Effectiveness of various Vitamin D protocols on raising and maintaining blood serum 25(OH)D3 levels over a three month period

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Introduction

- Rise in interest regarding the health benefits of Vitamin D supplementation
  - Increased appreciation of Vitamin D and its importance in musculoskeletal health and other medical conditions
  - Primary role of Vitamin D is to maintain serum calcium homeostasis

Introduction

- Vitamin D sufficiency is estimated by measuring serum 25-hydroxyvitamin D (25[OH]D) and optimal serum concentrations are controversial
- National Osteoporosis Foundation (NOF) and American Geriatric Society (AGS) recommend minimum of 30ng/ml
- No clear consensus on optimal Vitamin D dosing

Methods

- Randomized, prospective study to evaluate three vitamin D dosing regimens and their effect on serum 25 OH-D over a span of three months
- Funding provided by Brentwood Foundation
- Subjects were then assigned one of three dosing regimens:
  - **Group 1: 100,000U IU Vit D2 once**
  - **Group 2: 100,000U IU Vit D2 once weekly x 12 weeks**
  - **Group 3: 50,000U IU Vit D2 daily x 10 days then 2000U Vit D3 daily**
- Lab Draws (Serum 25OH-D): 0,2,6, and 12 Weeks

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Methods

- Single hospital system
- Voluntarily enrolled subjects
- **Inclusion Criteria:**
  - Male or Female, 18 years of age or older
- **Exclusion Criteria:**
  - Pregnant
  - PMHx: endocrinopathies, granulomatous disorders, active cancer or any other vitamin d altering medical conditions
  - Patient taking any medication which interferes with Vitamin D absorption and metabolism including: Steroids (Prednisone), Orlistat (Xenical & Alli), Cholestyramine (Questran, LoCholest, Prevalite), Dilantin (Phenytoin), Phenobarbital, and any anti-tuberculosis drugs
  - Patient taking any medication which may increase Vitamin D levels such as cholesterol-lowering statin drugs and thiazide diuretics.
  - Initial Vitamin D levels over 30 ng/ml

Methods

- Participants were randomized into each of the 3 groups using an algorithm created on Redcap Database
- **Statistics:**
  - It was determined by our research statistician for a standardized effect size of 0.5 units, which may generally be considered clinically important between placebo and any other dose regimen, and a power of 95%, a total of 45 subjects (15 subjects per episode) would be required to achieves statistical significance among the three groups, using repeated measures ANOVA over 4 time points
  - Alpha was set at 0.05
  - Assuming that up to 5 subjects per group would be lost to follow-up; leaving 30 subjects in the study (10 per group), a reasonable power of 80% would still be achieved

Methods

- Study participants were given:
  - Dosing log
  - Side effects log
  - Post-study questionnaire
- Participants were monitored by research coordinator via phone throughout study
- If supra-therapeutic vit D blood levels were noted on lab draws participants were contacted to check for symptoms

Methods

Initial screening questionnaire for study eligibility

Total Participants Enrolled: 86

- 14 withdrew or cancelled after enrollment
  - 8 cancelled
  - 6 withdrew mid study

Total Participants that met inclusion/exclusion criteria: 72

- 32% (24) of participants excluded due to normal Vit D value on initial draw
  - Excluded from June-Sept: 63% (17 of 27)
  - Excluded from Oct-Mar: 27% (6 of 22)
- 1 participant was excluded due to missed doses during the study

Total Participants Included in Vitamin D study: 48

- Group 1 participants: 15
- Group 2 participants: 16
- Group 3 participants: 17

Methods

- **Beneficial Side Effects**
  - Improved mood
  - Improved energy
  - Decrease chronic pain
  - Improved musculoskeletal strength
  - Improved immune function and overall health

Methods

Vitamin D Toxicity - symptoms of acute intoxication are generally associated with hypercalcemia and can ultimately lead to renal damage and tissue calcifications

Mild Symptoms	Severe Symptoms
Fatigue	Confusion
Constipation	Polyuria
Irritability	Polydipsia
Insomnia	Anorexia
Nervousness	Nausea
Pruritis	Vomiting
	Muscle Weakness

Results

Factor	Total	Treatment Group 1		Treatment Group 2		Treatment Group 3		p-value
		N	Statistics	N	Statistics	N	Statistics	
Vitamin D Blood Level at Week 0 [a]	48	15	22.28 ± 4.73	16	22.92 ± 5.17	17	19.86 ± 5.02	0.19[A]
Vitamin D Blood Level at Week 2 (14 ±4 days) [a]	48	15	28.5 ± 7.65	16	43.52 ± 13.5	17	61.24 ± 18.08	< 0.001[A]
Vitamin D Blood Level at Week 6 (43 ±3 days) [a]	48	15	22.85 ± 6.22	16	57.06 ± 20.06	17	44.71 ± 14.2	< 0.001[A]
Vitamin D Blood Level at Week 12 (84 ±5 days) [a]	48	15	19.46 ± 5.61	16	59.13 ± 20.73	17	36.94 ± 14	< 0.001[A]

[a] *Mean ± SD*

A: Analysis of Variance

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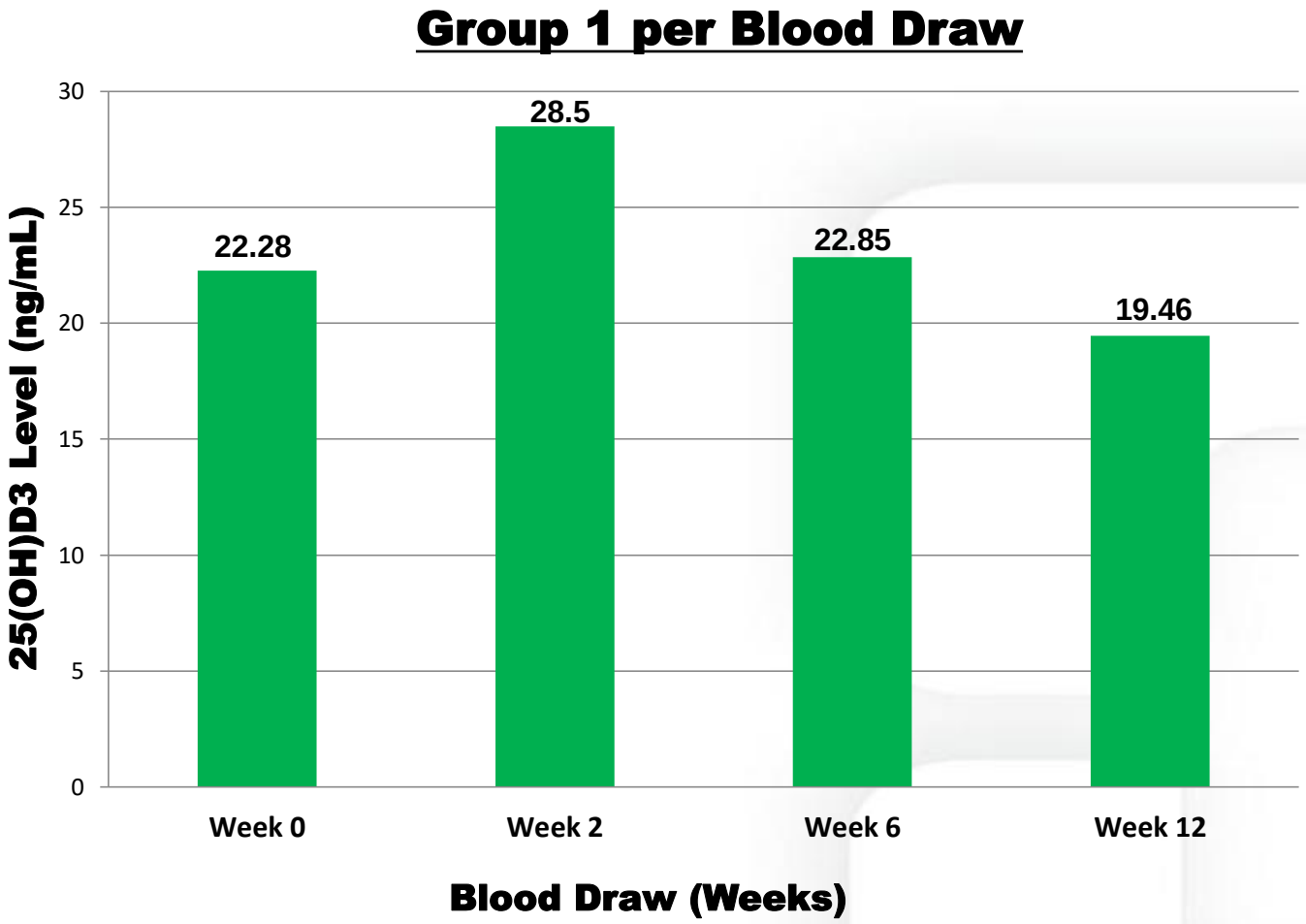
Results

Total Change in Vitamin D level throughout twelve week period per group

	Total Change 25(OH)D3	Standard Deviation
Group 1	-2.820	3.050
Group 2	36.212	2.953
Group 3	17.071	2.86

Results



		P-value
Group 1	Week 0 - Week 2	0.178
	Week 0 - Week 6	0.998
	Week 0 - Week 12	0.792

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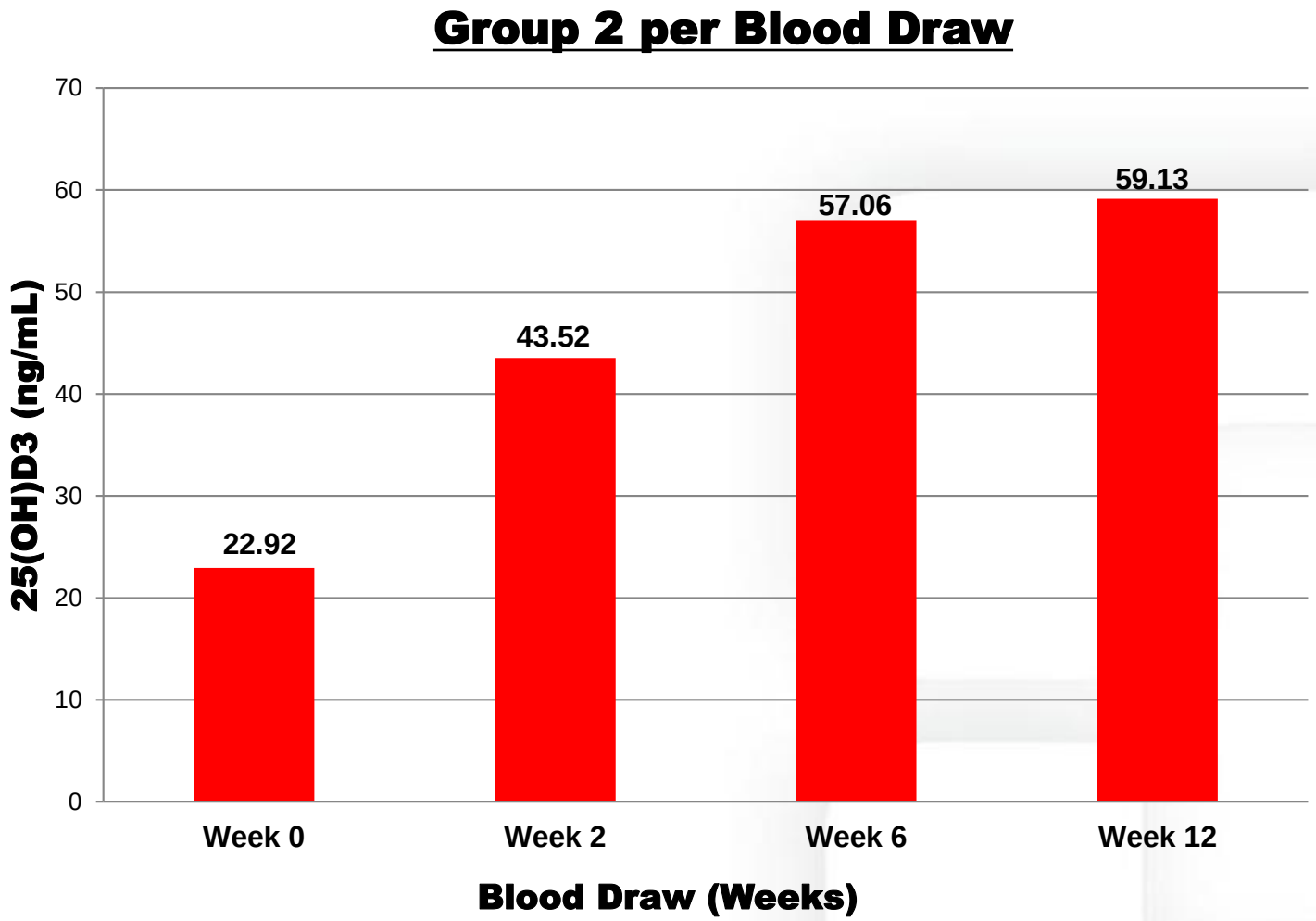
Results

Treatment Group	Contrast	Estimate	Std. Error	95% CI on Estimate	P-value
Group 1	Week 0 - Week 2	-6.220	3.050	-14.15 -- 1.71	0.178
	Week 0 - Week 6	-0.567	3.050	-8.49 -- 7.36	0.998
	Week 0 - Week 12	2.820	3.050	-5.11 -- 10.75	0.792
	Week 2 - Week 6	5.653	3.050	-2.27 -- 13.58	0.253
	Week 2 - Week 12	9.040	3.050	1.11 -- 16.97	0.018
	Week 6 - Week 12	3.387	3.050	-4.54 -- 11.31	0.684

Results



		P-value
Group 2	Week 0 - Week 2	<0.001
	Week 0 - Week 6	<0.001
	Week 0 - Week 12	<0.001

■ Group 2

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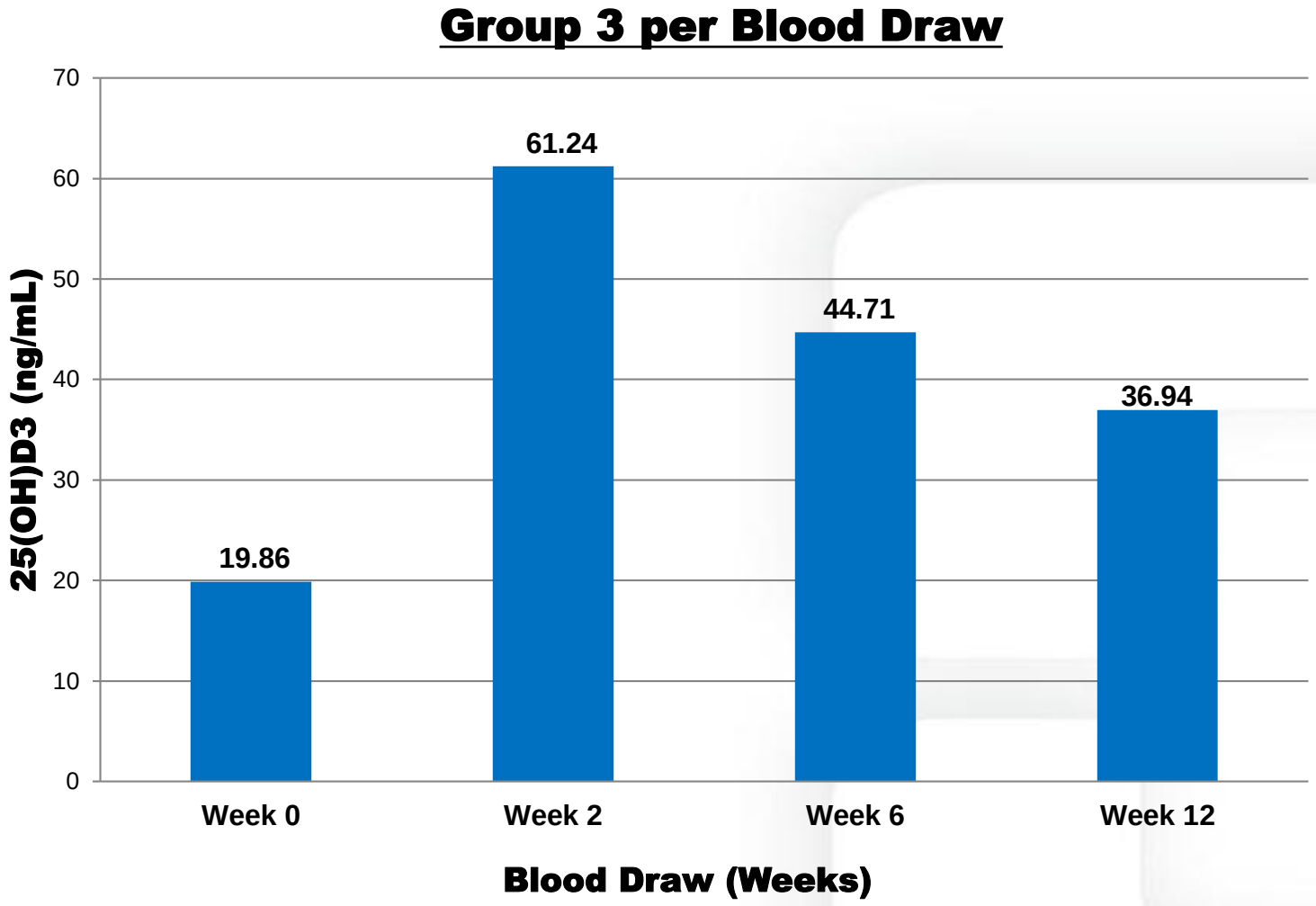
Results

Treatment Group	Contrast	Estimate	Std. Error	95% CI on Estimate	P-value
Group 2	Week 0 - Week 2	-20.606	2.953	-28.28 -- -12.93	<0.001
	Week 0 - Week 6	-34.144	2.953	-41.82 -- -26.47	<0.001
	Week 0 - Week 12	-36.212	2.953	-43.89 -- -28.54	<0.001
	Week 2 - Week 6	-13.537	2.953	-21.21 -- -5.86	<0.001
	Week 2 - Week 12	-15.606	2.953	-23.28 -- -7.93	<0.001
	Week 6 - Week 12	-2.069	2.953	-9.74 -- 5.61	0.897

Results



		P-value
Group 3	Week 0 - Week 2	<0.001
	Week 0 - Week 6	<0.001
	Week 0 - Week 12	<0.001

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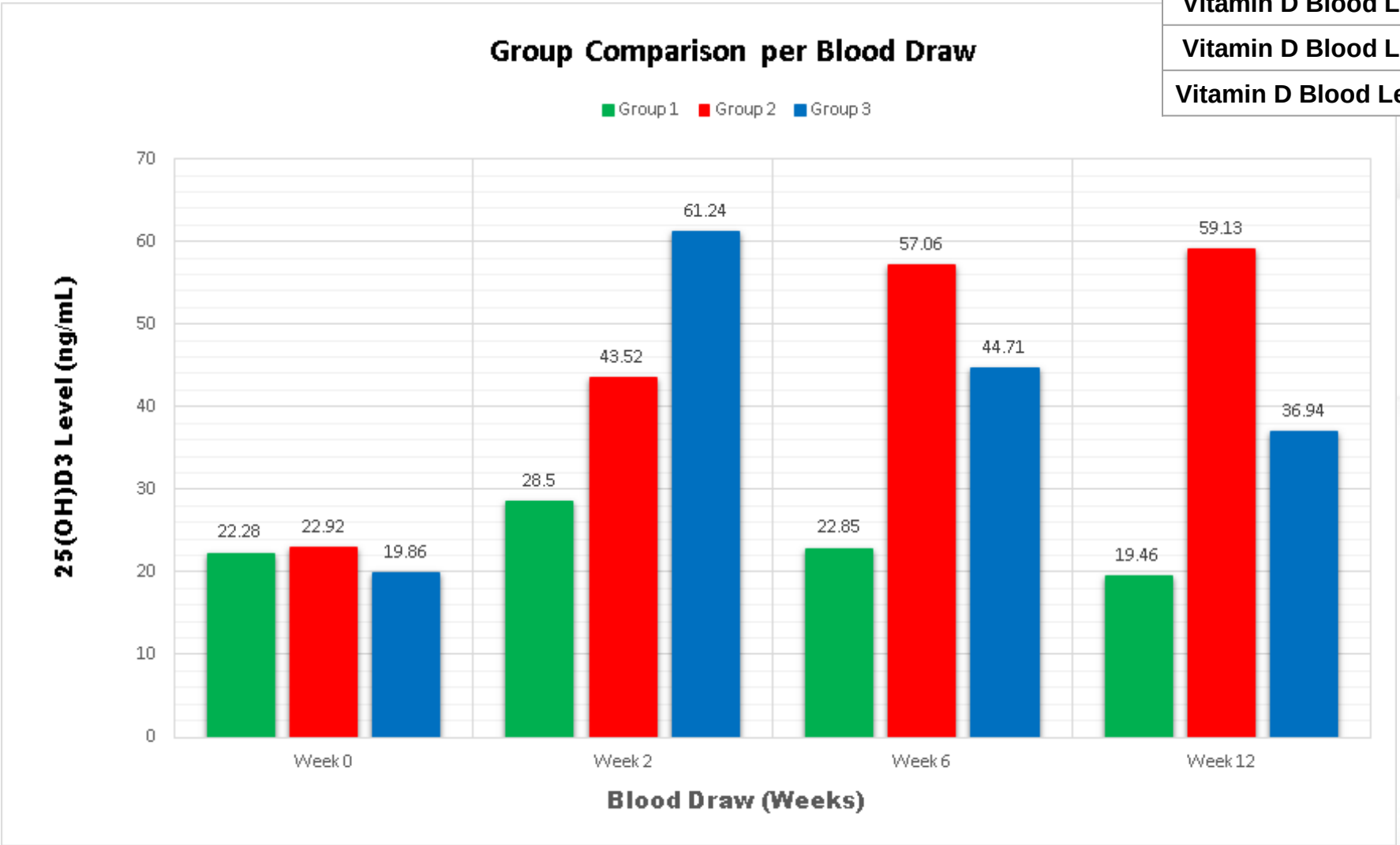
Results

Treatment Group	Contrast	Estimate	Std. Error	95% CI on Estimate	P-value
Group 3	Week 0 - Week 2	-41.371	2.865	-48.82 -- -33.92	<0.001
	Week 0 - Week 6	-24.841	2.865	-32.29 -- -17.40	<0.001
	Week 0 - Week 12	-17.071	2.865	-24.52 -- -9.62	<0.001
	Week 2 - Week 6	16.529	2.865	9.08 -- 23.98	<0.001
	Week 2 - Week 12	24.300	2.865	16.85 -- 31.75	<0.001
	Week 6 - Week 12	7.771	2.865	0.32 -- 15.22	0.037

Results

	P-value
Vitamin D Blood Level at Week 0	0.19[A]
Vitamin D Blood Level at Week 2	< 0.001[A]
Vitamin D Blood Level at Week 6	< 0.001[A]
Vitamin D Blood Level at Week 12	< 0.001[A]



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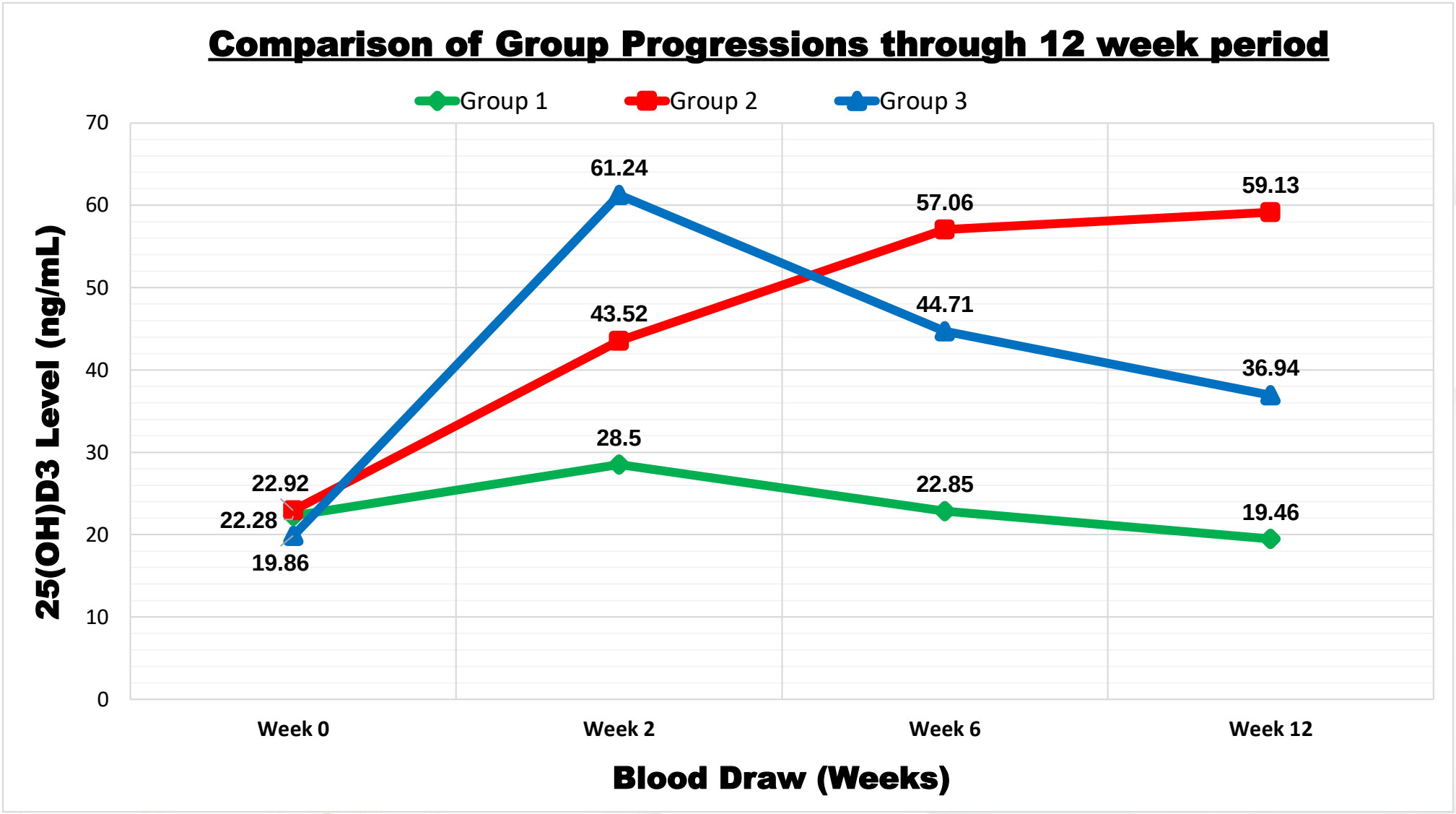
Results



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Results

Treatment Group	Contrast	Estimate	Std. Error	95% CI on Estimate	P-value
Week 0	Group 1 - Group 2	-0.639	4.472	-11.28 -- 10.00	0.989
	Group 1 - Group 3	2.415	4.408	-8.07 -- 12.90	0.848
	Group 2 - Group 3	3.054	4.334	-7.26 -- 13.36	0.761
Week 2	Group 1 - Group 2	-15.025	4.472	-25.66 -- -4.39	0.003
	Group 1 - Group 3	-32.735	4.408	-43.22 -- -22.25	<0.001
	Group 2 - Group 3	-17.710	4.334	-28.02 -- -7.40	<0.001
Week 6	Group 1 - Group 2	-34.216	4.472	-44.85 -- -23.58	<0.001
	Group 1 - Group 3	-21.859	4.408	-32.34 -- -11.37	<0.001
	Group 2 - Group 3	12.357	4.334	2.05 -- 22.67	0.014
Week 12	Group 1 - Group 2	-39.671	4.472	-50.31 -- -29.03	<0.001
	Group 1 - Group 3	-17.475	4.408	-27.96 -- -6.99	<0.001
	Group 2 - Group 3	22.196	4.334	11.89 -- 32.51	<0.001

Results

Post-study Questionnaire: Positive Side Effects

	Group 1		Group 2		Group 3		Total		
	Yes	No	Yes	No	Yes	No	Yes	No	P-value
Happier?	40%	60%	31.25%	68.75%	58.83%	41.18%	43.75%	56.25%	0.28
Stronger?	13.33%	86.67%	37.25%	62.5%	47.06%	52.94%	33.33%	66.67%	0.13
Better or Healthier?	26.67%	73.33%	43.75%	56.25%	58.82%	41.18%	43.75%	56.25%	0.21
Less Pain?	26.67%	73.33%	31.25%	68.75%	23.53%	76.47%	27.08%	72.92%	0.92
More Energy?	20.00%	80.00%	56.25%	43.75%	41.18%	58.82%	39.58%	60.42%	0.14
Will you continue taking Vitamin D supplements?	80.00%	20.00%	81.25%	18.75%	82.35%	17.65%	81.25%	18.75%	>0.99

Results

Negative Side Effects Documented by Participants

	Group 1		Group 2		Group 3		Total		
	Yes	No	Yes	No	Yes	No	Yes	No	P-value
Negative Side Effects	0.00%	100%	12.5%	87.5%	17.65%	82.35%	10.42%	89.58%	0.35
Side Effects Documented	**None**		**2 out of 16** - Occasional headaches (prior hx of migraines) - Occasional joint and muscle pain		**3 out of 17** - Fatigue - Headache - Constipation				

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Conclusions

- **Group 1: 100,000U IU Vit D2 once**
  - Group 1 did not have any significant statistical increase at any time point
- **Group 2: 100,000U IU Vit D2 once weekly x 12 weeks**
  - Group 2 showed a sustained and overall largest increase in Vit D levels over the twelve week period
  - Significantly higher at week 6 and 12 compared to other groups
- **Group 3: 50,000U IU Vit D2 daily x 10 days then 2000U Vit D3 daily**
  - Group 3 showed highest increase in Vit D levels at week 2

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Limitations

- Single center
- Study performed over 12 week time period

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Conclusion

- Large dosing regimens higher than previously studied protocols show safe to be given with zero severe adverse effects
- Not only is supplementation safe but shown to be beneficial
  - 25-45% of all participants stated they had positive effects
  - Some participants noted >50% positive effects on health
- 82.15% of all participants stated they will continue taking vitamin D supplementation post study

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Recommendations

- 100,000 IU Vitamin D2 weekly
- No baseline screening needed
  - 68% of healthy volunteers had low vit D
  - Dosing regimens shown to be safe with zero severe negative side effects and infrequent minor side effects

Future Applications

- Efficacy of Vitamin D supplementation on fracture healing
- Apply group 2 regimen to fractures in prospective multicenter study to compare non-union rates

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Thank You

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