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Dietary fat and the prevalence of hand osteoarthritis: data from the osteoarthritis initiative

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DIETARY FAT AND THE PREVALENCE OF HAND OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

by

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DEDICATION

To my mother, Cindy, who showed me that impossible is just a word.

DIETARY FAT AND THE PREVALENCE OF HAND OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

ALISSA LACY

ABSTRACT

Objective. To determine the effect of total dietary fat intake on the prevalence of hand osteoarthritis (HOA) utilizing data collected in the Osteoarthritis Initiative (OAI) study cohort.

Methods. This is an observational cross-sectional study. Subjects from the OAI cohort with hand radiographs were analyzed for HOA, defined as a Kellgren-Lawrence score of ≥2 in two or more joints on different fingers. Dietary data and socioeconomic factors were collected from the baseline study visit. Logistic regression analysis assessed the association of total fat intake and disease prevalence. Odds ratios were calculated from the coefficients and confidence intervals were calculated with log-likelihood.

Results. HOA was prevalent in 1,106 out of the 2,993 participants (37%). Total fat intake did not show a significant relationship to disease prevalence when adjusted for age,

education, income, race, smoking, BMI, prescription NSAID use, calcium intake, protein intake, total calories, saturated/monounsaturated fats, and alcohol consumption. There was a significant association of HOA with age, sex, education, race, total calories, and alcohol intake. Sex was analyzed independently to assess for effect modification, showing an association with age (P<0.01) OR (95%CI) 1.03 (1.02,1.03), race (P<0.01) 1.16 (1.09,1.23), and alcohol consumption (P<0.01) 1.06 (1.02,1.09) among only female subjects. Male subjects showed a strong association with age (P<0.01) 1.02 (1.01,1.02).

Conclusion. Total fat intake does not show a significant association with HOA prevalence with the study sample from the OAI cohort. Age, race, and alcohol consumption showed significant associations depending on sex. More research is needed to further investigation these associations among different groups.

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BMI	Body Mass Index
DIP	Distal interphalangeal joint
FFQ	Food frequency questionnaire
HOA	Hand osteoarthritis
KOA	Knee osteoarthritis
MCP	Metacarpophalangeal joint
NIH	National Institute of Health
NSAID	Nonsteroidal Anti-inflammatory Drug
OA	Osteoarthritis
OAI	Osteoarthritis Initiative
PIP	Proximal interphalangeal joint
UCSF	University of California San Francisco

I. BACKGROUND

A. Introduction

Osteoarthritis (OA) is a joint disease that can lead to pain, joint deformity, and disability. It can affect different joints in the body, targeting most commonly the knee, hip, and hand. In 2005 it was estimated that over 13 million Americans, age 26 and up, had symptomatic hand osteoarthritis (HOA).[1] Analysis of HOA data suggests that disease incidence increases significantly with age, therefore prevalence is growing in parallel to life expectancies of the U.S. population.[2] Current treatments only aim to relieve pain and reduce disability, but fail to address structural changes. Variability in disease manifestation further complicates treatment options and contributes to the need for better clinical options to improve public health.[3]

Osteoarthritis may be generalized, localized to one joint, or afflict multiple joints such as those located in the fingers of the hand. Joint space is composed of articular cartilage, an elastic tissue that protects bones from harmful friction and allows for fluid movements. As a person ages the cartilage begins to disintegrate leading to joint damage and weakness.[4] Symptomatic HOA is classified as pain, swelling, and stiffness in the hand, limiting use and leading to muscle wasting. Joints affected in HOA include: the metacarpophalangeal joint (MCP) at the base of the finger, the proximal interphalangeal joint (PIP) in the middle of the finger,

and the distal interphalangeal joint (DIP) closest to the fingertip. Disease progression can lead to severe sclerosis and definite bony deformity, resulting in greater disability.[4]

The etiology of the disease can result from a combination of systemic, extrinsic, and joint factors encompassing biomechanical, biochemical, and genetic aspects.[5,6] Systemic factors include gender, age, and ethnicity. Extrinsic factors pertain to occupational hazards, joint injury, and damage acquired from repetitive movements. Joint factors include abnormalities, deformities, and biochemical changes. These changes are under investigation, along with the nutritional factors that may influence them.

Non-modifiable systemic factors consisting of gender, age, and ethnicity have been linked to variability in OA prevalence and the clinical presentation in different anatomical locations.[7,8,9] These factors appear to influence the articular cartilage and cartilage extracellular matrix present in the joint, affecting the proteins involved in joint homeostasis.[10] The extracellular matrix, within the articular cartilage, aids in support and protection of the bone ends. Abnormal regulation and replenishment of this matrix can lead to joint dysfunction, degeneration, and joint space narrowing.[10] The underlying cause of abnormal changes are multifactorial and can be difficult to distinguish diagnostically.

Although less complex, extrinsic factors can also predispose individuals to OA. These factors involve occupational hazards, repetitive movements, and

injuries to joints acquired during these exposures. Excessive, repetitive stress, to joints cause wear and tear to the articular cartilage and changes in the bone structure, with the anatomical location dependent on type of activity, frequency, and duration of exposure. Careers that require manual dexterity are specifically associated with HOA, such as power grips or utilization of vibrating equipment.[11]

The study of another modifiable risk factor, diet, may reveal better targets for therapy other than ergonomical modifications. Current studies show that the stress from obesity increases risk to weight bearing joints, such as the knee and hip, but little information exists on the effects on non-weight bearing joints.[12] Excessive intake of dietary fat leading to weight gain can affect the biomechanics of joint integrity through load distribution, but may also contribute to the abnormal metabolism and regulation of the articular cartilage. A recent observational study showed that total fat, including saturated fat, polyunsaturated fatty acids, and monounsaturated fatty acids affects knee osteoarthritis (KOA).[13] This study followed over 2,000 subjects with moderate KOA from baseline to a 48 month follow up. Results concluded a positive association of dietary saturated fat with structural KOA progression.

Animal interventional studies have also supported that body fat, not body mass, can increase KOA development.[9,14] This may be due to an adipose derived cytokine, leptin, which is elevated in human OA patients.[15] Leptin is positively associated with cartilage degradation and plays a role in the inflammatory process

within a joint.[5] This evidence suggests that an increase in adipose tissue due to fat consumption, not weight alone, influences OA risk and progression through metabolism. Therefore dietary impact on pro-inflammatory factors cannot be excluded.

Although once thought to be a non-inflammatory form of arthritis, this data has confirmed that OA involves several inflammatory pathways.[4] Inflammation is mild to moderate in presentation with an upregulation of proinflammatory cytokines leading to an imbalance within a joint.[10] This imbalance can cause synthesis of proteins capable of cartilage destruction and joint space narrowing that progresses with time.

Age, therefore, is another influential risk factor for HOA. The mean age for symptomatic HOA is estimated to be 60 years old, with a higher prevalence apparent among women.[16] This age group has a higher overall risk due to a combination of comorbidities, such as cardiovascular disease and diabetes (both of which may have independent influences on OA risk).[4] A low fat diet reduces such health risks, but little data is available on the direct effect of fat consumption on hand joint degeneration.[17]

Diagnosis of HOA can be made from a combination of clinical presentation and radiographic changes in finger joints. Radiographic classification is scored, 0-4, utilizing a standardized method developed by Kellgren and Lawrence, aka K-L score.[18] Radiographic indications include joint space

narrowing and osteophyte formation, a bony outgrowth associated with the degeneration of cartilage at the joint (see Table 1 for scoring details). HOA is defined by a K-L score of ≥2 in two or more joints on separate fingers.[16] Symptoms may occur prior to structural changes in the joints or vice versa, therefore challenging clinical diagnosis and treatment.

Table 1. K-L Scale

Grade	Description
0	No radiographic features of osteoarthritis
1	Possible joint space narrowing and osteophyte formation
2	Definite osteophyte formation with possible joint space narrowing
3	Multiple osteophytes, definite joint space narrowing, sclerosis and possible bony deformity
4	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity

The rise of healthcare costs, in combination with OA disease progression into disability, has resulted in an enormous cost to society, unchallenged by current treatments.[3] One study found that the cost to the United States economy alone to be more than $60 billion per year.[19] Current treatments to address symptoms of osteoarthritis include weight loss, physical therapy, surgery, and Nonsteroidal Anti-inflammatories (NSAIDs) such as naproxen, celecoxib, or over

the counter ibuprofen.[20] Side effects of NSAID use include gastrointestinal risks, bleeding, stomach pain, and potential cardiovascular risk. These risks increase with use and age, therefore increasing health risks in the elderly population most affected by HOA.[21]

Current research is aimed at finding disease-modifying therapies, as none currently exist. The Osteoarthritis Initiative (OAI), initiated by The National Institute of Health (NIH), was launched in 2002 to investigate possible treatment targets and biomarkers primarily for KOA.[3] This cohort of subjects include those with measurable knee osteoarthritis or were at a high risk. Ample clinical data and samples were collected to address many of the confounding variables faced by researchers today. Although numerous publications have advanced our knowledge on knee OA, few studies have been completed pertaining to the available data on HOA.

B. Purpose

The purpose of this study was to investigate the relationship between total dietary fat consumption and the prevalence of HOA from the data collected in the OAI study. The aim of this research was to provide information on a modifiable risk factor, diet, and its possible influence on HOA.

C. Primary Study Question

How does total dietary fat intake affect the prevalence of radiographic hand osteoarthritis, at baseline, among subjects enrolled in the United States Osteoarthritis Initiative?

D. Study Rationale

Osteoarthritis is the most common form of arthritis, the hand being the most frequently affected site.[3] The role of diet is not fully understood in regard to osteoarthritis pathogenesis and progression. Total fat intake, specifically, is a modifiable factor that may be clinically important in the management of disease progression.[13] Current treatment options provide relief from symptoms, but do not prevent HOA structural progression or related disability. Surgical intervention and chronic NSAID use may impact health among an already high-risk population.[21] Consequently, here is a need for disease modifying therapies that not only alleviate symptoms, but manage joint degeneration and disease progression. Although human and animal models support a relationship between fat intake and KOA incidence, more studies are needed to better understand this process in non-weight bearing joints. Data collected from the OAI may provide valuable information on a potential association between dietary fat consumption and HOA prevalence.

II. MATERIAL AND METHODS

A. Population

The study sample included in the analysis for this study was gathered from the publicly available data entered into the Osteoarthritis Initiative (OAI), uploaded to a secure site housed on the University of California San Francisco (UCSF) web-server. As per the OAI protocol, participants were enrolled from February 2004 to May 2006 into the OAI at four clinical sites located in Baltimore, MD; Columbus, OH; Pittsburgh, PA; and Pawtucket, RI. Full ethical approval was granted by the institutional review board (IRB) of the OAI Coordinating Center, at UCSF. Participants in the OAI study were recruited by brochures distributed to targeted groups, through mail, and in person. Participants who self-identified as eligible were interviewed by telephone and advanced through a screening clinic visit to enrollment if eligible. Participants were consented at their corresponding study site with IRB-approved forms. For more details on the recruitment process, interview components, and screening measures please refer to the full OAI Protocol.[3]

OAI enrolled 4,796 males and females, between the ages of 49 to 79 years. The primary purpose of the OAI cohort was to investigate progression in previously diagnosed adult KOA subjects, as well as incidence in adults at a high risk for osteoarthritis. Participants deemed eligible in the OAI cohort had either:

1) Clinically significant knee OA who were at risk for progression, or

2) A high risk of initiation of clinically significant knee OA

As per the OAI protocol all participant information was de-identified and assigned a study number corresponding to information secured at the affiliated study site. All data was transferred electronically. Datasets composed of clinical measures and questionnaire information were placed on public access on the OAI website: https://oai.epi-ucsf.org/datarelease/. All staff training, certifications, and performance standards were monitored and updated through the OAI quality assurance committee.

Baseline data collected in the OAI study, and included for analysis in this study included demographic and socioeconomic factors. Participants self identified as White non-Hispanic, African American, or other racial/ethnic group. Each participant recorded yearly income and education status. The use of prescription NSAIDs (e.g., Ibuprofen, Diclofenac) was recorded for joint pain or arthritis more than half the days of the month, within the past 30 days.

Nutritional data, including 60 food groups, was collected at baseline in the OAI program through a Block Brief (2000) Food Frequency Questionnaire (FFQ) by the OAI. This was a self-administered reduced length food frequency questionnaire developed from the NHANES III dietary intake data.[3] Results from the questionnaire validation showed the absolute value of macronutrients to be underestimated by the FFQ as compared to food record estimates.[23] Most micronutrients, however, were not underestimated. As per the OAI program, the

commonly used unit or portion size was assigned to each food group and participants were asked to report frequency of consumption; never, a few times per year, once per month, 2-3 times per month, once per week, twice per week, 3-4 times per week, 5-6 times per week, and every day.[13] The FFQ was mailed to all subjects then reviewed for completion status by study nurses. All dietary data was calculated through NutritionQuest (www.nutritionquest.com). Dietary categories selected from the OAI for the purpose of this study included: total fat, saturated fat, monounsaturated fat, total calories, protein, dietary calcium, supplemental calcium, and alcohol consumption (drinks per week).[13]

For the purpose of this study, variables collected from the OAI were further categorized for analysis. Race was categorized as White, non-Hispanic or as other ethnicities. Education was categorized as follows: some high school/graduate, some college/graduate, or graduate school. Income was stratified into <$25,000, $25-49,000, $50-99,000, and ≥$100,000 per year. BMI was categorized into <25, 25-30 (overweight), and >30 kg/m^2 (obese).[13] Smoking was categorized as never or current/past smoker. Alcohol consumption per week was further categorized from the FFQ as 0 drinks, <1 to 3 drinks, or ≥4 drinks based off of the CDC's guideline for occasional to moderate dirnking.[22] In total all variables included in the analysis were sex, age, education, income, race, smoking status, BMI, prescription NSAID use, calcium intake (dietary/supplemental), protein intake, total calories per day, alcoholic drinks per week, saturated fat,

monounsaturated fat, and total fat intake.

In this study participants who did not report dietary data, answered less than 50% of the questionnaire, or had implausible total daily calorie intake (women with <500 or >3,500Kcal and men with <800 or >4,200Kcal) were excluded. Participants missing hand K-L scores or relevant health history information were not included in the study's analysis.

B. Study Design

This was an observational, multicenter, cross-sectional study designed to investigate HOA prevalence and total fat consumption at the baseline OAI visit. The outcome measure of this investigation was HOA and the exposure was total fat intake.

C. Analysis

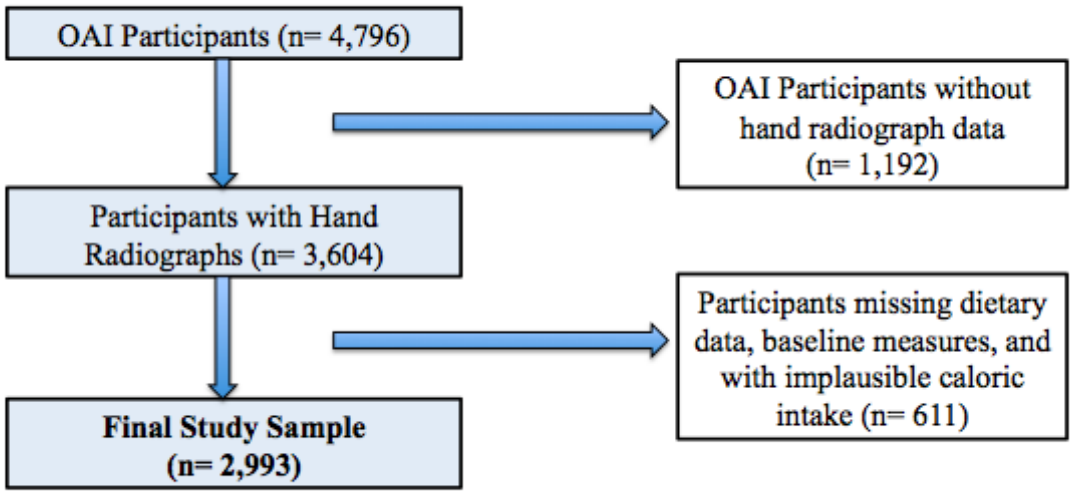
To evaluate for structural HOA the K-L grading scale was used to analyze all dominant hand radiographs for structural changes. HOA was defined as a K-L score of ≥2 in two or more joints on separate fingers, therefore excluding single finger OA and the three thumb joints.[18] K-L scores were assigned based on the radiographic findings assessed by one investigator who read the posteroanterior radiographs of the dominant hand. Intra-reader agreement was good (weighted kappa >0.84).

Statistical analysis was completed on R Studio programming software. Prevalence was filtered from OAI public data utilizing the previously defined K-L score. All subject health history and nutritional data was downloaded from OAI and merged by ID number. Analysis was done using a logistic regression, adjusting for multiple variables. Odds ratios (ORs) were calculated from the analysis coefficients and were aligned with 95% confidence intervals (CIs), calculated by log-likelihood. Analysis was not controlled for treatments, other than prescription NSAID use at baseline, as no current treatments reduce structural progression with relation to total fat intake.

III. RESULTS

Out of the 4,796 OAI participants, the final study sample analyzed for this study consisted of 2,993 participants. OAI participants without hand radiograph data, dietary data, or with implausible caloric intake excluded a total of 1,803 subjects (Figure 1). The mean age of the study population was 61 years old. Out of the 2,993 participants 1,312 were male (43.8%) and 1,681 were female (56.2%). The study population had 1,106 subjects with HOA (37%) and 1,887 without HOA (63%) (Table 2). A majority of the participants attended college and/or graduate school (87%) and had a yearly income of ≥ $50,000 (64%). The majority of the study sample was white, non-Hispanic (83%), while African Americans, Asians, and other ethnic groups comprised only 17%. Most of the subjects were non-smokers (78%) and few recorded NSAID use within the

Figure 1. Study Sample



past 30 days (10%). About 24% of individuals had a BMI of <25 kg/m^2, while a majority were overweight or obese, 40% and 36% respectively.

Dietary analysis showed a mean consumption of 677.5 mg/d of calcium with supplemental calcium consumption at 475.8 mg/d. Average protein consumption measured at 61.3 g/d and mean total caloric intake was 1,423 Kcal/d. The majority of participants consumed <1-3 alcoholic drinks per week (54%), while 29% consumed 4 or more. Participants who did not drink alcohol accounted for the last 17%. The mean intake of saturated fat was 19 g/d, monounsaturated fat was 20.4 g/d, and total fat was 55.1 g/d.

Participants with radiographic HOA were older in age, mean of 66.7 years old, and female (63%) as compared to those without HOA (57.9 years old and 52% respectively). Both age and sex showed a significant association (P value of <0.05) with prevalence of HOA; with P <0.01 OR of 1.03(1.02,1.03) and P <0.01 OR of 1.09(1.05,1.14), respectively. These results predict that with each year of age the subject is 3% more likely to have HOA, while females are 9% more likely to have HOA than males. Education also showed a significant association (P = 0.01) with OR of 0.97(0.94,0.99) predicting that participants who were more educated will be 3% less likely to develop HOA with each category. Percentage of White, non-Hispanic subjects was 9% higher in the HOA group and had a P value <0.01. Interpretation of the OR showed that these participants were 13% more likely to have HOA than other ethnicities. BMI categories showed significant association with HOA (P = 0.03) with a

2% increase in probability from <25 to 25-29 and from 25-29 to >30, respectively. NSAID use was three times higher in the HOA participants (18%) than in participants without HOA (5%). Mean calcium and protein intake was similar between the two groups, but mean supplemental calcium was slightly higher in HOA participants. These dietary variables did not show a significant association, with 95% CI including the null (1.00). Alcohol consumption was higher in the HOA group, with 33% of subjects consuming 4+ drinks per week; drink categories were significant with 1.04(1.02,1.07) (P<0.01). Each category of drinks per week increased probability by 4%.

Total fat showed no significant difference between groups the mean was slightly lower than the disease free group, 53.2 versus 56.3 grams/day. The odds ratios showed no difference between participants with and without HOA 1.00(0.99,1.01). Mean intake of saturated fat and monounsaturated fat were slightly lower in subjects with HOA, possibly due to a lower mean intake of total calories (P = 0.03).

In order to determine the effects of sex on the relationship between total fat intake and HOA prevalence, similar models were performed by separating sex into two strata. The results from these regression models show a difference in association of the same variables (Table 3). The male subgroup showed significant association with age (P <0.01) OR 1.02(1.01,1.02), while the female subgroup showed association with age (P <0.01) 1.03(1.02,1.03), race (P <0.01) 1.16(1.09,1.23), and alcohol consumption (P <0.01) 1.06(1.02,1.09). Each year of age increased the likelihood of HOA by 2% in men and 3% in women. The probability for HOA in white females is 16%. Results also

showed that females who consumed alcohol had an increased probability of HOA (6%) for each drink category (<1 to 3, and 4 or more). Dietary fat was not statistically associated with HOA in either sex.

Table 2. Association of total fat intake with the prevalence of hand osteoarthritis.

	All (N=2,993)	No HOA (N=1,886)	Prevalent HOA (N=1106)	P value	Odds Ratio (95% CI)*
Age in years, mean (SD)	61.2 (9.1)	57.9 (8.3)	66.7 (7.5)	<0.01	1.02(1.02,1.03)
Sex (% female)	56	52	63	<0.01	1.09(1.05,1.14)
Education, %				0.01	0.97(0.94,0.99)
</= High School	13	11	17		
College	45	45	44		
>College	42	46	39		
Income, %				0.25	0.99(0.94,1.01)
<25K	11	10	14		
25-49K	25	21	31		
50-99K	39	40	37		
100K	25	28	18		
Race, %				<0.01	1.13(1.08,1.18)
White, non-hispanic	83	80	89		
Other ethnicities	17	20	11		
Smoke, %				0.84	0.99(0.95,1.04)
Never	78	77	79		
Current/Past	22	23	21		
BMI[a] (kg/m^2) %				0.03	1.02(1.00,1.04)
<25	24	24	23		
25-29	40	39	42		
>30	36	37	35		
NSAID[b] use, %	10	5	18	0.14	0.96(0.92,1.01)
Dietary Calcium (mg/d), mean (SD)	677.5 (324.4)	678.1 (326.1)	676.4 (321.6)	0.80	1.00(0.99,1.00)
Supplement Calcium (mg/d), mean (SD)	475.8 (474.3)	421.5 (458.1)	568.6 (487.3)	0.36	1.00(0.99,1.00)
Protein (g/d), mean	61.3 (24.3)	62.0 (24.3)	60.1 (24.1)	0.27	1.00(0.99,1.00)
Total Calories (Kcal/d), mean (SD)	1428 (527.5)	1454 (542.8)	1385 (497.7)	0.03	0.99(0.99,0.99)
Alcohol (drinks/week) %				<0.01	1.04(1.02,1.07)
0	17	17	16		
<1-3	54	55	51		
4+	29	28	33		
Saturated Fat (g/d) mean (SD)	19.0 (9.2)	19.4 (9.40	18.3 (8.8)	0.39	1.00(0.99,1.00)
Monounsaturated Fat (g/d)	20.4 (10)	20.9 (10.3)	19.7 (9.6)	0.15	1.01(0.99,1.02)
Total Fat (g/d), mean (SD)	55.1 (25.6)	56.3 (26.1)	53.2 (24.6)	0.93	1.00(0.99,1.01)

a. Body Mass Index.
b. Non-steroidal anti-inflammatory drugs used in the past 30 days.
*Confident Intervals were calculated using log likelihood

Table 3. Assocaition of total fat intake and HOA by sex.

Variable	Female (N= 1,681)		Male (N= 1,312)	
	P. value	Odds Ratio (95% CI)*	P. value	Odds Ratio (95% CI)*
Age (years)	<0.01	1.03(1.02,1.03)	<0.01	1.02(1.01,1.02)
Education	0.09	0.97(0.94,1.00)	0.08	0.97(0.93,1.00)
Income	0.12	0.98(0.96-1.01)	0.63	1.01(0.98,1.04)
Race	<0.01	1.16(1.09,1.23)	0.22	1.05(0.97,1.13)
Smoker	0.99	1.00(0.89,1.13)	0.85	1.00(0.96,1.05)
BMI[a] Category (kg/m^2)	0.17	1.02(0.99,1.05)	0.07	1.03(0.99,1.07)
NSAID[b] use	0.06	0.94(0.88,1.00)	0.96	1.00(0.92,1.08)
Dietary Calcium (mg/d)	0.55	1.00(0.99,1.00)	0.18	1.00(0.99,1.00)
Supplemental Calcium (mg/d)	0.65	1.00(0.99,1.00)	0.05	1.00(0.99,1.00)
Protein (g/d)	0.23	1.00(0.99,1.00)	0.98	1.00(0.99,1.00)
Total Calories (Kcal/d)	0.07	1.00(0.99,1.00)	0.26	1.00(0.99,1.00)
Alcohol Category (drinks/week)	<0.01	1.06(1.02,1.09)	0.12	1.03(0.99,1.07)
Saturated Fat (g/d)	0.12	0.99(0.98,1.00)	0.66	1.00(0.99,1.01)
Monounsaturated Fat (g/d)	0.44	1.01(0.99,1.02)	0.45	1.00(0.99,1.02)
Total Fat (g/d)	0.61	1.00(0.99,1.00)	0.85	1.00(0.99,1.01)

a. Body Mass Index.
b. Non-steroidal anti-inflammatory drugs used in the past 30 days.
*Confident Intervals were calculated using log likelihood

IV. DISCUSSION

In this cross-sectional study of subjects with radiographic hand data, significant associations between total fat intake and HOA prevalence were not observed. The association seen with education, BMI, and total calories consumed may have been due to an effect modifier; sex. The strong association between sex with HOA prevalence was investigated by performing a separate analysis on the male and female subgroups. The difference in association with the same variables suggests that sex is an effect modifier for previously discussed variables, but not the primary exposure of dietary fat. The implication of this result is that females may have a higher overall risk of HOA, specific factors found in this study included race and alcohol consumption. Both may be clinically significant in women, while men may have other risk factors no addressed in this study or a decreased risk of HOA overall.

Although previous research suggests that dietary fat intake may be associated with osteoarthritis, the results of this study show no statistical association with total fat and HOA prevalence (P = 0.93) OR 1.00 (0.99.1.01). This suggests that HOA may not be affected by fat intake, but by other variables including age, race, and alcohol consumption. Other dietary variables did not show associations with disease prevalence in this model. This may be due to a decrease in total calories and fats within HOA participants, a result of diagnosis and dietary modification for treatment. Since the study sample was confined to previously collected information more detailed hand data was not available for analysis; a limitation of this study's design.

Participants with HOA showed patterns consistent with current data, an older study sample with a mean age of 66.7 years. The status of subjects around this age group may influence variables assessed in the models. Elderly or retired individuals may be less active, consume fewer calories, and have other health conditions requiring regular medical treatment and monitoring. This may complicate clinical care and require individual treatment plans to address non-compliance and co-morbidities. This age group may falsely decrease the association of HOA with fat intake if dietary changes occurred after HOA onset, such as a decrease in fatty foods. Structural damage to the joint cannot be reversed by current therapies, therefore HOA prevalence may appear increased in participants with a seemingly healthy baseline diet. More information in regard to current occupation, health care, and hand use is needed.

The HOA group also had an increased percentage of female subjects. This may be due to an earlier onset of disease and progression from different biological changes occurring among sexes, such as menopause. Alcohol metabolism may vary between sex and age, therefore influencing the association seen in the results.[24,25] Difference in specific alcohol types, such as wine, beer, or liquor, may be seen between sexes. If female participants drink more liquor or wine as compared to the male participants it may falsely elevate significance. Stratification of different drink types may allow for a better analysis in combination with investigating each subgroup.

A. Strengths:

Strengths of the study include the large sample size utilized from the OAI, as the high participant numbers adds significant power to the results. All data was previously gathered and analyzed into tables allowing for easy access. The study analysis timeline was therefore decreased as data was quickly collected and organized. All IRB approval was previously obtained and a central committee ensured consistency in results and measurements taken (hand radiographs, clinical data, etc.).

The multicenter design of the study allowed for data collection from multiple states in different regions of the United States. This difference in enrollment locations increases generalizability of the study, as participants are not restricted to one specific region in America. A more diverse cohort allows for extension of these research findings to a larger population.

B. Limitations:

A limiting factor was the cohort utilized for the study sample. All subjects enrolled were either diagnosed with knee osteoarthritis or were categorized as a high-risk individual. This could lead to an overestimate of prevalence as inclusion criteria was specific to the knee joint, therefore excluding subjects without KOA risk and diagnosis. The relationship between KOA and HOA prevalence is not completely understood, therefore more information is needed to understand the

effects this may have on the study sample utilized for this research. The data collected during the OAI study included many variables in regard to knee osteoarthritis and therefore were not specific to just the hand joints. Due to the study design more information on hand use and injury could not be obtained. The study sample was predominately Caucasian and therefore was lacking in an adequate sample of other ethnicities for comparison. This could result in a false association of HOA and race.

The dietary intake questionnaire could be subject to false data as there is the possibility of recall bias. This could lead to underestimation of fatty food portions, or possible overestimation of other nutrients. Incorrect reporting would therefore influence any associations if total fat were falsely recorded. The questionnaire was only a snapshot of each individual's dietary intake and, as previously discussed, may underestimate macronutrients. Nutritional consumption was not monitored or recorded over time and was limited to a 12-month recollection; therefore changes in diet throughout a subject's lifetime cannot be captured. Long-term dietary patterns, changed due to recent health issues, may have had lasting effects on joint damage and degeneration. This can result in HOA participants with recently lowered fat intake and therefore a lack of association between total fat and disease prevalence.

C. Future Directions:

The future of OAI research may hold the key to disease management and potentially unveil preventative measures for high-risk patients. Investigation into HOA incidence and nutrition may show a relationship between disease severity and diet quality. Another observational study, prospective in nature, would be useful to determine if increased fat consumption or other dietary factors lead to a more advanced K-L score from baseline to the 48-month follow-up visit. Total fat intake could be stratified into quartiles to further investigate any possible associations in this study.

The relationship between alcohol consumption and HOA prevalence may also reveal important information. Utilizing the same study sample a cross-sectional observational study should be performed investigating the type of alcohol consumed among the female subjects. Wine, beer, and hard liquor may have different effects on males and females as well as different age groups.

A prospective cohort study following a large population could identify dietary patterns and changes to these patterns, showing long-term effects on HOA prevalence. Logging dietary data into an online system, such as the USDA's diet tracker (https://www.supertracker.usda.gov/foodtracker.aspx), would decrease recall bias and provide a more accurate collection of data. Evaluation of pain scores in relation to this dietary data may provide information regarding strategies to limit disease symptoms and decrease disability in the hands. In this regard other

dietary factors that may decrease pain, such as fish oil, could be included.[13]

V. CONCLUSION

Osteoarthritis is a multifactorial disease, affecting millions of people globally and costing billions of dollars to the economy annually. There are currently no disease modifying treatments, but the study of modifiable risk factors may suggest a new approach to disease management. Data analysis from the OAI cohort did not show a significant association of total fat intake and the prevalence of HOA. There was, however, a strong association with age, sex, education, race, BMI, total calories, and alcohol consumption. Due to the numerous associations found further analysis was done to determine the true significance of these results.

To assess for the possibility of an effect modifier, sex was analyzed into two separate models with the same variables. Although age remained significantly associated with HOA in both groups, White, non-Hispanic females were 16% more likely to have HOA. Females who consumed alcoholic drinks were 6% more likely with each increment of consumption, however, no association was seen between alcohol consumption in males. These results conclude that specific dietary factors may influence HOA prevalence, but more data is needed to address the numerous variables involved.

This data may aid clinical strategies in regard to HOA risk and progression. Nutrition is an important part of daily life, influencing each individual's metabolism and immune system through multiple pathways. Diet modification may hold the key to decreasing HOA risk and slowing progression, therefore improving public health.

REFERENCES

1. Murphy L, Helmick C. "The Impact of Osteoarthritis in the United States: A Population-Health Perspective." American Journal of Nursing. March 2012; 112(3).

2. Dillon CF, Hirsch R, Rash EK, Gu Q. Symptomatic hand osteoarthritis in the United States: prevalence and functional impairment estimates from the thirst U.S. National Health and Nutrition Examination Survey, 1991-1994.American Journal of Physical Medicine & Rehabilitation. January 2007;86(1), 12-21.

3. Nevitt M, Felson D, Lester G. "The Osteoarthritis Initiative: Protocol for the Cohort Study." OAI: A Knee Health Study, 2013. https://oai.epi-ucsf.org/datarelease/docs/StudyDesignProtocol.pdf

4. Leung GJ, KD Rainsford, and WF Kean. "Osteoarthritis of the hand I: aetiology and pathogenesis, risk factors, investigation and diagnosis." Journal of Pharmacy and Pharmacology, November 2013;66, 339-346.

5. Charlier E, et. al. "Insights on Molecular Mechanisms of Chondrocytes Death in Osteoarthritis." *International Journal of Molecular Sciences.* 2016, *17*(12), 2146; doi:10.3390/ijms17122146

6. Lane, et al. "OARSI-FDA Initiative: Defining the Disease State of Osteoarthritis." Osteoarthritis and Cartilage 19 (2011) 478e482. doi:10.1016/j.joca.2010.09.013

7. Yucesoy B., Charles LE, Baker B, Burchfiel. "Occupational and genetic risk factors for osteoarthritis: A review." PubMed Central. Jan. 1, 2015; 50(2): 261–273. doi:10.3233/WOR-131739

8. Loughlin, J. "The genetic epidemiology of human primary osteoarthritis: current status." *Expert Reviews in Molecular Medicine*. 2005. 7(9), pp. 1–12. doi: 10.1017/S1462399405009257.

9. Collins JE, Deshpande BR, Katz JN, Losina E."Race- and Sex-Specific Incidence Rates and Predictors of Total Knee Arthroplasty: Seven-Year Data From the Osteoarthritis Initiative." Arthritis Care and Research (Hoboken). 2016 Jul;68(7):965-73. doi: 10.1002/acr.22771.

10. Fernandez-Moreno M, Rego I, Carreira-Garcia V, Blanco FJ. "Genetics in

osteoarthritis. Current Genomics." 2008;9:542–547. doi: 10.2174/138920208786847953.

11. Neogi T, Zhang Y. "Epidemiology of Osteoarthritis." Rheumatic Disease Clinics of North America. 39 (2013) 1–19 http://dx.doi.org/10.1016/j.rdc.2012.10.004

12. Centers for Disease Control and Prevention. "Osteoarthritis (OA)". http://www.cdc.gov/arthritis/basics/osteoarthritis.htm October 28, 2015.

13. Lu, et al."Dietary Fat and Progression of Knee Osteoarthritis Dietary Fat Intake and Radiographic Progression of Knee Osteoarthritis: Data from the Osteoarthritis Initiative." Arthritis Care and Research (Hoboken). 2016 Jun 6. doi: 10.1002/acr.22952.

14. Griffin TM, Guilak F. "Why is obesity associated with osteoarthritis? Insights from mouse models of obesity." *Biorheology*. 2008;45(3-4):387-398.

15. Poonpet T, Honsawek S. "Adipokines: Biomarkers for osteoarthritis?" *World Journal of Orthopedics*. 2014;5(3):319-327. doi:10.5312/wjo.v5.i3.319.

16. Haugen IK, et al. "Prevalence, incidence and progression of hand osteoarthritis in the general population: the Framingham Osteoarthritis Study." *Annals of Rheumatic Diseases.* doi:10.1136/ard.2011.150078

17. Hu, et al. "Prospective study of major dietary patterns and risk of coronary heart disease in men." American Journal of Clinical Nutrition. 2000 Oct;72(4):912-21.

18. Kellgren JH, Lawrence JS. "Radiologic assessment of osteoarthrosis." Annals of Rheumatic Diseases. 1957; 16, 494-501.

19. Buckwalter JA, Saltzman C, Brown T. "The impact of osteoarthritis: implications for research." Clinical Orthopaedics and Related Research. 2004 Oct;(427 Suppl):S6-15.

20. Hochberg MC, et al. "American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee." Arthritis Care & Research, April 2012. Vol. 64:4 pp 465-474. DOI 10.1002/acr.21596

21. Scarpignato C, Lanas A, Blandizzi C, et al. "Safe prescribing of non-steroidal anti-inflammatory drugs in patients with osteoarthritis – an expert consensus

addressing benefits as well as gastrointestinal and cardiovascular risks." *Boston Medical Center Medicine*. 2015;13:55. doi:10.1186/s12916-015-0285-8.

22. "Alcohol Use and Your Health." Center for Disease Control. July 25, 2016. https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm

23. Block G, Hartman AM, Naughton D. "A reduced dietary questionnaire: development and validation." Epidemiology 1990; 1:58-64.

24. "Alcohol Metabolism." National Institute on Alcohol Abuse and Alcoholism. No. 35; PH 371 January 1997, Updated Oct. 2000. https://pubs.niaaa.nih.gov/publications/aa35.htm

25. Magnusson K, et al. "Smoking and alcohol use are associated with structural and inflammatory hand osteoarthritis features." Scandinavian Journal of Rheumatology. 2017 Feb 1:1-8. doi: 10.1080/03009742.2016.1257736.

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