Project Title:

Do GLP-1 agonists, a new weight loss drug, cost us muscle? : A Python simulation study.

New Mexico Supercomputing Challenge

Final Report

April 1, 2026

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Executive Summary

Problem Investigated: This project studied whether GLP-1 receptor agonists (which are used to treat obesity and diabetes), may cause significant muscle loss. Previous research suggests that about 40% of the weight lost with these medications may come from lean mass, and about half of that may be muscle. This raises concerns because muscle is important for strength, movement, and overall health, especially in fall prevention in older adults. However, there is still a gap in understanding how much muscle is lost in different people and how strategies like protein intake and physical activity might help prevent it.

Method: A computational simulation model was built using Python. The model used mathematical calculations, probability, pseudorandom generated data to simulate real-life patients. Each simulated patient included factors such as age, sex, body weight, fat mass, muscle mass, BMI, activity level, and protein intake. The model tested different weight loss scenarios (9%, 13%, 16%, and 17%) and estimated how much muscle would be lost in each case.To strengthen the model, a “physiologic aging” component was added. This translated muscle loss into an estimated decline in functional age, helping show how muscle loss may affect overall health, not just body composition.

Verification and Validation: The model was checked to make sure all calculations worked correctly and produced consistent results. The results were then compared with published studies, including major GLP-1 trials such as STEP 1 and SURMOUNT, as well as other research on muscle loss and prevention strategies.

Results**:** The model showed that muscle loss increases as total weight loss increases, ranging from about 4.4% to 8.6% of original muscle mass. Protein intake helped reduce muscle loss, preserving up to about 15% of muscle. Physical activity had the strongest effect. People with high activity levels lost much less muscle (about 4%) compared to those with low activity levels (about 12.6%).The model also showed that greater muscle loss was linked to accelerated aging, suggesting that muscle loss may have important long-term side effects.

Conclusions: GLP-1 medications can reduce both fat and muscle. Eating enough protein helps protect muscle, but staying physically active is the most effective way to preserve it. These results suggest that patients using GLP-1 therapy should also focus on exercise and good nutrition to prevent muscle loss.

Background:

Obesity and diabetes are major health problems in the United States and around the world. In recent years, a new group of medications called GLP-1 receptor agonists has been developed to help treat these conditions. These medications help people lose weight by slowing digestion, reducing appetite, and lowering overall caloric intake.

Although these medications are effective for weight loss, research shows that not all of the weight lost is fat. About 40% of the weight loss may come from lean mass, and about half of that may be muscle. Muscle is important for strength, movement, balance, and overall health. Losing too much muscle can lead to weakness, increased risk of falls, and long-term health problems, especially in older adults.

Another important concern is that losing muscle may affect how the body functions over time. Muscle loss can act like faster aging in the body, leading to decreased strength and physical performance leading to frailty, and increased risk of falls.

While several clinical studies have measured weight loss and body composition, there is still a gap in understanding how muscle loss varies between individuals, how it affects overall function, and how it can be reduced. In particular, there is limited research on how factors such as protein intake and physical activity can help protect muscle.

This project uses a computational simulation model to better understand these questions and explore possible strategies to reduce muscle loss and its impact on health.

Research Questions:

This study focuses on two main questions:

A) Can muscle loss during GLP-1–use be estimated using a computational simulation model?

B) Can muscle loss be reduced by increasing protein intake and physical activity?

Hypothesis

A Python-based simulation model can be used to estimate muscle loss during GLP-1–related weight loss. The model will show that increasing protein intake and physical activity can reduce muscle loss during treatment. It will also show that greater muscle loss is associated with increased physiologic aging, meaning a decline in physical function over time and morbidity.

Methods:

A computational simulation model was developed using Python to estimate muscle loss during GLP-1 treatment and to test how protein intake and physical activity may reduce that loss. We planned initially to use data NAHNES data based but this data set did not have information on patients using GLP agonists meds. Because individual patient data from clinical trials is not publicly available, we turned to models that used simulated patient profiles designed to reflect realistic human characteristics.

Each simulated patient included variables such as age, sex, height, weight, body mass index (BMI), muscle mass, fat mass, activity level (low, medium, high), and daily protein intake ranging from (0.8g/kg per day for the lowest intake to 1.6 g/kg/day for the highest intake). Low activity was defined as daily, casual activities that keep you moving but require minimal effort, such as slow walking, light chores, or stretching; medium activity as activities requiring 3.0–5.9 metabolic equivalents (METs). Your heart beats faster, you breathe harder, and you may sweat, but you can still hold a conversation (like brisk walking, water aerobics), whereas high activity was defined as Activities requiring 6.0+ METs. These cause fast breathing and a significantly elevated heart rate, making it hard to speak (like running, jogging fast, cycling fast, etc) . These values were generated using probability distributions and random sampling to create a realistic population of 100 individuals.

The model then applied different weight-loss scenarios (9%, 13%, 16%, and 17%) and estimated how much of that weight loss came from muscle versus fat. A base assumption was used that approximately 40% of weight loss comes from lean mass, based on published studies. This value was then adjusted depending on each patient's activity level and protein intake.

Various concepts were incorporated including , simulation modeling, pseudo-random data generation, probability and statistics, scenario analysis, data transformations, Mathematical modeling, summary analysis and various visualization techniques.

To make the model more meaningful, a physiologic aging component was added. This converted muscle loss into an estimated “functional age decline,” helping show how loss of muscle could impact strength, mobility, and overall health.

Python libraries including NumPy, pandas, and Matplotlib were used for simulation, data analysis, and visualization.

Validation and verification of model:

Verification was performed by ensuring that the model behaved logically and consistently. For example, larger weight-loss scenarios produced greater muscle loss, and higher activity levels and protein intake reduced muscle loss. These checks confirmed that the equations and code were working as intended.

Validation was done by comparing the model’s results with published clinical studies. Major GLP-1 trials such as STEP 1 (semaglutide) and SURMOUNT (tirzepatide) show that a significant portion of weight loss comes from lean mass, which supports the assumptions used in this model. Additional review articles also show that protein intake and resistance exercise can help reduce muscle loss, which matches the patterns seen in the simulation.

One limitation of the model is that it estimates muscle loss based on body composition and does not directly measure muscle strength or function. However, this reflects a similar limitation in many clinical studies, which often measure lean mass but not physical performance.

Results

The simulation showed a clear trend: as total weight loss increased on GLP1 medications, muscle loss also increased.

Across the weight-loss scenarios:

- 9% weight loss → ~4.44% muscle loss
- 13% weight loss → ~6.42% muscle loss
- 16% weight loss → ~7.90% muscle loss
- 17% weight loss → ~8.64% muscle loss

This shows that greater weight loss is associated with greater muscle loss.

Protein intake helped reduce muscle loss. In the model, higher protein intake preserved up to about 15% of muscle compared to lower intake levels.

Physical activity had the strongest effect. Individuals with high activity levels had much lower muscle loss (~4.10%) compared to those with low activity (~12.61%). Medium activity levels also showed strong protection (~3.98%).

The physiologic aging model showed that greater muscle loss was associated with greater functional decline. For example:

- Low activity → ~31 years of functional decline
- High activity → ~10 years
- Medium activity → ~9.6 years

This does not represent actual aging, but instead shows how muscle loss, caused by GLP1 medications, may impact physical health over time.

Overall, the results suggest that both protein intake and physical activity play important roles in preserving muscle, with activity having the strongest effect.

Conclusions:

This study suggests that GLP-1 medications can lead to loss of both fat and muscle. While weight loss is beneficial, losing too much muscle may negatively affect strength, mobility, and long-term health.

The model shows that muscle loss increases as total weight loss increases. However, this loss can be reduced with practical strategies. Protein intake provides moderate protection against losing muscle, while physical activity appears to be the most effective way to preserve muscle.

These findings support a more complete approach to treatment. Patients using GLP-1 medications may benefit most when the medication is combined with regular exercise and adequate nutrition.

Another important conclusion is that muscle loss should not be viewed only as a number. The physiologic aging model shows that muscle loss may have real functional consequences, which highlights the importance of prevention.

The most significant achievement of the project is:

The most significant achievement of this project was building a complete computational model from the ground up and using it to study a real medical problem.

I learned how to use Python to generate realistic patient data, simulate different scenarios, and analyze results. I was able to combine computer science, mathematics, and medical research into one model.

Another important achievement was adding the physiologic aging component, which made the project more meaningful by connecting the results to real-world health effects.

This project showed how computer modeling can be used to prove and simulate real-life scenarios and their solutions.

Software and Outputs: Python (NumPy, Pandas, Matplotlib) was used for mathematical operations, simulation modeling, data analysis, and visualization.

Tables and Graphs

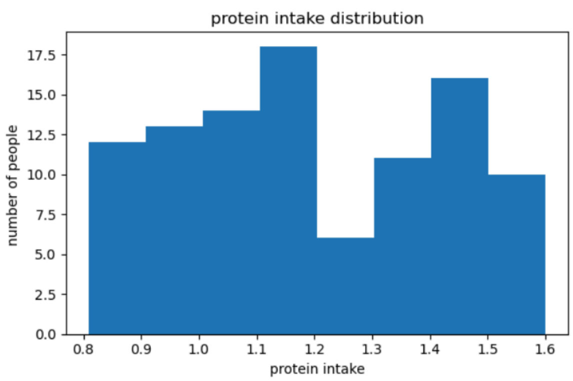
Table 1 - Dataframe printed to show first 20 entries of simulated control group

	ID	Age	sex	height_cm	weight_kg	muscle_kg	fat_kg	activity level	protein per day	BMI
0	1	44	female	170.0	82.9	29.6	53.3	low	0.95	28.69
1	2	52	female	155.9	81.8	31.2	50.6	medium	1.45	33.66
2	3	35	female	170.0	80.0	25.0	55.0	medium	1.58	27.68
3	4	69	male	152.5	81.0	31.5	49.5	low	0.91	34.83
4	5	62	male	153.4	98.6	33.5	65.1	medium	1.48	41.90
5	6	40	male	165.9	99.2	32.6	66.6	low	1.08	36.04
6	7	57	male	170.0	99.8	32.0	67.8	medium	1.32	34.53
7	8	53	female	170.0	80.0	31.7	48.3	low	1.34	27.68
8	9	68	female	152.0	83.7	29.9	53.8	low	1.49	36.23
9	10	25	female	164.6	101.2	37.9	63.3	low	1.49	37.35
10	11	64	male	150.0	92.7	36.9	55.8	low	0.85	41.20
11	12	68	male	163.2	98.0	31.2	66.8	medium	1.51	36.79
12	13	54	female	170.0	96.1	29.6	66.5	high	1.06	33.25
13	14	53	male	155.5	88.0	28.6	59.4	high	1.29	36.39
14	15	31	female	165.7	84.5	29.3	55.2	high	0.99	30.78
15	16	24	female	160.3	81.9	27.4	54.5	low	1.32	31.87
16	17	27	male	160.9	83.0	30.0	53.0	low	1.08	32.06
17	18	46	female	152.9	96.6	36.0	60.6	low	1.09	41.32
18	19	45	female	170.0	95.0	32.8	62.2	medium	1.21	32.87
19	20	27	female	165.1	87.3	28.5	58.8	medium	1.17	32.03
20	21	59	male	170.0	93.7	36.9	56.8	medium	1.45	32.42

Table 2 - Concatenated scenario table, First 20 entries

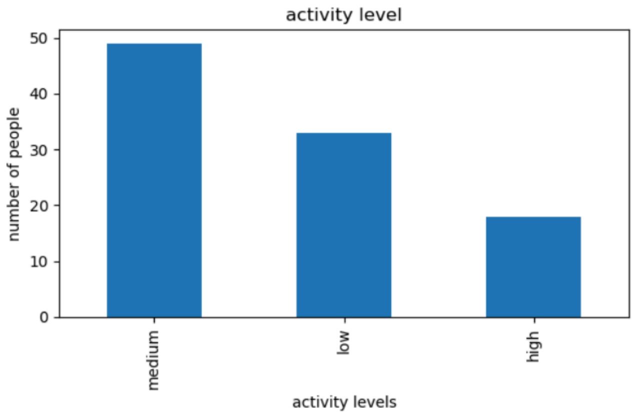
	ID	Age	sex	height_cm	weight_kg	muscle_kg	fat_kg	activity level	protein per day	BMI	total_loss_kg	muscle_fraction	muscle_loss_kg	fat_loss_kg	new_muscle_kg	new_weight	muscle_loss_pct_of_original	age_decline_years	scenario
0	1	44	female	170.0	82.9	29.6	53.3	low	0.95	28.69	7.461	0.45	3.35745	4.10355	26.24255	79.54255	11.342736	30.7	9% Weight loss
1	2	52	female	155.9	81.8	31.2	50.6	medium	1.45	33.66	7.362	0.10	0.73620	6.62580	30.46380	81.06380	2.359615	6.4	9% Weight loss
2	3	35	female	170.0	80.0	25.0	55.0	medium	1.58	27.68	7.200	0.10	0.72000	6.48000	24.28000	79.28000	2.880000	7.8	9% Weight loss
3	4	69	male	152.5	81.0	31.5	49.5	low	0.91	34.83	7.290	0.45	3.28050	4.00950	28.21950	77.71950	10.414286	22.2	9% Weight loss
4	5	62	male	153.4	98.6	33.5	65.1	medium	1.48	41.90	8.874	0.10	0.88740	7.98660	32.61260	97.71260	2.648955	5.6	9% Weight loss
5	6	40	male	165.9	99.2	32.6	66.6	low	1.08	36.04	8.928	0.30	2.67840	6.24960	29.92160	96.52160	8.215951	17.5	9% Weight loss
6	7	57	male	170.0	99.8	32.0	67.8	medium	1.32	34.53	8.982	0.10	0.89820	8.08380	31.10180	98.90180	2.806875	6.0	9% Weight loss
7	8	53	female	170.0	80.0	31.7	48.3	low	1.34	27.68	7.200	0.25	1.80000	5.40000	29.90000	78.20000	5.678233	15.3	9% Weight loss
8	9	68	female	152.0	83.7	29.9	53.8	low	1.49	36.23	7.533	0.25	1.88325	5.64975	28.01675	81.81675	6.298495	17.0	9% Weight loss
9	10	25	female	164.6	101.2	37.9	63.3	low	1.49	37.35	9.108	0.25	2.27700	6.83100	35.62300	98.92300	6.007916	16.2	9% Weight loss
10	11	64	male	150.0	92.7	36.9	55.8	low	0.85	41.20	8.343	0.45	3.75435	4.58865	33.14565	88.94565	10.174390	21.6	9% Weight loss
11	12	68	male	163.2	98.0	31.2	66.8	medium	1.51	36.79	8.820	0.10	0.88200	7.93800	30.31800	97.11800	2.826923	6.0	9% Weight loss
12	13	54	female	170.0	96.1	29.6	66.5	high	1.06	33.25	8.649	0.10	0.86490	7.78410	28.73510	95.23510	2.921959	7.9	9% Weight loss
13	14	53	male	155.5	88.0	28.6	59.4	high	1.29	36.39	7.920	0.10	0.79200	7.12800	27.80800	87.20800	2.769231	5.9	9% Weight loss
14	15	31	female	165.7	84.5	29.3	55.2	high	0.99	30.78	7.605	0.10	0.76050	6.84450	28.53950	83.73950	2.595563	7.0	9% Weight loss
15	16	24	female	160.3	81.9	27.4	54.5	low	1.32	31.87	7.371	0.25	1.84275	5.52825	25.55725	80.05725	6.725365	18.2	9% Weight loss
16	17	27	male	160.9	83.0	30.0	53.0	low	1.08	32.06	7.470	0.30	2.24100	5.22900	27.75900	80.75900	7.470000	15.9	9% Weight loss
17	18	46	female	152.9	96.6	36.0	60.6	low	1.09	41.32	8.694	0.30	2.60820	6.08580	33.39180	93.99180	7.245000	19.6	9% Weight loss
18	19	45	female	170.0	95.0	32.8	62.2	medium	1.21	32.87	8.550	0.10	0.85500	7.69500	31.94500	94.14500	2.606707	7.0	9% Weight loss
19	20	27	female	165.1	87.3	28.5	58.8	medium	1.17	32.03	7.857	0.10	0.78570	7.07130	27.71430	86.51430	2.756842	7.5	9% Weight loss
20	21	59	male	170.0	93.7	36.9	56.8	medium	1.45	32.42	8.433	0.10	0.84330	7.58970	36.05670	92.85670	2.285366	4.9	9% Weight loss

Graphic 1



Graphic 2

Graphic 3



activity level
number of people
50
40
30
20
10
0
medium
low
high
activity levels

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Acknowledgment: Arfa Khan, data analyst from Renal Medicine Associates, Albuquerque Academy, judges for their valuable feedback and parents.

Code:

[Hyperlink for code]()

```
import numpy as np
import matplotlib.pyplot as plt
import pandas as pd
np.random.seed(88)
pd.set_option('display.max_rows',420)
pd.set_option('display.max_columns',20)
n=100
ID = np.arange(1, n+1)
age= np.random.randint(20,70,size=n)
sex=np.random.choice(['male','female'],size = n)
height_cm=np.clip (np.random.normal(165,10,size=n),150, 170).round(1)
weight_kg=np.clip (np.random.normal(90,10,size=n),80,None).round(1)
muscle_kg=(weight_kg*np.random.uniform(0.3 ,0.4 , size=n)).round(1)
fat_kg=(weight_kg-muscle_kg).round(1)
activity= np.random.choice(['low' , 'medium' ,'high'],size=n ,p=[0.3,0.5,0.2])
protein_day_kg=np.random.uniform(0.8,1.6,size=n).round(2)
height_cm_sq=(height_cm*height_cm)
BMI= ((weight_kg/height_cm_sq)*10000).round(2)
Df=pd.DataFrame({"ID":ID,
"Age":age,
"sex":sex,
"height_cm":height_cm,
"weight_kg":weight_kg,
"muscle_kg":muscle_kg,
"fat_kg":fat_kg,
"activity level":activity,
"protein per day":protein_day_kg,
```

```
"BMI":BMI})
def adj_muscle_pct(base_muscle_pct,activity, protein_per_day):
adjustment=0
if activity == "high":
adjustment -= 0.95
elif activity == "medium":
adjustment -= 0.5
if protein_per_day >= 1.3:
adjustment -=0.15
elif 1.0 < protein_per_day <= 1.2:
adjustment -= 0.10
else:
adjustment += 0.05
final_pct=base_muscle_pct+adjustment
return max(0.10,min(final_pct,0.60))
def simulation_func(Df,weight_loss_pct,base_muscle_pct):
out=Df.copy()
out['total_loss_kg']=Df['weight_kg']*weight_loss_pct
out['muscle_fraction']=out.apply(
lambda row : adj_muscle_pct(
base_muscle_pct,
row['activity level'],
row['protein per day']
),
axis = 1
)
out['muscle_loss_kg']=out['total_loss_kg']*out['muscle_fraction']
out['fat_loss_kg']=out['total_loss_kg']-out['muscle_loss_kg']
out['new_muscle_kg']=Df['muscle_kg']-out['muscle_loss_kg']
out['new_weight']=Df['weight_kg']-out['muscle_loss_kg']
out['muscle_loss_pct_of_original']=(out['muscle_loss_kg']/Df['muscle_kg'])*100
```

```
out['age_decline_years'] = np.where(out['sex']==
'male',out['muscle_loss_pct_of_original']/0.47,out['muscle_loss_pct_of_original']/0.37).ro
und(1)
return out
scenarios = [
(0.09,0.40),
(0.13,0.40),
(0.16,0.40),
(0.175,0.40)
]
results=[]
for pct_loss,base_pct in scenarios:
simulated_values=
simulation_func(Df,weight_loss_pct=pct_loss,base_muscle_pct=base_pct)
simulated_values['scenario']=f'{int (pct_loss*100)}% Weight loss'
results.append(simulated_values)
all_sim_values = pd.concat(results, ignore_index=True)
```