

Effects Of Weight Change On Knee And Hip Radiographic Measurements And Pain Over 4 Years: Data From The Osteoarthritis Initiative

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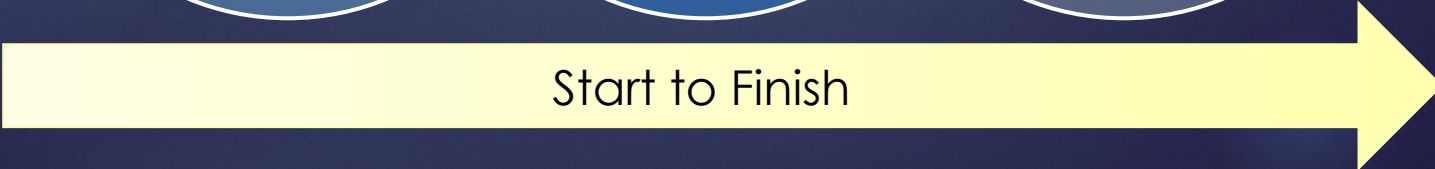
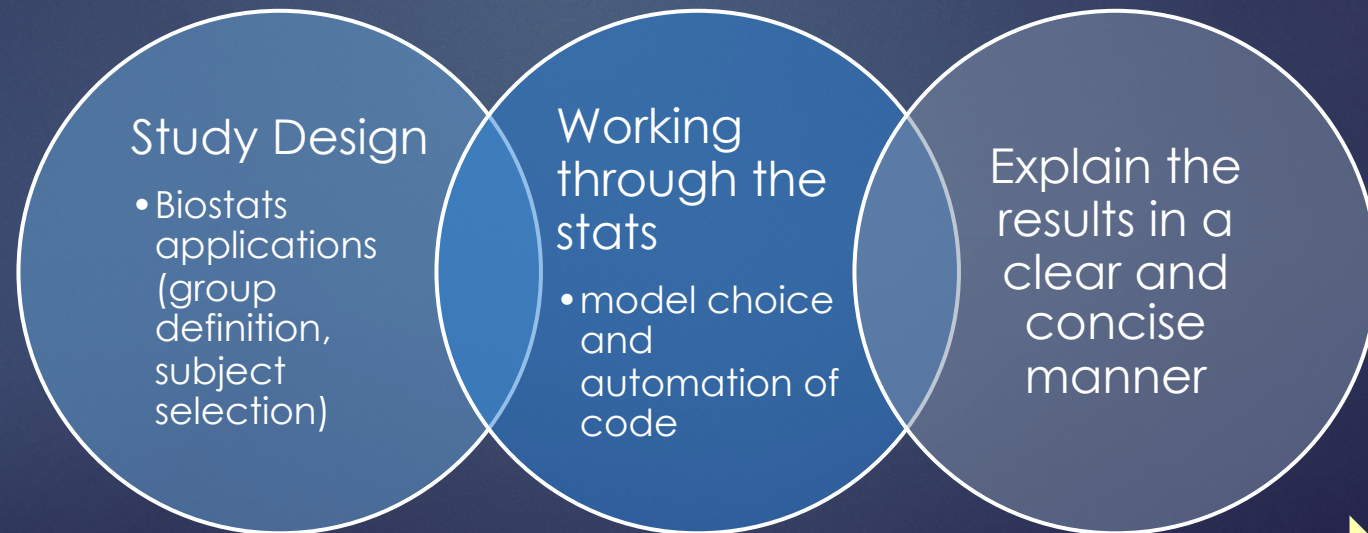
²Department of Epidemiology and Biostatistics, University of California, San Francisco

³Department of Medicine, University of California, Davis



Effects Of Weight Change On Knee And Hip Radiographic Measurements And Pain Over 4 Years: Data From The Osteoarthritis Initiative

Outline:

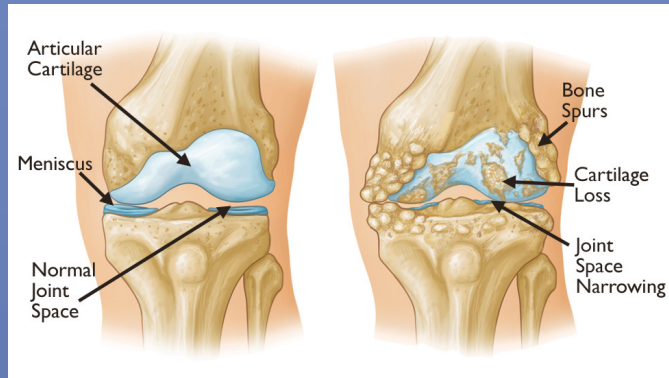


Osteoarthritis

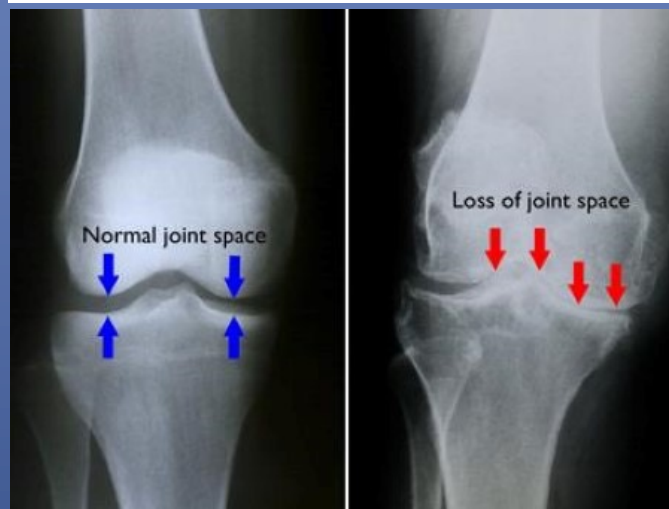
Affects 9.3 million U.S. adults, leads to severe disability & joint degeneration

Anatomy

Knee

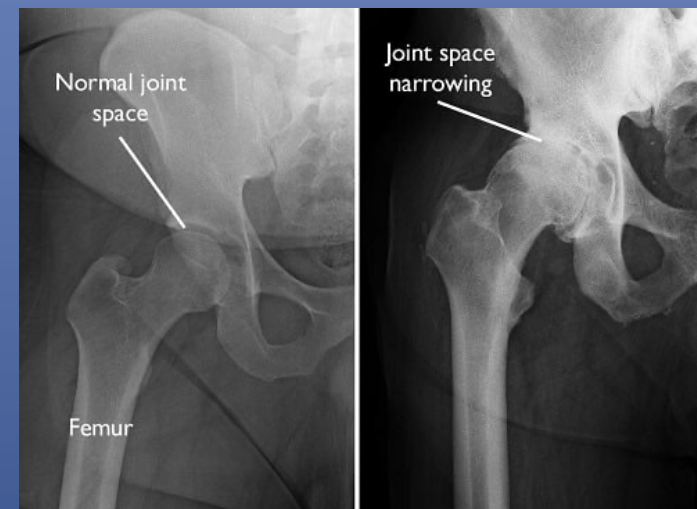
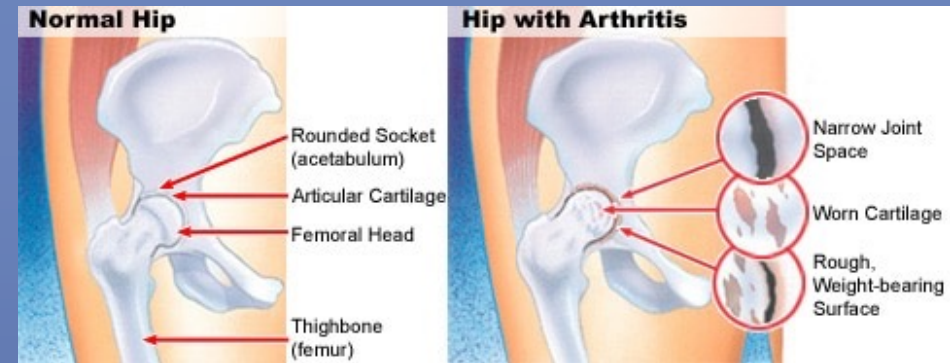


Radiography



<https://orthoinfo.aaos.org/en/diseases--conditions/arthritis-of-the-knee/>
<https://orthoinfo.aaos.org/en/diseases--conditions/osteoarthritis/>

Hip



<https://orthoinfo.aaos.org/en/diseases--conditions/osteoarthritis-of-the-hip/>
<https://roberthowells.com.au/conditions-and-treatment/hip-osteoarthritis-an-overview/>

Background

Purpose

Methods

Results

Discussion

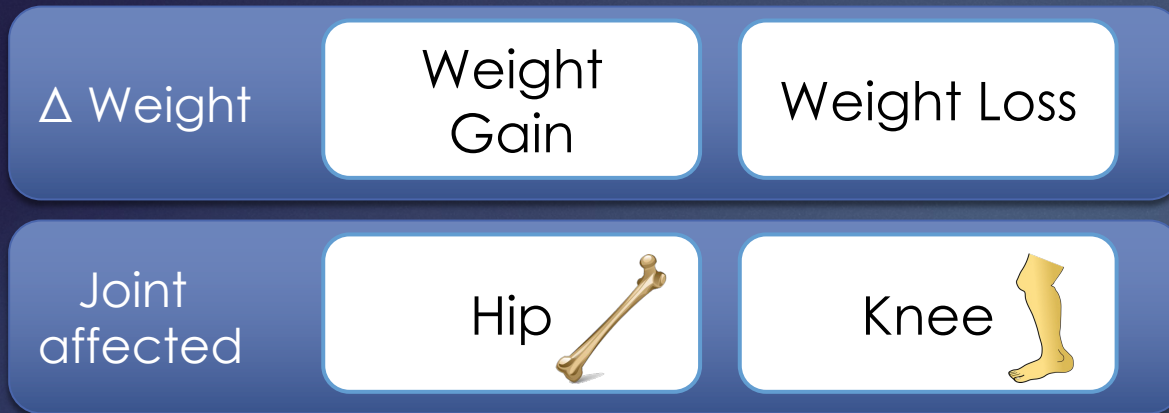
Conclusion

Background



¹Obese individuals have a 2.63 (95% CI 2.28, 3.05) odds of knee OA development compared to normal-weight controls

Modifiable risk factor



¹Blagojevic M, et al; Osteoarthritis Cartilage. 2010

²Messier SP, et al. Osteoarthritis Cartilage. 2011

³Gersing et al. Osteoarthritis Cartilage. 2016

Background



¹Obese individuals have a 2.63 (95% CI 2.28, 3.05) odds of knee OA development compared to normal-weight controls

Modifiable risk factor



²18-month changes in knee joint space width were not significantly different between “high” weight loss (10.2%), “low” weight loss (2.7%) and controls (1.5% gain)

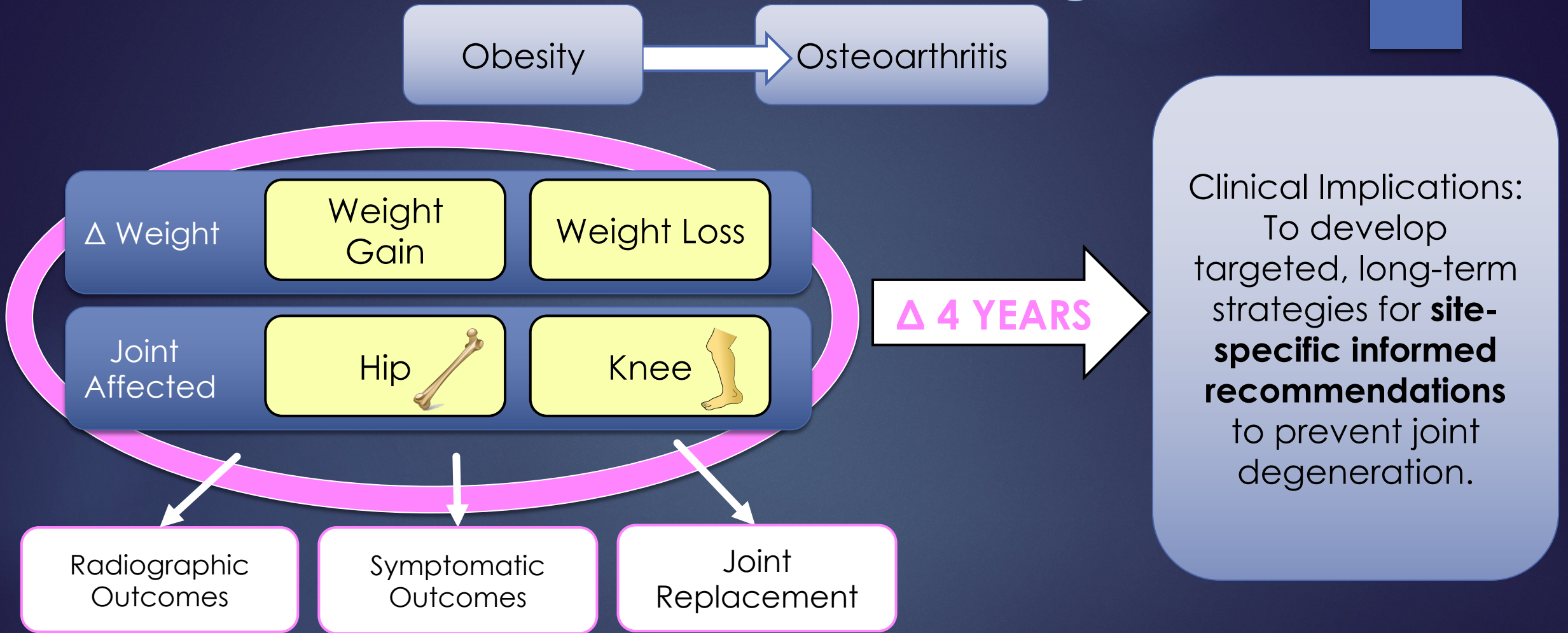
³Weight loss over 48 months was associated with slowed knee cartilage degeneration and improved knee symptoms

¹Blagojevic M, et al; Osteoarthritis Cartilage. 2010

²Messier SP, et al. Osteoarthritis Cartilage. 2011

³Gersing et al, Osteoarthritis Cartilage. 2016

Background



Purpose

- ▶ To assess the effects of weight loss and weight gain on hip and knee radiographic changes, pain, and joint replacement over 4 years.

Osteoarthritis Initiative Database

Goals: prevention and treatment of *osteoarthritis*



Observational Study:
A type of study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome (for example, no treatment is given).

Multi-center,
observational study sponsored
by the National
Institutes of
Health

N=4,796

Timepoints:
Baseline → 10
years

Data:

- clinical
- patient reported outcomes,
- radiographs
- MRIs

Background

Purpose

Methods

Results

Discussion

Conclusion

Participant Selection

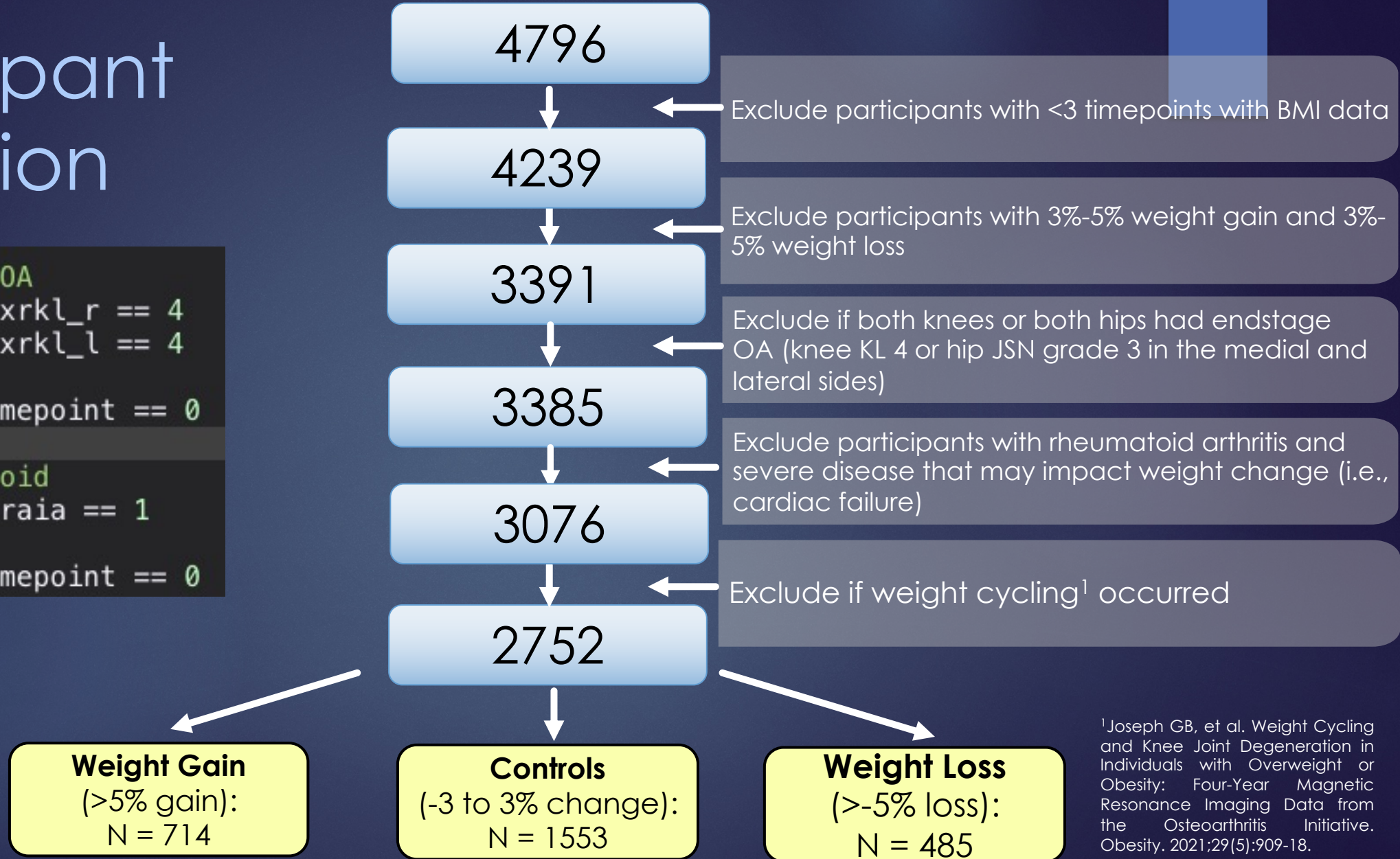
```
// drop severe OA
drop if v00xrkl_r == 4
drop if v00xrkl_l == 4

count if timepoint == 0

// drop rheumatoid
drop if p01raia == 1

count if timepoint == 0
```

All Participants in the OAI Database



¹Joseph GB, et al. Weight Cycling and Knee Joint Degeneration in Individuals with Overweight or Obesity: Four-Year Magnetic Resonance Imaging Data from the Osteoarthritis Initiative. Obesity. 2021;29(5):909-18.

All Participants in the OAI Database



Background

Purpose

Methods

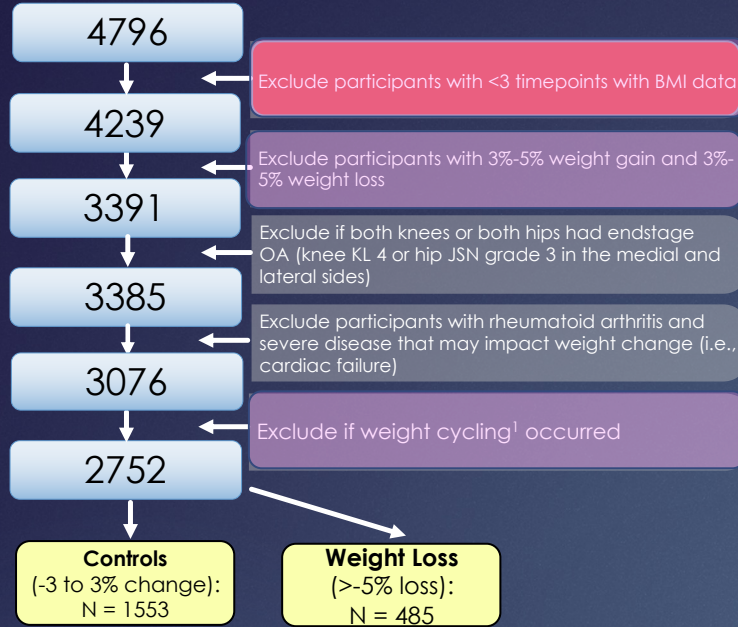
Results

Discussion

Conclusion

Statistical Methods

All Participants in the OAI Database



Sample Data - Wide

```
list id v00bmi v01bmi v03bmi v05bmi v06bmi v08bmi in 1/5, clean noobs
```

id	v00bmi	v01bmi	v03bmi	v05bmi	v06bmi	v08bmi
9000099	23.8	24.1	23.4	23.7	24.7	24.5
9000296	29.8	29.4	.	28.8	28.4	28.2
9000622	22.7	22.2
9000798	32.4	32.8	34.3	33.6	34.2	36.2
9001104	30.7	28.7

Long format

Sample Data - Long

id	timepoint	bmi	cnt_bmi
9000099	0	23.79999924	7
9000099	1	24.10000038	7
9000099	3	23.39999962	7
9000099	5	23.70000076	7
9000099	6	24.70000076	7
9000099	8	24.5	7
9000099	10	21.7	7
9000296	0	29.79999924	6
9000296	1	29.39999962	6
9000296	3	.	6
9000296	5	28.79999924	6
9000296	6	28.39999962	6
9000296	8	28.20000076	6
9000296	10	28.1	6

Exclude participants with < 3 timepoints with BMI Data

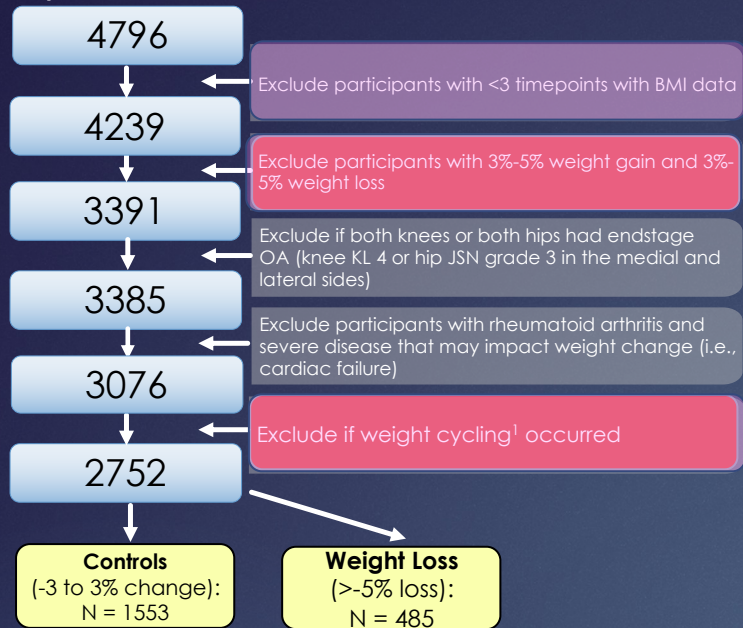
```
bysort id: egen cnt_bmi=count(bmi)
tab cnt_bmi timepoint
drop if cnt_bmi<3
```

```
. reshape long v0@bmi, i(id) j(timepoint)
(j = 0 1 3 5 6 8 10)
v010bmi: 2490 values would be changed; not changed

Data                                Wide  ->  Long
-----
Number of observations                4,796 -> 33,572
Number of variables                   26   -> 21
j variable (7 values)                 -> timepoint
xij variables:
      v00bmi v01bmi ... v010bmi -> v0bmi

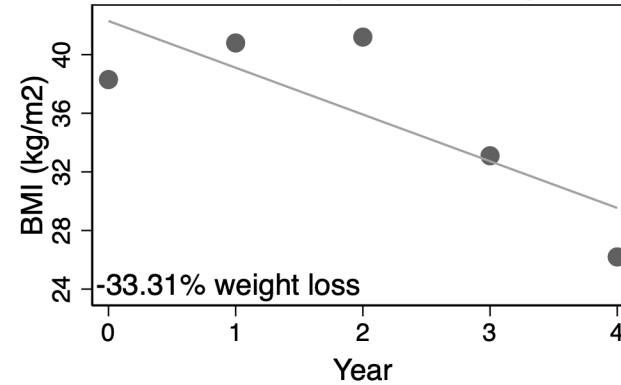
. rename v0bmi bmi
```

All Participants in the OAI Database

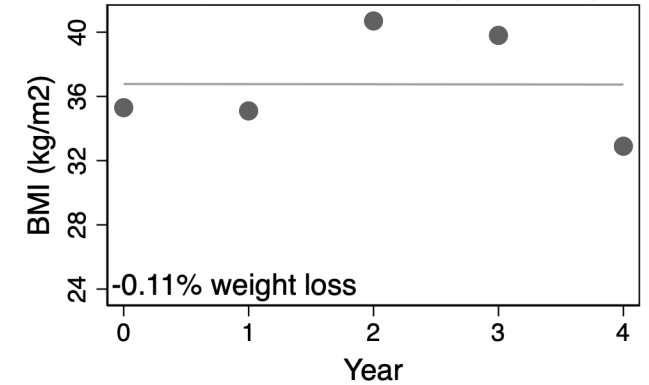


Statistical Methods

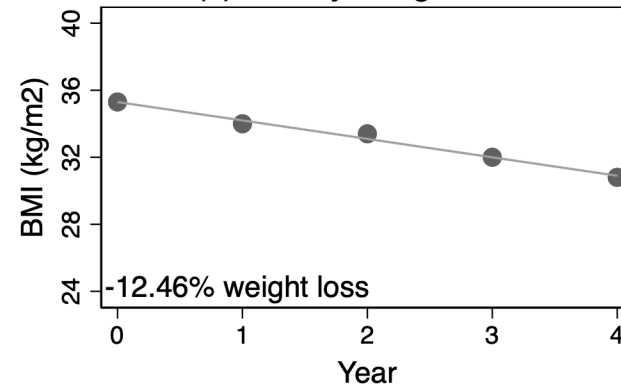
(a) Cyclers with Significant Weight Loss



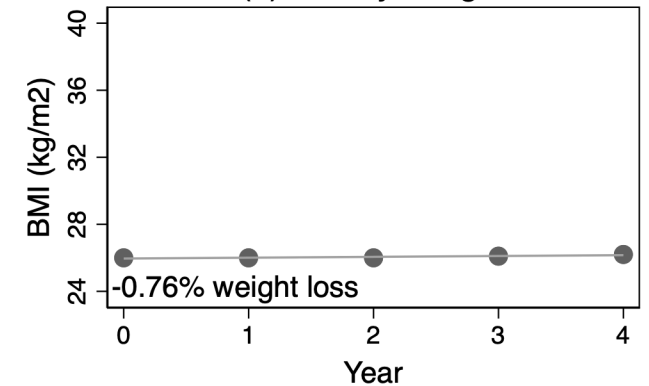
(b) Cyclers without Weight Change



(c) Steady Weight Loss



(d) Steady Weight



Regression models: Individual annual changes in BMI **over 4 years**

- Controls (-3 to 3% change)
- Weight loss (>5% loss)
- Weight Gain (>5% gain)

Top 10% of RMSE¹ (residuals) were designated as cyclers

Cyclers

Non-cyclers

Background

Purpose

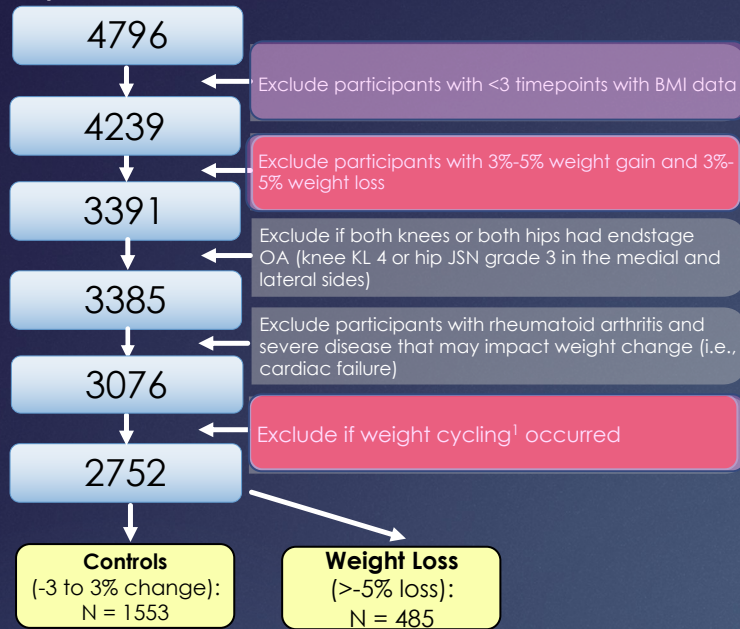
Methods

Results

Discussion

Conclusion

All Participants in the OAI Database



Regression models: Individual annual changes in BMI **over 4 years**

Controls (-3 to 3% change)

Weight loss (>5% loss)

Weight Gain (>5% gain)

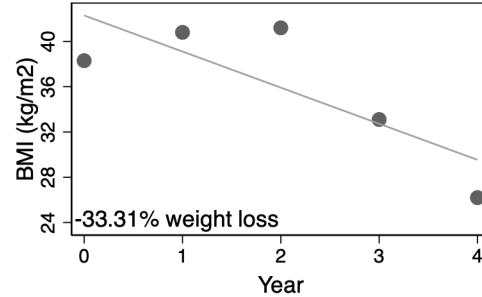
Top 10% of RMSE¹ (residuals) were designated as cyclers

Cyclers

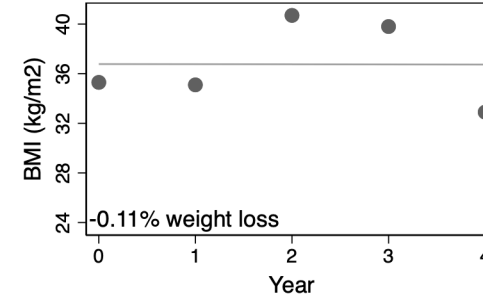
Non-cyclers

Statistical Methods

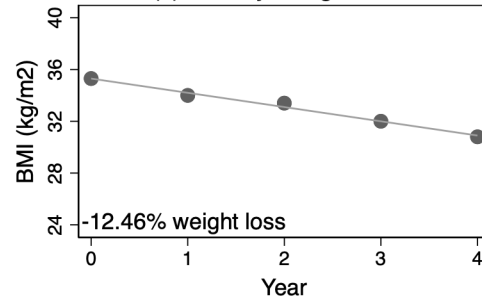
(a) Cycler with Significant Weight Loss



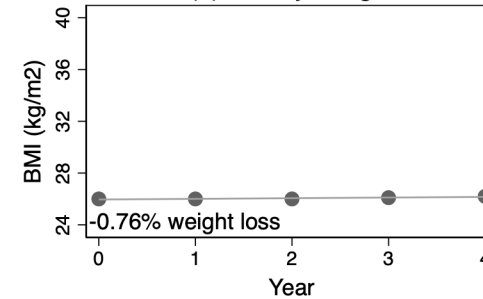
(b) Cycler without Weight Change



(c) Steady Weight Loss



(d) Steady Weight



```
for values var = 9000000/9999999 { // loop through all IDs
  capture quietly: regress bmi year if id == `var' // regression
  capture replace b_year = _b[year] if id == `var' // slope
  capture replace d_48_bmi_modl_new = b_year*4 if id == `var' // change over 4 years
  capture replace d_48_bmi_modl_perc_new = (((bmi + d_48_bmi_modl_new) - bmi)/bmi)*100 if year == 0 & id == `var' // % change
  capture replace e_rmse8_new = e(rmse) if id == `var' // RMSE
}
```

Background

Purpose

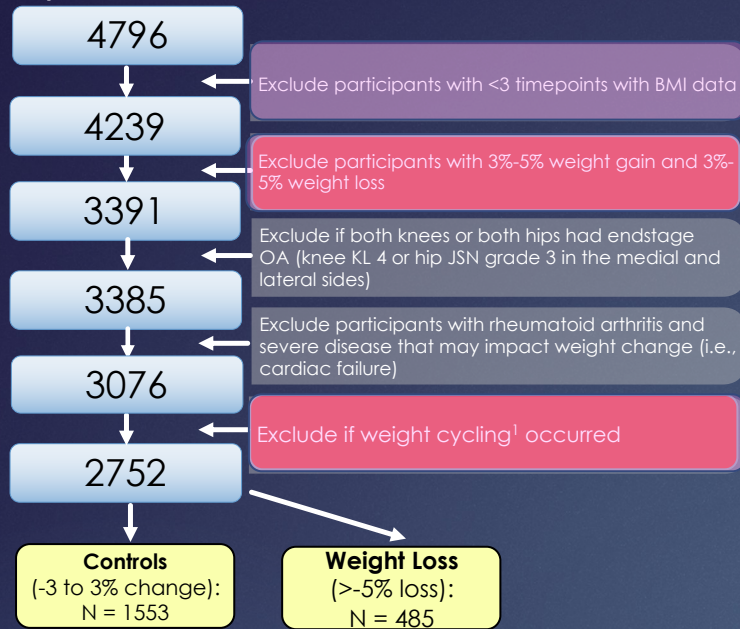
Methods

Results

Discussion

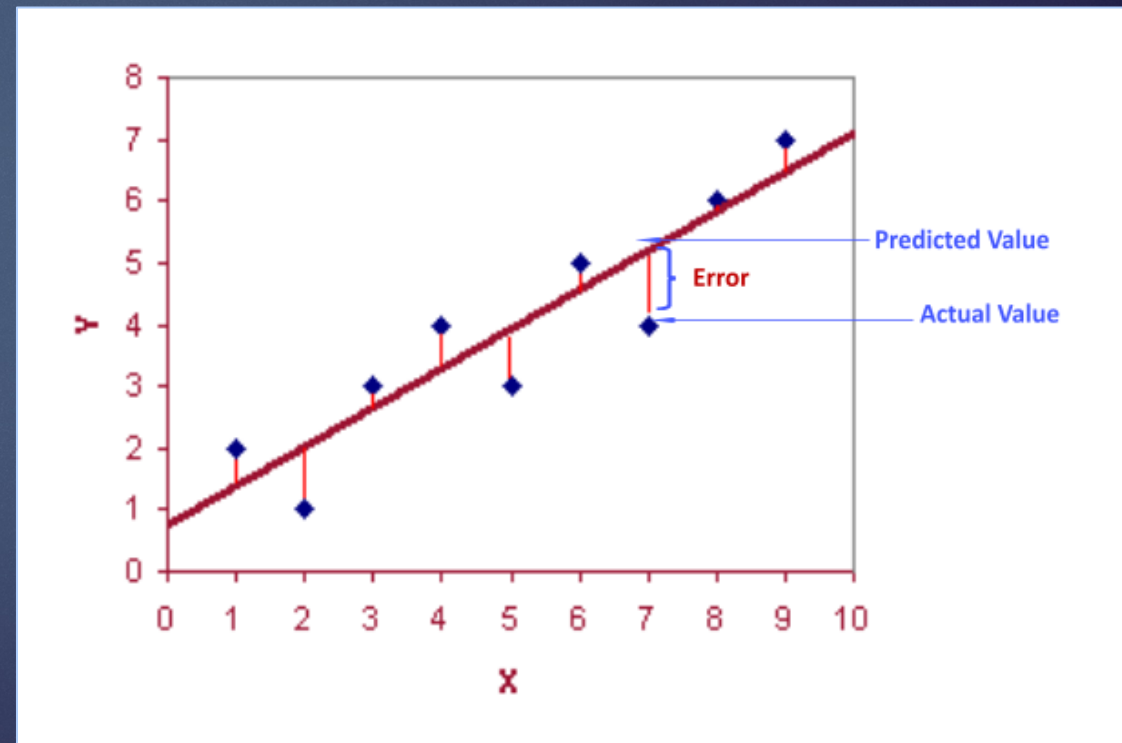
Conclusion

All Participants in the OAI Database



Statistical Methods

$$RMSE = \sqrt{\frac{\sum_{i=1}^N (\text{Predicted}_i - \text{Actual}_i)^2}{N}}$$



Regression models: Individual annual changes in BMI **over 4 years**

Controls (-3 to 3% change)

Weight loss (>5% loss)

Weight Gain (>5% gain)

Top 10% of RMSE¹ (residuals) were designated as cyclers

Cyclers

Non-cyclers

Background

Purpose

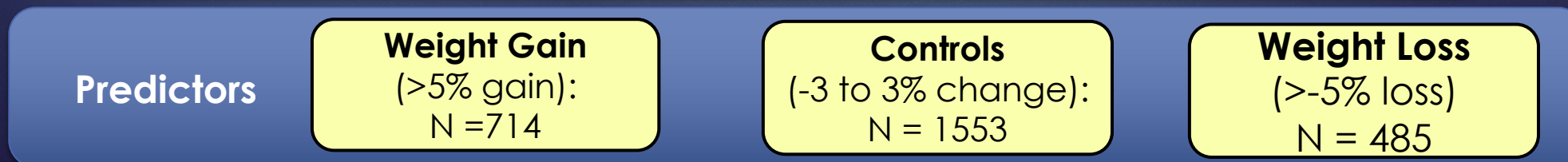
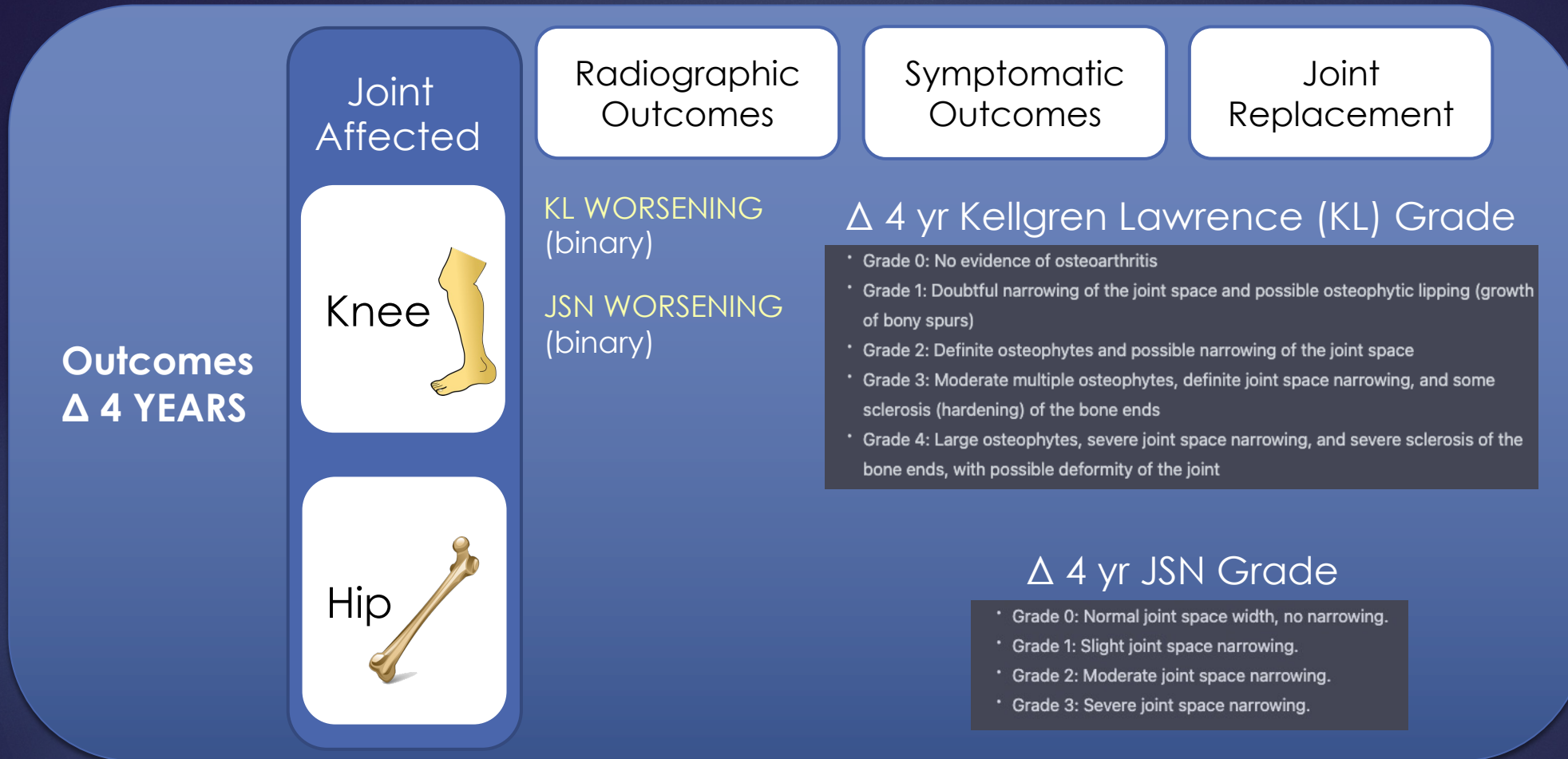
Methods

Results



Discussion

Conclusion

Predictor and Outcome Definitions



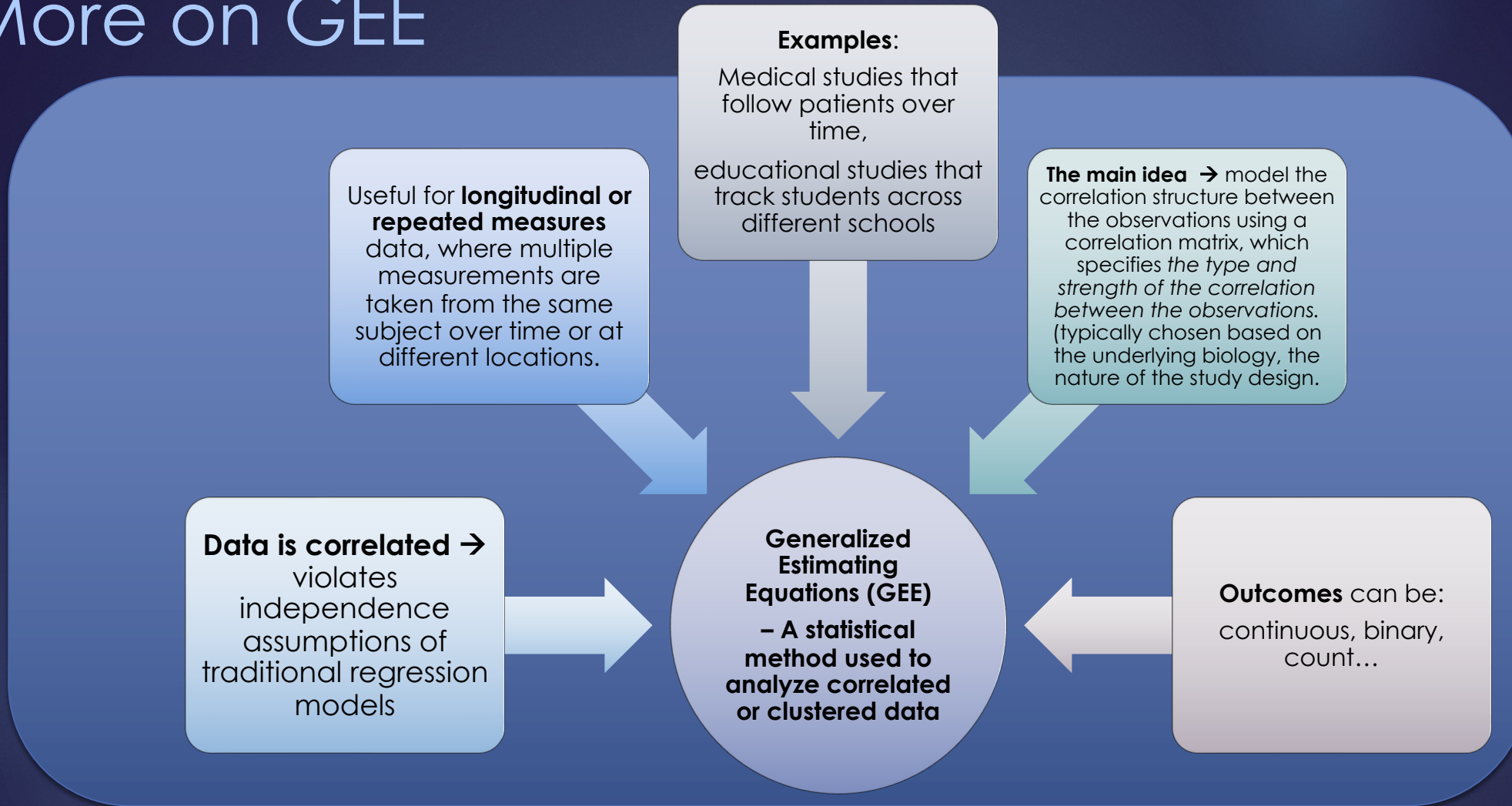
Predictor and Outcome Definitions

	Joint Affected	Radiographic Outcomes	Symptomatic Outcomes	Joint Replacement
Outcomes Δ 4 YEARS	Knee 	KL WORSENING (binary) JSN WORSENING (binary)	No Pain $NoPain_{BL}, NoPain_{4-years}$ Developed Pain $NoPain_{BL}, Pain_{4-years}$	Total Knee Replacement during any annual visit between BL and 4-years
	Hip 	Modified Croft Grade (binary) JSN WORSENING (binary)	Pain Resolved $Pain_{BL}, NoPain_{4-years}$	Total Hip Replacement during any annual visit between BL and 4-years

Statistics

GEE with logistic regression accounting for two knee/hips per person
 Adjustments: age, sex, BMI at baseline

More on GEE



Statistics

GEE with logistic regression accounting for two knee/hips per person
Adjustments: age, sex, BMI at baseline

Background

Purpose

Methods

Results

Discussion

Conclusion

Data – long format

```
listsome id weight_change side p01bmi v00age del_hip_status_bin del_HJSNSM_HJSNSL_bin if del_hip_status_bin ~=., random clean noobs ab(20)
```

id	weight_change	side	p01bmi	v00age	del_hip_status_bin	del_HJSNSM_HJSNSL_~n
9010308	controls	1	22.5	70	0	0
9010308	controls	2	22.5	70	0	0
9010370	controls	2	26.9	51	0	0
9010370	controls	1	26.9	51	0	0
9010952	controls	1	20.9	66	0	0
9010952	controls	2	20.9	66	0	0
9011115	controls	2	24.3	54	0	0
9011115	controls	1	24.3	54	0	0
9011420	weight_gain	2	32.6	72	0	0
9011420	weight_gain	1	32.6	72	0	0
9011661	weight_loss	1	32	64	0	0
9011661	weight_loss	2	32	64	0	0
9011918	weight_loss	1	23.1	62	0	0
9011918	weight_loss	2	23.1	62	1	1
9011949	weight_loss	1	39.5	58	0	0
9011949	weight_loss	2	39.5	58	0	0
9012435	controls	2	31.8	68	0	0
9012435	controls	1	31.8	68	0	0
9013634	weight_gain	1	21.6	49	0	0
9013634	weight_gain	2	21.6	49	0	0

<-- Binary Outcome

Statistics

GEE with logistic regression accounting for two knee/hips per person
Adjustments: age, sex, BMI at baseline

Background

Purpose

Methods

Results

Discussion

Conclusion

Predictor and Outcome Definitions

Joint Affected

Knee



Hip



Outcomes
Δ 4 YEARS

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

```
. tab weight_change side
```

weight_change	Side		Total
	1	2	
controls	1,555	1,553	3,108
weight_gain	713	714	1,427
weight_loss	486	485	971
Total	2,754	2,752	5,506

Statistics

GEE with logistic regression accounting for two knee/hips per person
Adjustments: age, sex, BMI at baseline

Background

Purpose

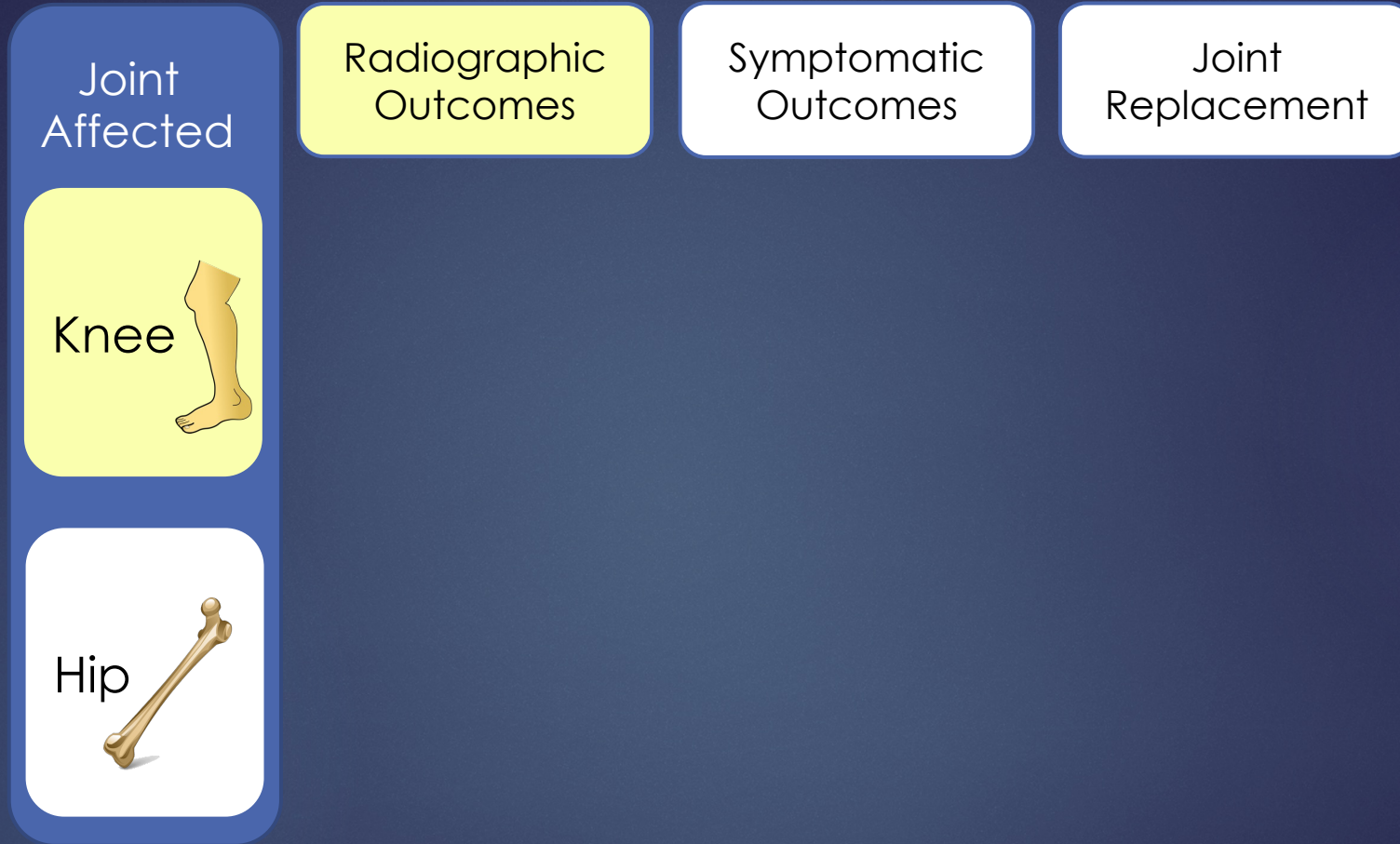
Methods

Results

Discussion

Conclusion

Results – Knee Radiographic



Background

Purpose

Methods

Results

Discussion

Conclusion


Results – Knee Radiographic


Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee 

Hip 

KNEE	KL worsening		
	OR	95% CI	P
Controls		Reference	
Weight Gain	0.95	0.76 – 1.19	0.652
Weight Loss	0.69	0.53 – 0.91	0.009

Participants with weight loss have a 0.69 odds of **Knee** KL worsening compared to controls without weight change


Results – Knee Radiographic


Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee 

Hip 

KNEE	Medial JSN		
	OR	95% CI	P
Controls		Reference	
Weight Gain	1.29	1.01 – 1.64	0.038
Weight Loss	0.85	0.63 – 1.13	0.263

Participants with weight gain have a 1.29 odds of **Knee** JSN worsening compared to controls without weight change

Results – Knee Radiographic


Correlation Structure
Specification of the correlation between the repeated measurements or observations within the same subject or cluster


Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee 

Hip 

```
. xtgee del_XRKL_bin_01 i.weight_change_num i.p02sex v00age p01bmi, i(id) family(binomial) link(logit) corr(independent) eform
```

GEE Binary Outcome Predictor Adjustments Rep. measure Error distribution for logistic regression Responses w/i subject are equally correlated to each other OR

Binary Outcome
Predictor
Adjustments

del_XRKL_bin_01	Odds ratio	Robust std. err.	z	P> z	[95% conf. interval]
weight_change_num					
weight_gain	.94935	.1081822	-0.46	0.648	.7593265 1.186927
weight_loss	.6926761	.0969866	-2.62	0.009	.5264381 .9114085
2.p02sex	1.460378	.1446028	3.82	0.000	1.202767 1.773165
v00age	1.017995	.0049338	3.68	0.000	1.008371 1.027712
p01bmi	1.078997	.0103212	7.95	0.000	1.058956 1.099417
_cons	.0048366	.00207	-12.46	0.000	.0020905 .0111904

Note: _cons estimates baseline odds (conditional on zero random effects).

Participants with weight loss have a 0.69 odds of Knee KL worsening compared to controls without weight change

How to Automate GEE with predictor/outcome combos

```
local outcomes del_XRKL_bin_01 del_XRJSM_bin
local adjustments i.p02sex v00age p01bmi

foreach out in `outcomes'{
  di "*****"
  di "the outcome is `out'"
  qui tab `out' weight_change_num, chi
  di "xtgee `out' i.weight_change_num `adjustments', i(id) family(binomial) link(logit) corr(independent) vce(robust) eform"
  xtgee `out' i.weight_change_num `adjustments', i(id) family(binomial) link(logit) vce(robust) corr(independent) eform
  di "*****"
}
```

Background

Purpose

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How to Automate GEE with predictor/outcome combos

```
local outcomes del_XRKL_bin_01 del_XRJSM_bin
local adjustments i.p02sex v00age p01bmi

foreach out in `outcomes'{
  di "*****"
  di "the outcome is `out'"
  qui tab `out' weight_change_num, chi
  di "xtgee `out' i.weight_change_num `adjustments', i(id) family(binomial) link(logit) corr(independent) vce(robust) eform"
  xtgee `out' i.weight_change_num `adjustments', i(id) family(binomial) link(logit) vce(robust) corr(independent) eform
  di "*****"
}
```

```
the outcome is del_XRKL_bin_01
xtgee del_XRKL_bin_01 i.weight_change_num i.p02sex v00age p01bmi, i(id) family(binomial) link(logit) corr(independent) vce(robust) eform
```

del_XRKL_bin_01	Odds ratio	Robust std. err.	z	P> z	[95% conf. interval]	
weight_change_num						
weight_gain	.94935	.1081822	-0.46	0.648	.7593265	1.186927
weight_loss	.6926761	.0969866	-2.62	0.009	.5264381	.9114085
2.p02sex	1.460378	.1446028	3.82	0.000	1.202767	1.773165
v00age	1.017995	.0049338	3.68	0.000	1.008371	1.027712
p01bmi	1.078997	.0103212	7.95	0.000	1.058956	1.099417
_cons	.0048366	.00207	-12.46	0.000	.0020905	.0111904

How to Automate GEE with predictor/outcome combos

```

local outcomes del_XRKL_bin_01 del_XRJSM_bin
local adjustments i.p02sex v00age p01bmi

foreach out in `outcomes'{
  di "*****"
  di "the outcome is `out'"
  qui tab `out' weight_change_num, chi
  di "xtgee `out' i.weight_change_num `adjustments', i(id) family(binomial) link(logit) corr(independent) vce(robust) eform"
  xtgee `out' i.weight_change_num `adjustments', i(id) family(binomial) link(logit) vce(robust) corr(independent) eform
  di "*****"
}

```

```

the outcome is del_XRKL_bin_01
xtgee del_XRKL_bin_01 i.weight_change_num i.p02sex v00age p01bmi, i(id) family(binomial) link(logit) corr(independent) vce(robust) eform

```

```

the outcome is del_XRJSM_bin
xtgee del_XRJSM_bin i.weight_change_num i.p02sex v00age p01bmi, i(id) family(binomial) link(logit) corr(independent) vce(robust) eform

```

del_XRKL_bin_01	Odds ratio	Robust std. err.	z	P> z	[95% conf. interval]	
weight_change_num						
weight_gain	.94935	.1081822	-0.46	0.648	.7593265	1.186927
weight_loss	.6926761	.0969866	-2.62	0.009	.5264381	.9114085
2.p02sex	1.460378	.1446028	3.82	0.000	1.202767	1.773165
v00age	1.017995	.0049338	3.68	0.000	1.008371	1.027712
p01bmi	1.078997	.0103212	7.95	0.000	1.058956	1.099417
_cons	.0048366	.00207	-12.46	0.000	.0020905	.0111904

del_XRJSM_bin	Odds ratio	Robust std. err.	z	P> z	[95% conf. interval]	
weight_change_num						
weight_gain	1.287926	.157711	2.07	0.039	1.013114	1.637282
weight_loss	.8472146	.1260778	-1.11	0.265	.6328814	1.134134
2.p02sex	1.022499	.1070983	0.21	0.832	.8327347	1.255507
v00age	1.033336	.0055857	6.07	0.000	1.022446	1.044342
p01bmi	1.100024	.0116146	9.03	0.000	1.077494	1.123025
_cons	.0010945	.0005217	-14.30	0.000	.0004301	.0027857

Background

Purpose

Methods

Results

Discussion

Conclusion

How to Automate the code – tables command

```
collect clear
local adjustment i.p02sex v00age p01bmi
local outcomes del_XRKL_bin_01 del_XRJSM_bin
local varnames i.weight_change_num

foreach out of local outcomes{
    local i=1
    foreach var of local varnames {
        collect, tags(out[`out'] var[`var']): xtgee `out' `var' `adjustment', i(id) family(binomial) link(logit) corr(independent) eform
        collect label levels var `var' "model `i'", modify
        local i=`i'+1
    }
}

collect style column, nodelimiter dups(center)
collect style cell result[_r_b _r_ci], warn nformat(%9.3f) // formatting
collect label levels result _r_b "Odds Ratio", modify
collect layout (var#colname[`varnames' `adjustment']) (out#result[_r_b _r_ci _r_p]) // with adjustments.
```

	del_XRKL_bin_01			del_XRJSM_bin		
	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
model 1						
controls	1.000			1.000		
weight_gain	0.949 0.759	1.187	0.648	1.288 1.013	1.637	0.039
weight_loss	0.693 0.526	0.911	0.009	0.847 0.633	1.134	0.265
P02SEX=1	1.000			1.000		
P02SEX=2	1.460 1.203	1.773	0.000	1.022 0.833	1.256	0.832
V00AGE	1.018 1.008	1.028	0.000	1.033 1.022	1.044	0.000
p01bmi	1.079 1.059	1.099	0.000	1.100 1.077	1.123	0.000

More info here (webinar):

https://www.stata.com/training/webinar_series/examples-of-table-and-collect1/

Background

Purpose

Methods

Results

Discussion

Conclusion

Results – Hip Radiographic

Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee

Hip



HIP	Worsening of hip ROA		
	OR	95% CI	P
Controls		Reference	
Weight Gain	1.31	0.88-1.85	0.181
Weight Loss	1.02	0.64-1.63	0.925

No significant associations between weight change and hip ROA or JSN (results not shown)

Results - Knee Symptomatic

Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee

Hip

KNEE	Develop Frequent Knee Pain		
	OR	95% CI	P
Controls		Reference	
Weight Gain	1.34	1.08-1.67	0.009
Weight Loss	1.00	0.76-1.32	0.976

Participants with weight gain have a 1.34 odds of developing frequent knee pain compared to controls without weight change


Results - Knee Symptomatic


Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee 

Hip 

KNEE		<i>Knee pain resolution - any over 12 months</i>		
	OR	95% CI	P	
Controls		Reference		
Weight Gain	1.04	0.79-1.36	0.775	
Weight Loss	1.40	1.06-1.86	0.019	

Participants with weight loss have a 1.40 odds of **knee** pain resolution compared to controls without weight change


Results - Hip Symptomatic


Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

Knee 

Hip 



HIP	Develop Frequent Hip Pain		
	OR	95% CI	P
Controls		Reference	
Weight Gain	1.08	0.84-1.38	0.561
Weight Loss	0.95	0.70-1.63	0.720

No significant associations between weight change and hip pain for all pain outcomes

Results – Joint Replacement

Joint Affected

Radiographic Outcomes

Symptomatic Outcomes

Joint Replacement

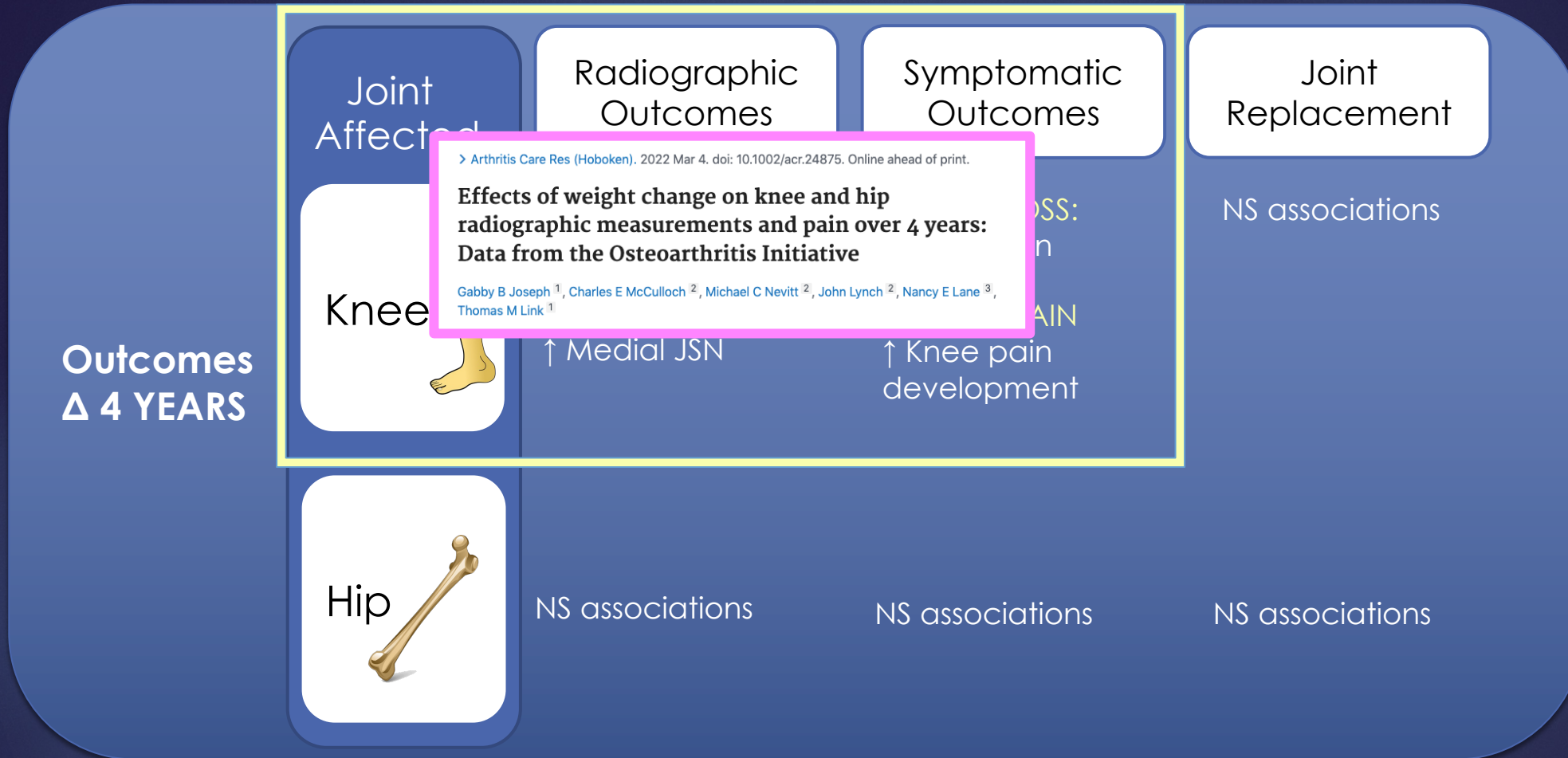
Knee

Hip

	Total Knee Replacement			Total Hip Replacement		
	OR	95% CI	P	OR	95% CI	P
Controls		Reference			Reference	
Weight Gain	1.50	0.90 – 2.49	0.121	1.37	0.74 – 2.55	0.315
Weight Loss	1.11	0.59 – 2.07	0.748	1.22	0.65 – 2.30	0.529

No significant associations between weight change and total knee or total hip replacement

Conclusion



This large, longitudinal study (n=2752 with 4-year follow-up) suggests that weight loss may protect against, and weight gain may exacerbate radiographic and symptomatic *knee* OA, while weight change (5% threshold) does not have significant effects on hip OA.

Study Design

- Start to Finish
- Group definitions & selecting participants in an observational study

Working through the stats

- model choice and automation of code (GEE and tables)

Explain the results in a clear and concise manner





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Thank you!

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