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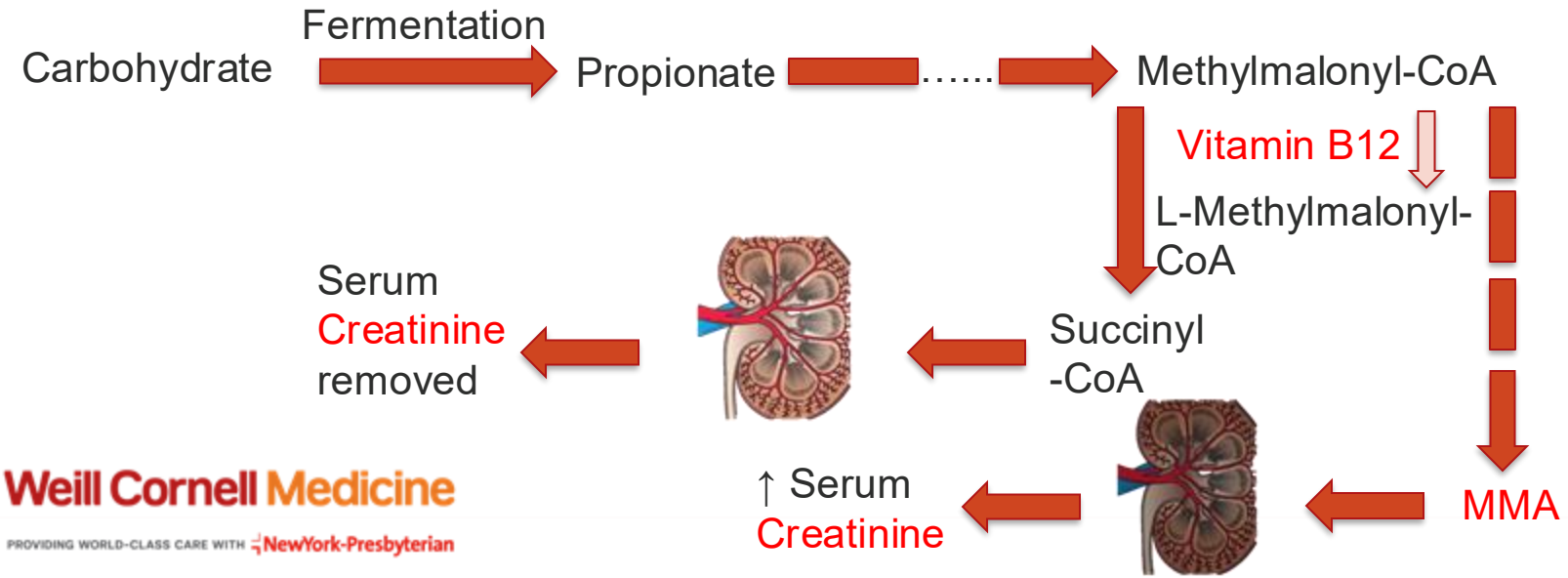
MMA and Lung Cancer

Final Project Presentation

Introduction

- Cancer
  - Uncontrollable cell growth, metastatic
- Lung Cancer
  - Cigarette smoking
- Methylmalonic Acid (MMA): Propionate metabolism byproduct



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Introduction

- Scientific Question
    - **Primary analysis:** Is there any association between cancer history and MMA level? Is this association be affected by different age or creatinine level?
    - **Secondary analysis:** Does the strength of the association between MMA levels and cancer history vary based on how recent the cancer diagnosis is?

- Approach
    - Linear regression model (Univariable, Multivariable)

Methods

- **National Health and Nutrition Examination Survey, NHANES (2001-2014)**
  - Random US population
  - Self-reported personal interview data
  - Demographic, Metabolic characteristics (Vitamin B12, MMA, Creatinine), Cancer history (all cancers incl. lung cancer), Cancer diagnosis age
- **Data manipulation**
  - Subset lung cancer patients
  - Keep only 'Yes' or 'No' responses for the cancer history question and responses within valid value range for cancer diagnosis detail questions
  - 0.05 significance level
- **Demographic**
  - Descriptive characteristics:
    - Age – Wilcoxon rank-sum test; Gender/Race and Ethnicity – Chi-square test
  - Metabolic characteristics:
    - Vitamin B12, Creatinine, MMA – Kruskal-Wallis rank sum test

Methods

- **Dataset support literature or not**
  - Cancer and Vitamin B12: Wilcoxon rank-sum test
  - Vitamin B12 and MMA, MMA and Creatinine: correlation test

- **MMA and age association:**
  - Correlation test (spearman)

- **MMA and history of cancer: interaction with age and creatinine**
  - Linear regression
  - Box-cox transformation for MMA

$$y' = \begin{cases} \frac{y^\lambda - 1}{\lambda}, & \text{if } \lambda \neq 0, \\ \ln(y), & \text{if } \lambda = 0. \end{cases}$$

- **MMA and cancer diagnosis recency**
  - Linear regression
  - Log - transformation for both MMA and Cancer diagnosis recency.
  - MMA and type of cancer: Wilcoxon rank-sum test

Results - Demographic

For cancer history:

- Age, Race/Ethnicity: Significant
- Gender: Not significant

Table 1: Demographic Characteristics by Cancer History

Variables	N	Cancer History		p-value[1]
		Cancer N = 1,734	No cancer N = 17,686	
Age, Median (Q1, Q3)	19,420	69 (57, 78)	46 (32, 62)	<0.001
Gender, n (%)	19,420			0.3
Female		917 (53%)	9,114 (52%)	
Male		817 (47%)	8,572 (48%)	
Race/Ethnicity, n (%)	19,420			<0.001
Mexican American		103 (5.9%)	3,011 (17%)	
Non-Hispanic Black		227 (13%)	3,779 (21%)	
Non-Hispanic White		1,267 (73%)	7,792 (44%)	
Other Hispanic		73 (4.2%)	1,237 (7.0%)	
Other race, including multi-racial		64 (3.7%)	1,867 (11%)	

[1] Wilcoxon rank sum test; Pearson's Chi-squared test

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Results – Metabolic

Density of three metabolic characteristics comparing between three type of patients

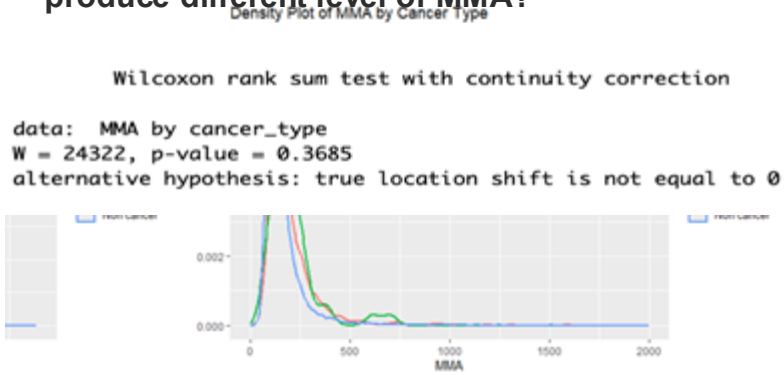
Summary of hypothesis test

Table 2: Metabolic Characteristics by Cancer History

Variables	N	Cancer History: Lung cancer N = 55	Cancer History: No cancer N = 17,686	Cancer History: Other cancer N = 1,679	p-value[1]
Vitamin B12, Median (Q1, Q3)	15,116	514 (401, 662)	499 (371, 680)	519 (369, 732)	0.010
Missing values (N)		16	3,903	385	
MMA, Median (Q1, Q3)	14,971	188 (138, 248)	134 (103, 180)	164 (123, 228)	<0.001
Missing values (N)		16	4,029	404	
Creatinine, Median (Q1, Q3)	19,351	1.01 (0.90, 1.24)	0.85 (0.70, 1.00)	0.90 (0.77, 1.10)	<0.001
Missing values (N)		0	60	9	

[1] Kruskal-Wallis rank sum test

Compare to other cancers, does lung cancer produce different level of MMA?



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Results – Literature check, MMA and age

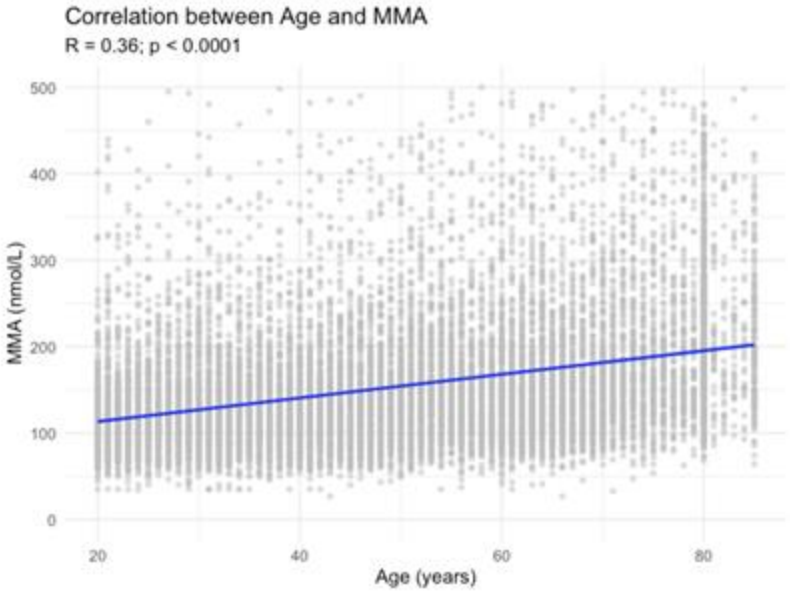
Does our dataset conforms to the literature?

A tendency for cancer patients to have smaller Vitamin B12 observations compared to participants with no cancer.

Test	Group	Cancer & Vitamin B12	Vitamin B12 & MMA	MMA & Creatinine
Wilcoxon rank-sum test		p = 0.00125		
Correlation test	Cancer		r = -0.0645 p = 0.01947	r = 0.156 p < 0.0001
	No-cancer		r = -0.0618 p < 0.0001	r = 0.264 p < 0.0001

Association between age and MMA level

r(Spearman): 0.359 p < 0.001



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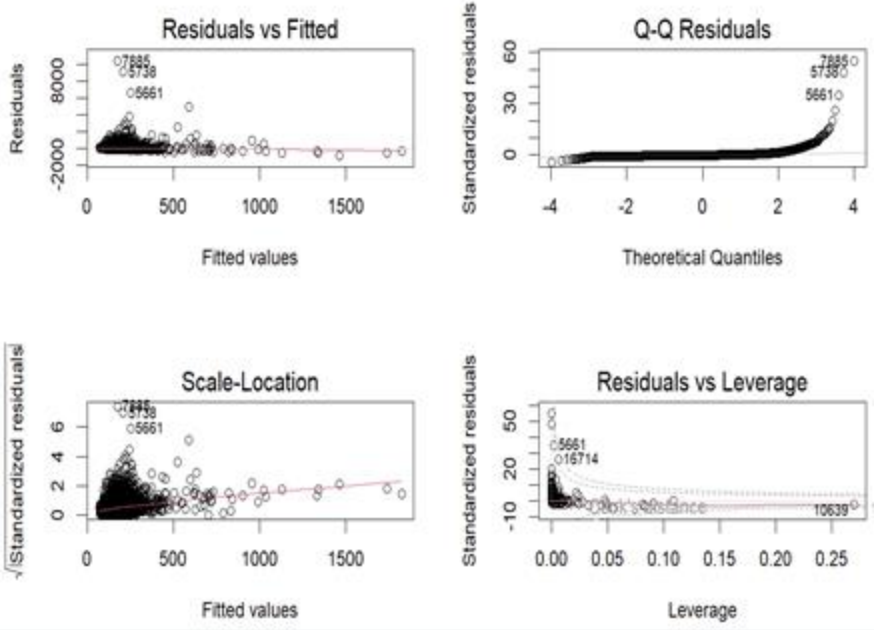
Results – MMA and cancer history

Regression	Coefficient	Estimate	F test	R-squared
Association regression	History of cancer	-34.99 (p<0.001)	37.3 (p<0.001)	0.02422
Baseline regression	Intercept	7.7664 (p=0.877)	288.1 (p < 0.001)	0.0879
	History of cancer	-4.1493 (p=0.971)		
	Age	2.6024 (p =0.006)		
	Creatinine	23.7363 (p=0.329)		
	Age * History of cancer	-0.4728（ p=0.221）		
	Creatinine * History of cancer	37.4477（ p=0.0027 7）		

- History of cancer: Had cancer is reference group



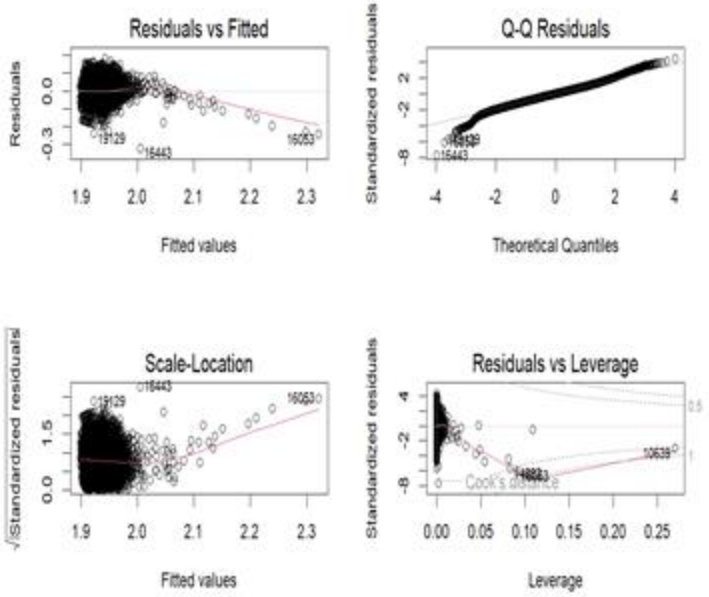
Results – MMA and cancer history

Box-cox transformation: $$y' = \begin{cases} \frac{y^\lambda - 1}{\lambda}, & \text{if } \lambda \neq 0, \\ \ln(y), & \text{if } \lambda = 0. \end{cases}$$

λ = -0.464

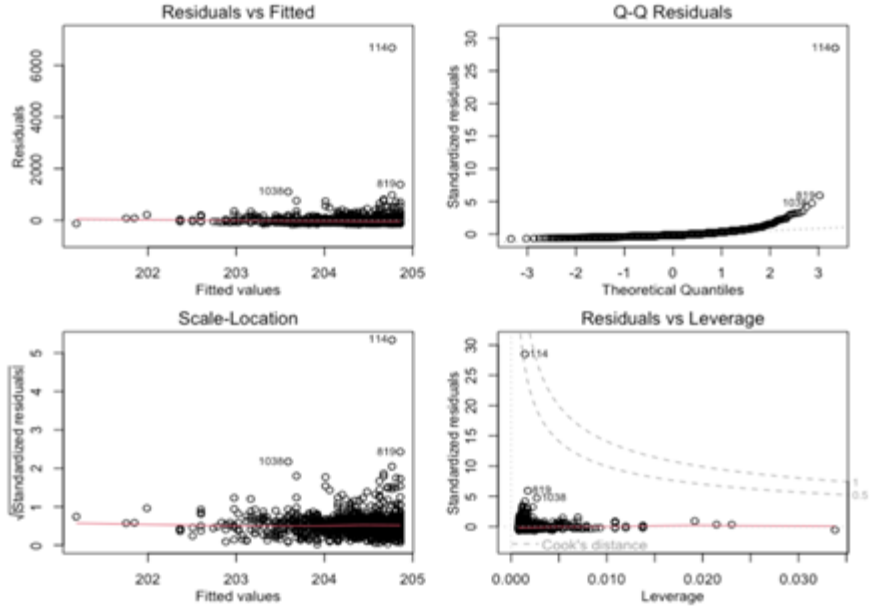
Regression	Coefficient	Estimate	F test	R-squared
Box-cox transformation regression	Intercept	1.868 (p<0.001)	659.6 (p<0.001)	0.181
	History of cancer	0.00255 (p=0.651)		
	Age	0.00110 (p<0.001)		
	Creatinine	0.0149 (p=0.00534)		
	Age * History of cancer	-0.000153 (p=0.0729)		
	Creatinine * History of cancer	0.00390 (p=0.157)		

- History of cancer: Had cancer is reference group

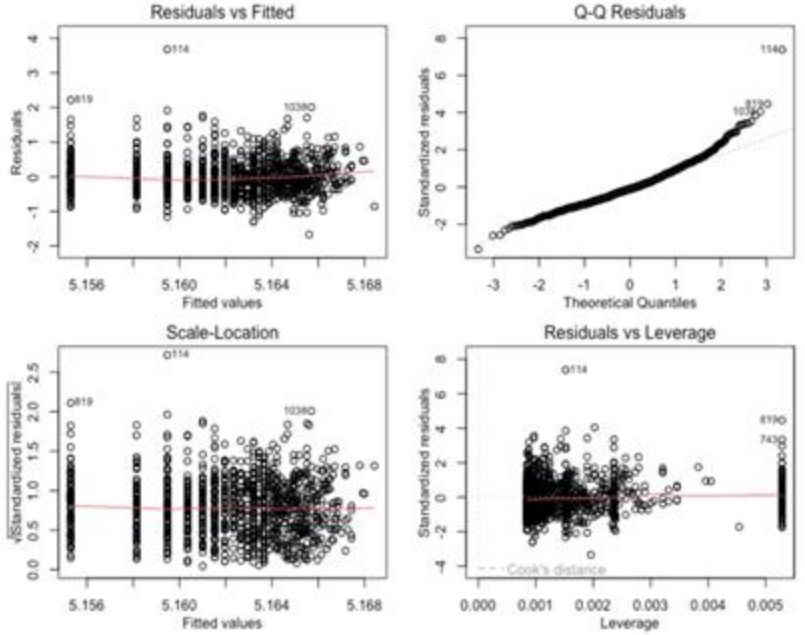


Results – MMA and recency of diagnosis

Simple linear regression



Log transformation linear regression



Coefficient	Estimate	F test	R-squared
Intercept	5.157 (p<0.001)	0.004272 (p= 0.836)	3.599e-05
Cancer recency	-0.002598 (p=0.836)		

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Conclusion

- Cancer and cancer-free participants differ significantly for age, race/ethnicity, and all metabolic characteristics.
- MMA level is associated with cancer history or age alone but not recency of diagnosis.
- Age and creatinine do not appear to impact the association between MMA and cancer history.
- People with cancer have higher MMA level but having lung cancer do not show different MMA level.

Conclusion – Limitations and Implications

- **Limitations:**
  - Unable to confirm the validity of metabolic data points
  - Detection method of metabolic characteristics might vary through time
  - Dataset might be biased (More Non-Hispanic White)

- **Implications:**
  - MMA is not a good indicator for lung cancer
  - More direct biomarkers is better for diagnosis Eg: Carcinoembryonic Antigen (CEA), CA125, CA15-3

References

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Thank you!

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Questions?

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