metabolic control. Those with ketotic HGSD types required 3 doses or less in 24 hours.

What were the long-term results

- **Long-term use of Glycosade was found to be safe, well-tolerated, and metabolic control was found to be maintained with fewer doses.**
- **Trends in data indicate participants taking Glycosade had fewer biochemical parameters outside of normal ranges.**

Conclusion

As the first randomised double-blind international multi-centre study of Glycosade use, the results from the Glyde trial have shown:

- **Glycosade improved the duration of fasting, in all age groups and HGSD types without impacting metabolic control. This was most notable in those with GSD type Ia who were able to maintain normoglycaemia of 6 hours or longer.**
- **Glycosade delayed ketosis by at least 1 hour in the ketotic HGSD types when compared to UCCS.**
- **A trend towards a reduced number of biochemical parameters outside the normal range was observed in those taking Glycosade.**
- **Glycosade was the preferred starch for the majority of participants.**
- **Fewer doses of Glycosade could be used over 24 hours without impacting metabolic control.**

The results from the Glyde study add to the evidence base supporting the longer term safety and efficacy of Glycosade for the dietary management of HGSD.

The study findings also supported the need for an additional flavour of Glycosade.
Two flavour options are now available; unflavoured and lemon flavour.

Unflavoured Glycosade is suitable from 2 years of age onwards. Lemon flavour Glycosade is suitable from 3 years of age onwards.

The full Glyde publication (July 2024) is open access and can be found here:
Short and long-term acceptability and efficacy of extended-release cornstarch in the hepatic glycogen storage diseases: results from the Glyde study | Orphanet Journal of Rare Diseases | Full Text (biomedcentral.com)

The dietary aspects of the Glyde trial will be published as a separate journal paper.

This information is intended for healthcare professionals only.

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