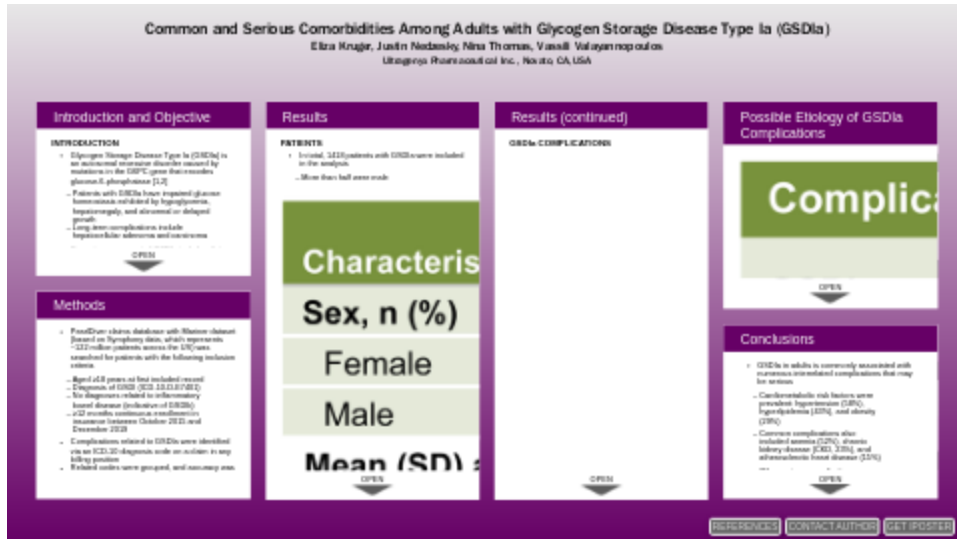


Common and Serious Comorbidities Among Adults with Glycogen Storage Disease Type Ia (GSDIa)



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PRESENTED AT:



INTRODUCTION AND OBJECTIVE

INTRODUCTION

- Glycogen Storage Disease Type Ia (GSDIa) is an autosomal recessive disorder caused by mutations in the G6PC gene that encodes glucose-6-phosphatase [1,2]
 - Patients with GSDIa have impaired glucose homeostasis exhibited by hypoglycemia, hepatomegaly, and abnormal or delayed growth
 - Long-term complications include hepatocellular adenoma and carcinoma
- Current management of GSDIa includes dietary supplementation (eg, cornstarch [3]); however, adherence over a 24-hour period may be difficult
- Quantitative studies are needed to assess chronic complications of GSDIa

OBJECTIVE

- This retrospective cohort study investigated complications in adults with GSDIa

METHODS

- PearlDiver claims database with Mariner dataset (based on Symphony data, which represents ~122 million patients across the US) was searched for patients with the following inclusion criteria
 - Aged ≥ 18 years at first included record
 - Diagnosis of GSDI (ICD-10-D-E7401)
 - No diagnoses related to inflammatory bowel disease (indicative of GSDIb)
 - ≥ 12 months continuous enrollment in insurance between October 2015 and December 2019
- Complications related to GSDIa were identified via an ICD-10 diagnosis code on a claim in any billing position
- Related codes were grouped, and accuracy was confirmed by clinical experts
- Data were summarized descriptively

RESULTS

PATIENTS

- In total, 1418 patients with GSDIa were included in the analysis
 - More than half were male

Characteristic	Patients N=1418
Sex, n (%)	
Female	645 (46)
Male	773 (55)
Mean (SD) age, years	46.0 (17.1)
Mean (SD) duration of enrollment, years	3.3 (0.8)
Type of insurance plan, n (%)	
Commercial	988 (70)
Medicare	170 (12)
Medicaid	161 (11)
US Department of Veterans Affairs	52 (4)
Not available	47 (3)
Region, n (%)	
South	549 (39)
Northeast	441 (31)
Midwest	251 (18)
West	171 (12)
Unknown	*(<1)

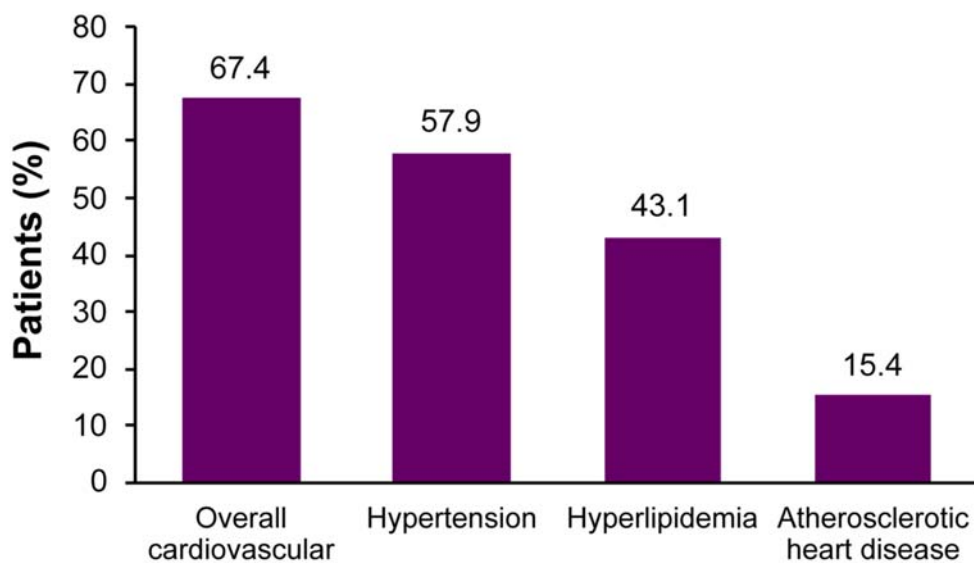
*Patient counts of 1–10 were not reported for privacy reasons.

RESULTS (CONTINUED)

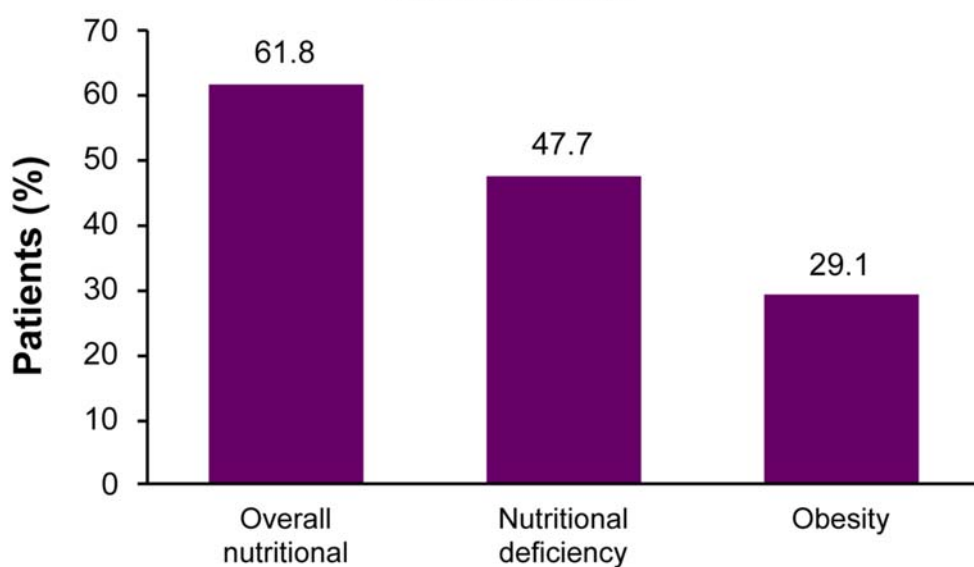
GSDIa COMPLICATIONS



Cardiovascular

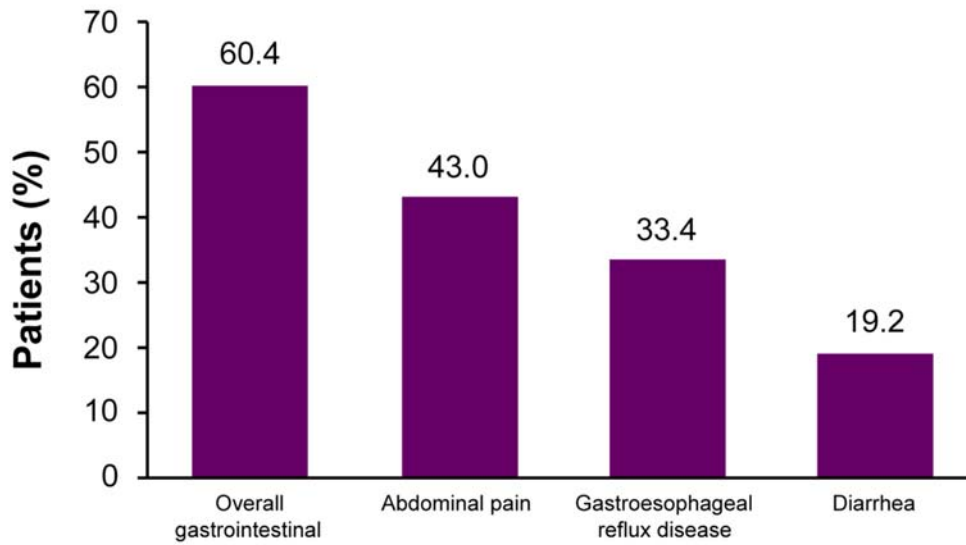


Nutritional

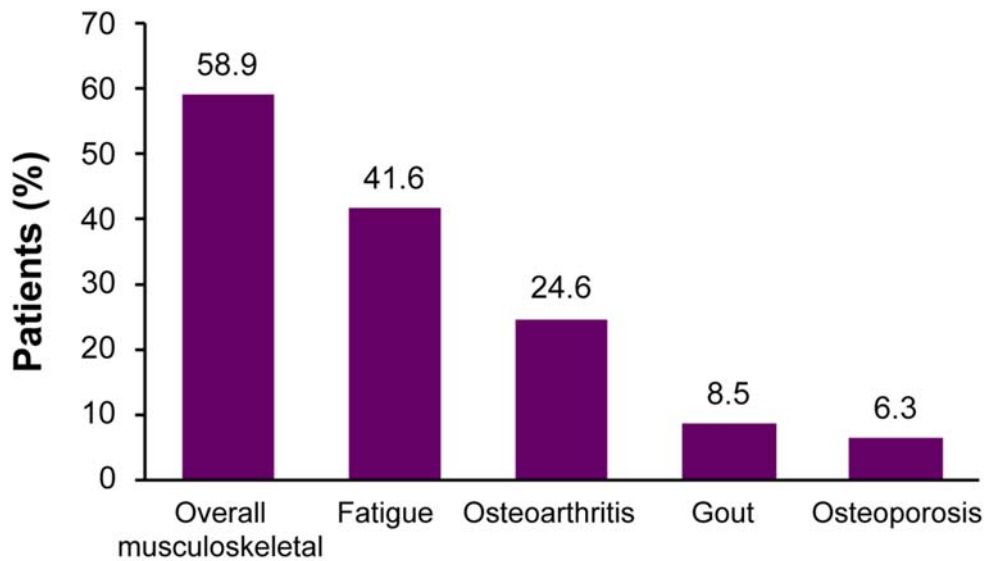




Gastrointestinal

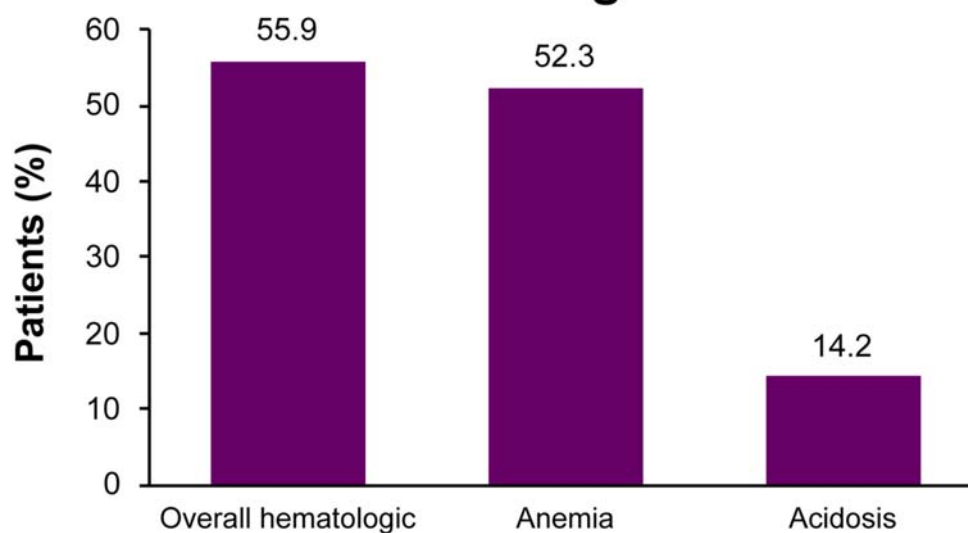


Musculoskeletal

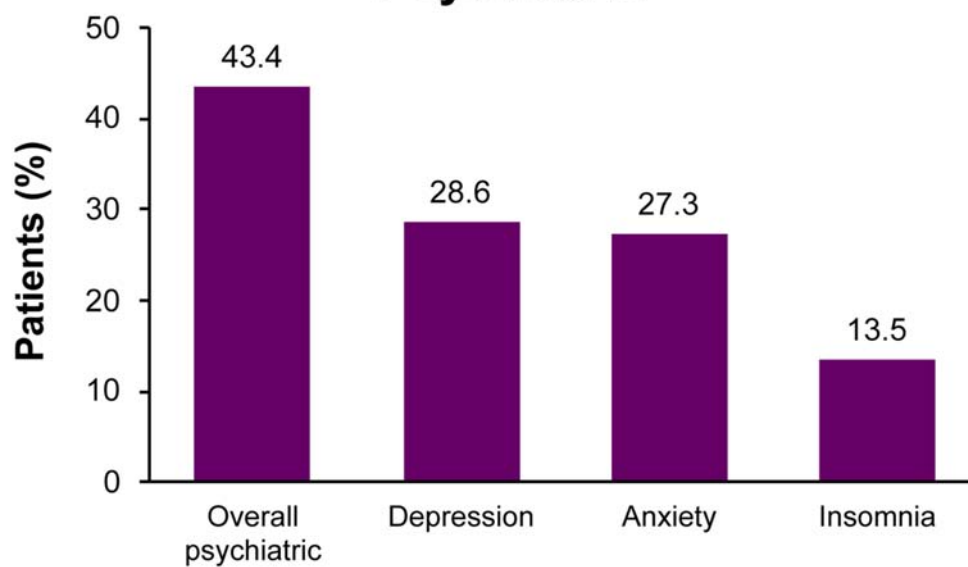




Hematologic

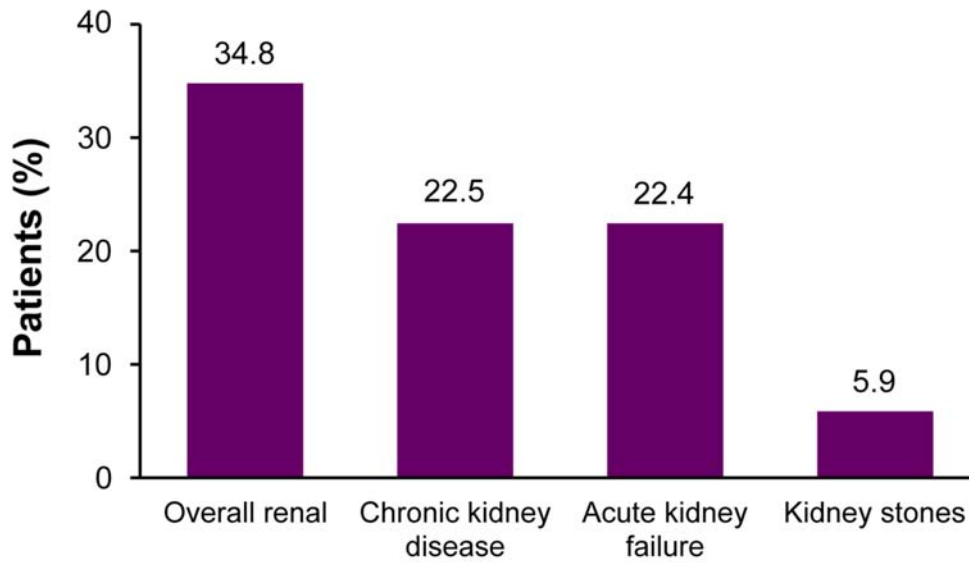


Psychiatric

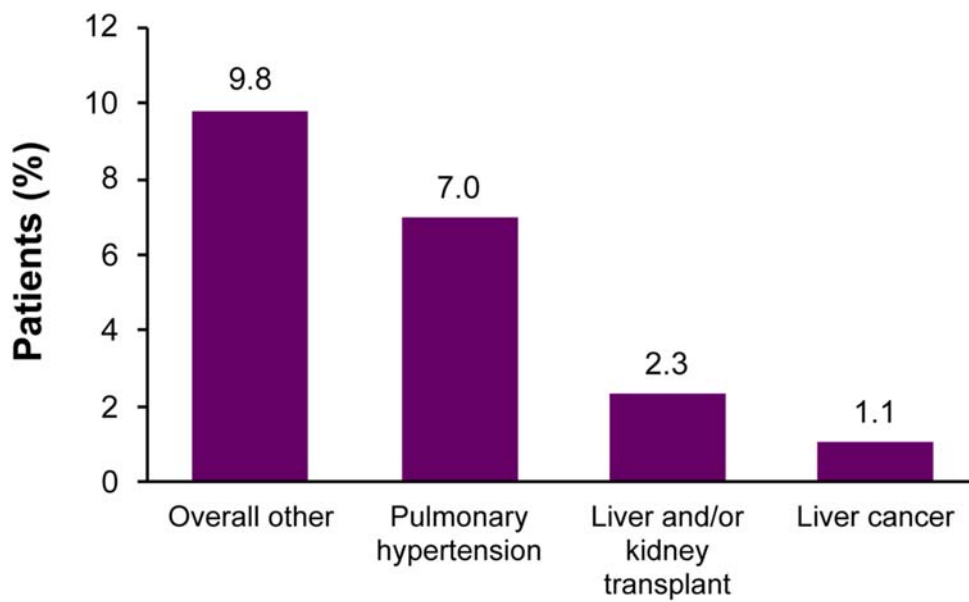




Renal



Other



POSSIBLE ETIOLOGY OF GSDIA COMPLICATIONS

Complication	Possible Etiology*
GSDIa	Genetic liver disorder resulting in G6Pase deficiency
Cardiovascular	
Hypertension	Progressive renal disease
Hyperlipidemia	Increased lipid synthesis, decreased lipid serum clearance, obesity
Atherosclerotic heart disease	Hypertension, hyperlipidemia
Gastrointestinal	
Abdominal pain	Large amounts of raw cornstarch have been found to cause flatulence and abdominal pain
Gastroesophageal reflux disease	Obesity and anxiety may contribute
Diarrhea	Large amounts of raw cornstarch can modify microbiota leading to diarrhea

Hematologic

Anemia	Decreased production of erythropoietin due to renal insufficiency, chronic lactic acidosis, iron deficiency (cornstarch reduces iron bioavailability in the gastrointestinal tract), complications of hepatic adenoma
Acidosis	Progressive renal disease, hypoglycemia

Musculoskeletal

Fatigue	Nutritional deficiency, hypoglycemia
Osteoarthritis	Obesity, gout, low exercise tolerance related to risk of hypoglycemia
Gout	Hyperuricemia due to progressive renal disease
Osteoporosis	Lactic acidosis and cortisol release secondary to hypoglycemia, inadequate calcium intake due to dietary restrictions

Nutritional

Nutritional deficiency	Dietary restrictions and management with cornstarch, digestive complications
Obesity	Consumption of large amounts of raw cornstarch which is high in calories, reduced exercise capacity

Psychiatric	
Depression/ Anxiety	Diagnosis of rare disease, highest emotional burden in those with a rare disease where there are no available treatments
Insomnia	Ingestion of raw cornstarch every 4 –5 hours including at night, recommended to prevent hypoglycemia in adults
Renal	
Chronic kidney disease	Accumulation of glycogen and fat in the kidneys leading to progressive organ failure
Acute kidney failure	Activation of the renin -angiotensin system, prolonged oxidative stress, and profibrotic cytokines may be implicated in glomerular injury
Kidney stones	Hyperuricemia due to progressive renal disease
Other	
Pulmonary hypertension	Abnormal production of serotonin, a vasoconstrictive amine
Liver and/or kidney transplant	Accumulation of glycogen and fat in the liver and kidneys leading to progressive organ failure and tumors (adenomas and malignancies)
Liver cancer	Etiology of hepatocellular adenomas and transformation to hepatocellular carcinoma likely multifactorial, metabolic control may play a role

*Etiologies were determined by literature review.

CONCLUSIONS

- GSDIa in adults is commonly associated with numerous interrelated complications that may be serious
 - Cardiometabolic risk factors were prevalent: hypertension (58%), hyperlipidemia (43%), and obesity (29%)
 - Common complications also included anemia (52%), chronic kidney disease (CKD, 23%), and atherosclerotic heart disease (15%)
 - Other serious complications included pulmonary hypertension (7%), liver/kidney transplant (2%), and liver cancer (1%)
- Further research into potential cornstarch adverse effects is needed
- The high prevalence of complications suggests there could be an impact on mortality; however, this study did not capture this information
- This analysis reveals that GSDIa is associated with many complications and large unmet need

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2. Chou JY, et al. *Curr Mol Med.* 2002;121–143.
3. Kishnani PS, et al. *Genet Med.* 2014;16:e1.