

## 1) Supplementary Materials

### Melanoma Risk and Vitamin D level and status

First author	location	Study design	Control group	cases (%male)	control (%male)	age cases/controls	assessment of Vitamin D status
<b>Bade B., 2014</b>	Germany	Retrospective case-control study	Healthy controls	324 (54%)	141 (42%)	56.3 / 55.1	LIAISON-25-OH Vitamin D Immunoassay
<b>Befon A., 2019</b>	Greece	Prospective cohort study	Age and sex matched healthy patients	99 (46%)	97 (48%)	50/51	25-OH-Vitamin-D-Immunoassay
<b>Cattaruzza M., 2019</b>	Italy	case-control study	Age and sex matched healthy patients	137 (45%)	99 (32%)	13/129	LIAISON-25-OH Vitamin-D-Immunoassay
<b>Davies J., 2011</b>	UK	Case-control study	Age and sex matched healthy patients	880 (40%)	194 (40%)	NA	25-OH-vitamin-D-Immunoassay
<b>Ene C., 2015</b>	Romania	Case-control study	healthy controls of same geographic region as patients	88 (35%)	88 (38%)	18-45 both	25-OH-ELISA, Euroimmunkit Assay
<b>Kwon G., 2018</b>	USA	Embedded case-control study	Postmenopausal fair-skinned women from different centers	718 (0%)	718 (0%)	50-79	25-OH-D-liquid-chromatography with mass spectrometry
<b>Lombardo M., 2021</b>	Italy	retrospektive case-control study	Healthy controls	154 (51%)	125 (NA)	59.7 / NA	25-OH-D-liquid-chromatography with mass spectrometry
<b>Major J., 2012</b>	Finland	Embedded case-control study	Age-matched healthy patients	92 (100%)	276 (100%)	57.5 / 57	LIAISON 25-OH Vitamin-D-Immunoassay
<b>Navarette-Dechent C., 2012</b>	Chile	Case-control study	Age and sex matched healthy patients	40 (37,5%)	56 (37,5%)	48.5 / 48,4	25-OH-D-liquid-chromatography with mass spectrometry
<b>Nürnberg B., 2009</b>	Germany	Case-control study	Healthy controls	205 (55%)	141 (43%)	NA / NA	LIAISON 25-OH Vitamin-D-Immunoassay
<b>Skaaby T., 2014</b>	Denmark	Prospective cohort study	Cancer-free danish citizens	10485 (ca. 50%)	56 (NA)	40 - 71 both	25-OH-Vitamin-D-Immunoassay with HPLC
<b>Spath L., 2016</b>	Italy	Case-control study	Sex and age matched healthy controls of same geographic region as patients	105 (41%)	101 (ca. 41%)	54 both	LIAISON 25-OH Vitamin-D-Immunoassay
<b>Stenehjem J., 2020</b>	Norway	prospective embedded case-control study	Age and sex matched healthy patients	708 (57%)	708 (57%)	42 both	25-OH-D-liquid-chromatography with mass spectrometry
<b>Van der Pols J., 2013</b>	Australia	Prospective cohort study	Cancer-free citizens	17 (30%)	1174 (45%)	58 / 54	LIAISON 25-OH Vitamin-D-Immunoassay
<b>Vojdeman, F., 2019</b>	Denmark	Prospective cohort study	Cancer-free danish citizens	684 (NA)	216560 (34,7%)	NA / 48.8	LIAISON 25-OH Vitamin-D-Immunoassay

## Melanoma Prognosis and Vitamin D level and status

First author	location	study design	Recruitment of participants	Outcome(s)	Sample size	age	assessment of Vitamin D status
<b>Befon A., 2019</b>	Greece	Prospective cohort study	99 patients with histologically confirmed primary MM and serum vitamin D determination within one month after diagnosis were included (Athens Hospital, 2011-2014)	Tumor thickness <1 vs. >4 mm in vitamin D-deficient patients	66	50	25-OH-Vitamin-D-Immunoassay
<b>Fang S., 2016</b>	USA	Prospective cohort study	1042 patients with histologically confirmed primary MM and vitamin D serum determination within 07 months after diagnosis were included (Texas Hospital, 1997-2009)	SMD of vitamin D values for patients with >1 vs. ≤1mm tumor thickness SMD of vitamin D values for patients with vs. without ulceration SMD of vitamin D mean values for patients with tumor stage ≥3 vs. <3 SMD of vitamin D mean values for patients with vs. without evidence of mitosis	519 / 409 176 / 664 349 / 693 455 / 199	54.8	25-OH-Vitamin-D-Immunoassay
<b>Gambichler T., 2012</b>	Germany	Prospective cohort study	764 patients with histologically confirmed primary MM and vitamin D serum determination at the time of diagnosis were included (Bochum Hospital, 2009-2012)	Tumor thickness <1 vs. >4 mm in vitamin D deficient patients Tumor stage 0 vs. ≥1 in vitamin D deficient patients SMD of vitamin D values for patients with >1 vs. ≤1mm tumor thickness SMD of vitamin D mean values for patients with tumor stage 4 vs. 0	425 753 371 / 367 67 / 61	18-79	25-OH-Vitamin-D-Immunoassay
<b>Johansson H., 2021</b>	Italy	Case-control study	104 patients with histologically confirmed primary MM and serum vitamin D determination at the time of diagnosis were included (hospitals in northern Italy)	Tumor stage 2a vs. 2b/c in Vitamin-D-deficient patients	104	50	25-OH-Vitamin-D-Immunoassay

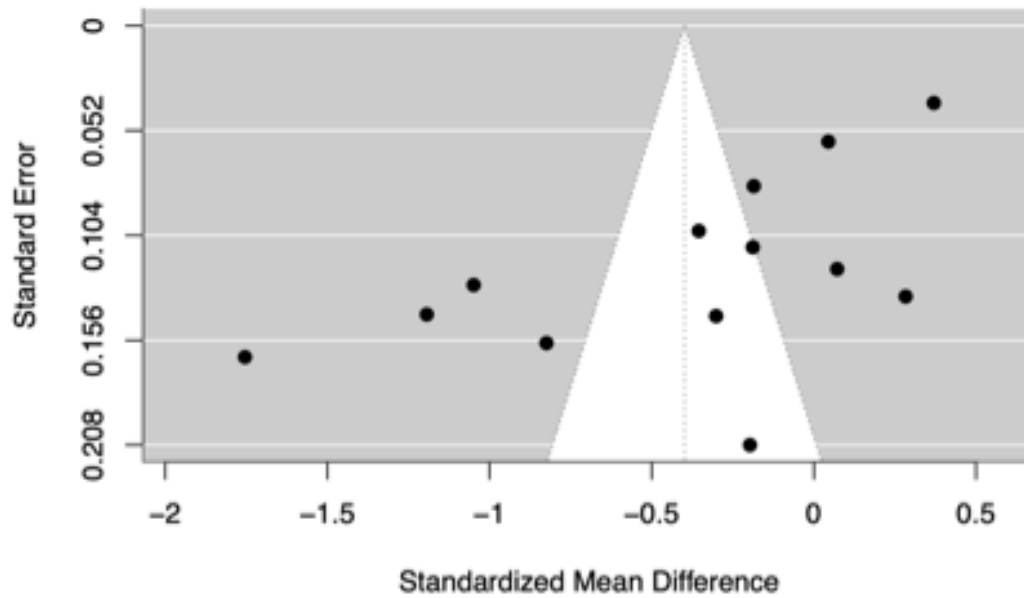
<b>Lim A., 2017</b>	Australia	retrospective cohort study	109 patients with histologically confirmed primary MM and vitamin D serum determination up to 6 months after diagnosis were included (Melbourne Hospitals, 2001-2013)	<p>SMD of vitamin D values for patients with &gt;1 vs. ≤1mm tumor thickness</p> <p>SMD of vitamin D mean values for patients with vs. without evidence of mitosis</p> <p>SMD of vitamin D mean values for patients with tumor stage &gt;2 vs. ≤2</p>	<p>55 / 54</p> <p>39 / 31</p> <p>22 / 62</p>	57.7	NA
<b>Lipplaa A., 2018</b>	UK	Retrospective cohort study	341 patients with histologically confirmed primary MM and vitamin D serum determination for diagnosis were included (2007-2012)	<p>SMD of vitamin D levels for patients with vs. without ulceration</p> <p>SMD of vitamin D mean levels for patients with tumor stage 3 vs. 2</p>	<p>137 / 151</p> <p>251 / 90</p>	<p>55</p> <p>stage 3: 53 stage 2: 64</p>	25-OH-D liquid chromatography with mass spectrometry
<b>Lombardo M., 2021</b>	Italy	Retrospective case-control study	154 patients with histologically confirmed primary MM and vitamin D serum determination for diagnosis were included (Varese Hospital)	<p>Mitoses positive vs. negative in vitamin D-deficient patients</p> <p>SMD of vitamin D values for patients with &gt;1 vs. ≤1mm tumor thickness</p> <p>SMD of vitamin D mean values for patients with tumor stage 3 vs. 1</p> <p>SMD of vitamin D mean values for patients with vs. without mitoses</p> <p>SMD of vitamin D values for patients with vs. without ulceration</p>	<p>153</p> <p>65 / 83</p> <p>22 / 104</p> <p>80 / 65</p> <p>23 / 131</p>	59.7	25-OH-D liquid chromatography with mass spectrometry
<b>Newton-Bishop J., 2009</b>	UK	Prospective cohort study	1132 patients with histologically confirmed primary MM and serum vitamin D determination at diagnosis (or within 3-6 months) were included (Northern England hospitals, 2000-2008)	SMD of vitamin D values for patients with >1 vs. ≤1mm tumor thickness.	719 / 411	NA	25-OH-D liquid chromatography with mass spectrometry
<b>Ogbah Z., 2013</b>	Spain	Retrospektive cohort studie	81 patients with histologically confirmed primary MM and serum vitamin D determination at diagnosis (or within 3 months) were included (Barcelona Hospital, 2000-2008)	SMD of vitamin D levels for patients with >1 vs. ≤1mm tumor thickness.	22 / 46	NA	LIAISON 25-OH Vitamin-D-Immunoassay

<b>Randerson-Moor J., 2009</b>	UK	Case-control study	1043 patients with histologically confirmed primary MM and serum vitamin D determination at diagnosis (or within 3-6 months) were included (Leeds Hospital, 2000-2006)	SMD of vitamin D values for patients with >1 vs. ≤1mm tumor thickness	477 / 342	18-75	25-OH Vitamin-D-Immunoassay
<b>Saiag P., 2015</b>	France	Prospective cohort study	1171 patients with histologically confirmed primary MM and vitamin D serum determination for diagnosis were included (Paris Hospital, 2003-2013)	SMD of vitamin D levels for patients with >1 vs. ≤1mm tumor thickness  SMD of mean vitamin D levels for patients with tumor stage 4 vs. 1  SMD of vitamin D levels for patients with vs. without ulceration	675 / 451  70 / 425  225 / 781	54,2	25-OH-D liquid chromatography with mass spectrometry
<b>Spath L., 2016</b>	Italy	Cohort study	105 patients with histologically confirmed primary MM and vitamin D serum determination for diagnosis were included (Rome Hospital, 2003-2013)	Tumor thickness >4 vs. <1mm in vitamin D-deficient patients  Tumor stage ≥3 vs. <3 in vitamin D-deficient patients  SMD of vitamin D values for patients with >1 vs. ≤1mm tumor thickness  SMD of vitamin D mean values for patients with tumor stage ≥3 vs. <3	105  49  45 / 60  14 / 36	53.7	LIAISON 25-OH Vitamin-D-Immunoassay
<b>Timmerman D., 2016</b>	USA	Retrospective cohort study	252 patients with histologically confirmed primary MM and vitamin D serum determination for diagnosis (up to a maximum of 1 year afterward) were included (Rome Hospital, 2003-2013)	Tumor thickness ≥0.75 mm vs. <0.75 mm in vitamin D-deficient patients  Tumor stage >1 vs. ≤1 in vitamin D-deficient patients  Mitotic detection positive vs. negative in vitamin D-deficient patients	81  252  196	55,4	NA
<b>Wyatt C., 2015</b>	Australia	Cohort study	100 patients with histologically confirmed primary MM and vitamin D serum determination for diagnosis were included (Brisbane Hospitals, 2003-2013)	Tumor thickness ≥0.75 vs. <0.75 mm in vitamin D-deficient patients  Mitotic evidence positive vs. negative in vitamin D-deficient patients  SMD of vitamin D mean values for patients with vs. without mitoses	100  100  23 / 77	61	LIAISON 25-OH Vitamin-D-Immunoassay

## 2) Egger's Tests and Funnel Plots:

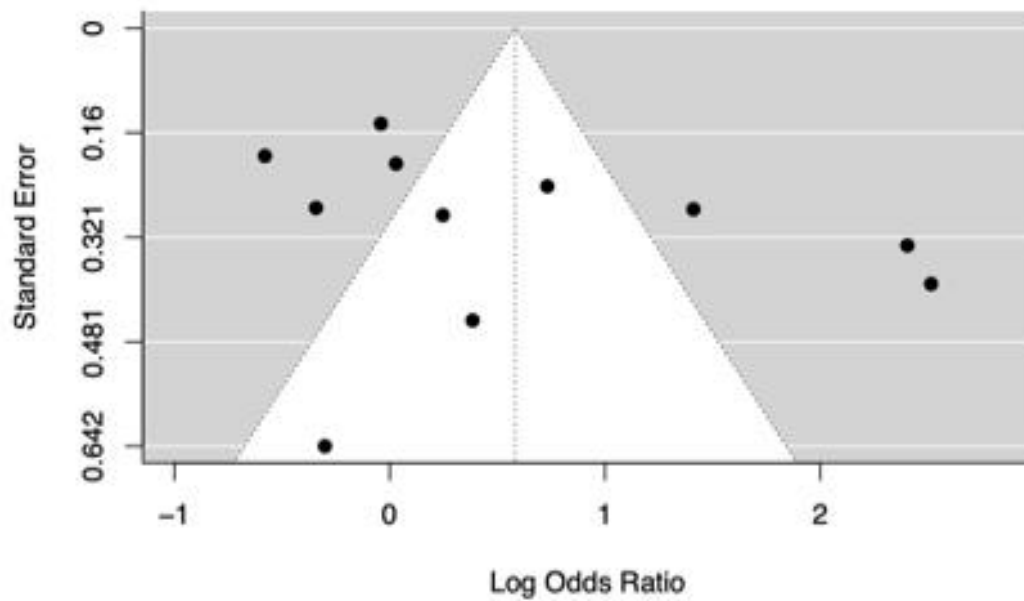
### Analysis – Melanoma Risk and Vitamin D levels:

Test for Funnel Plot Asymmetry (with modified standard error):  $p = 0.15$



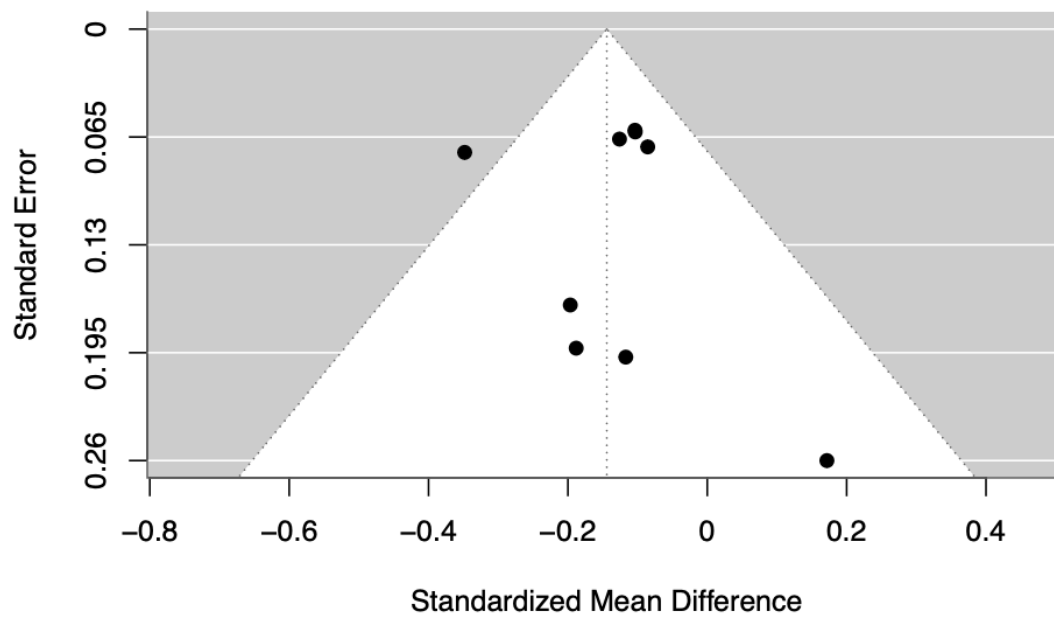
### Analysis – Melanoma Risk and Vitamin D Deficiency:

Test for Funnel Plot Asymmetry:  $p = 0.58$



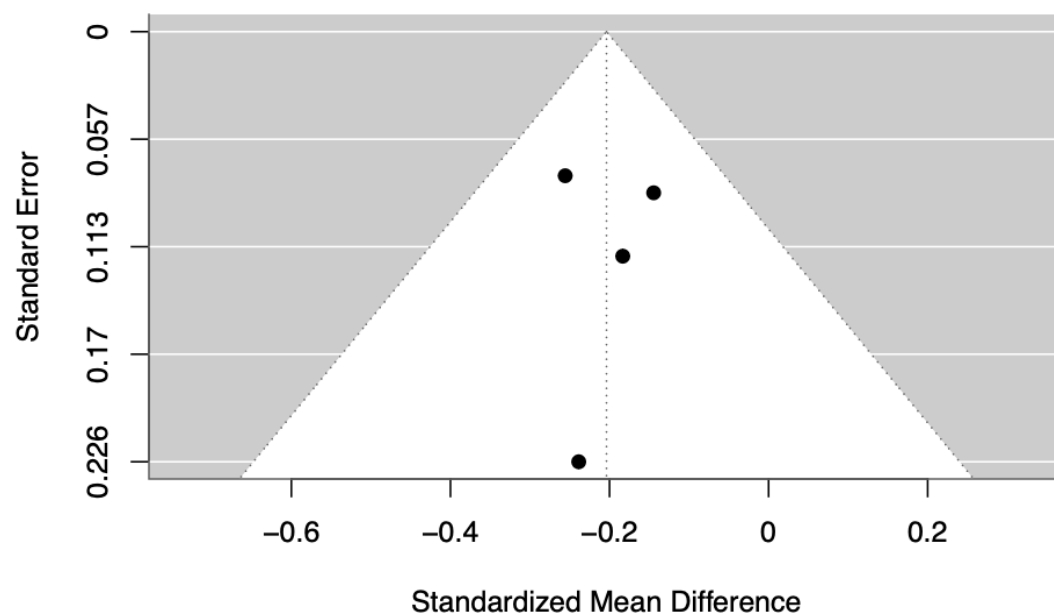
**Analysis – Melanoma Prognosis (Tumor thickness and Vitamin D level):**

**Test for Funnel Plot Asymmetry:  $p = 0.69$**



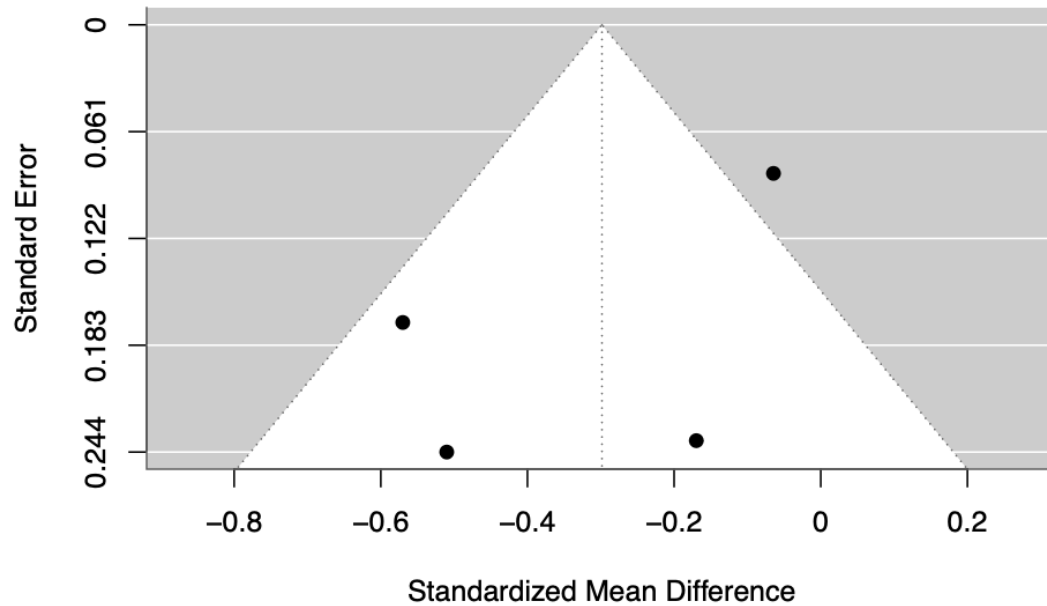
**Analysis – Melanoma Prognosis (Ulcerations status and Vitamin D level):**

**Test for Funnel Plot Asymmetry:  $p = 0.96$**



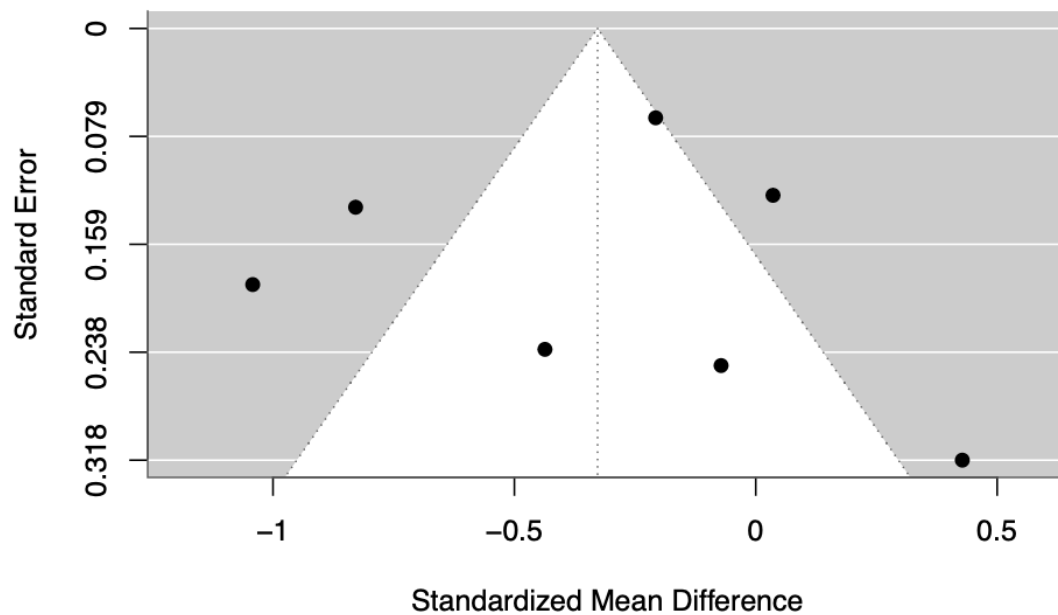
**Analysis – Melanoma Prognosis (Mitotic Rate and Vitamin D level):**

**Test for Funnel Plot Asymmetry:  $p = 0.37$**



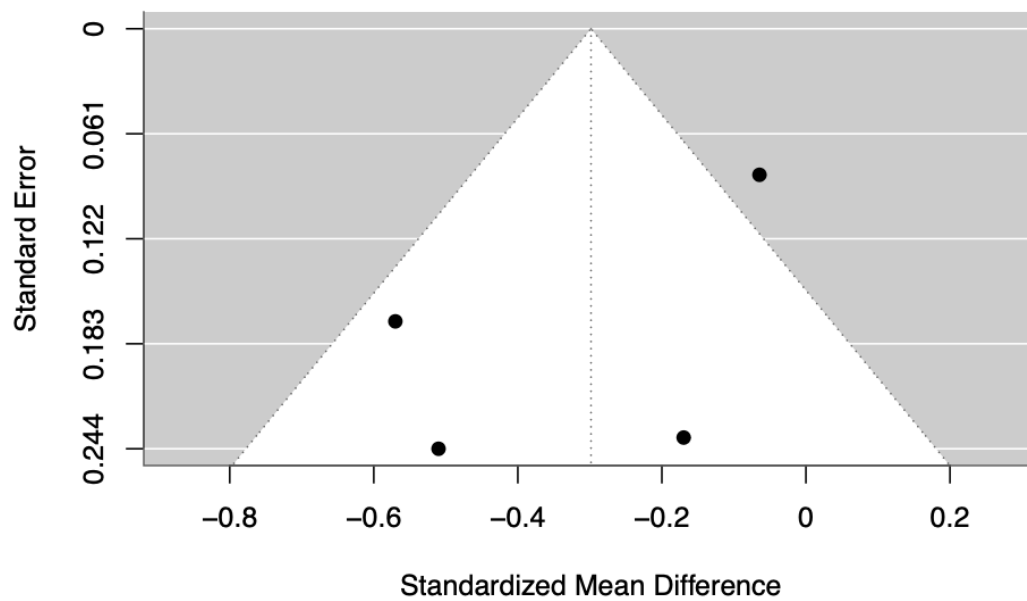
**Analysis – Melanoma Prognosis (Tumor stage and Vitamin D level):**

**Test for Funnel Plot Asymmetry:  $p = 0.43$**



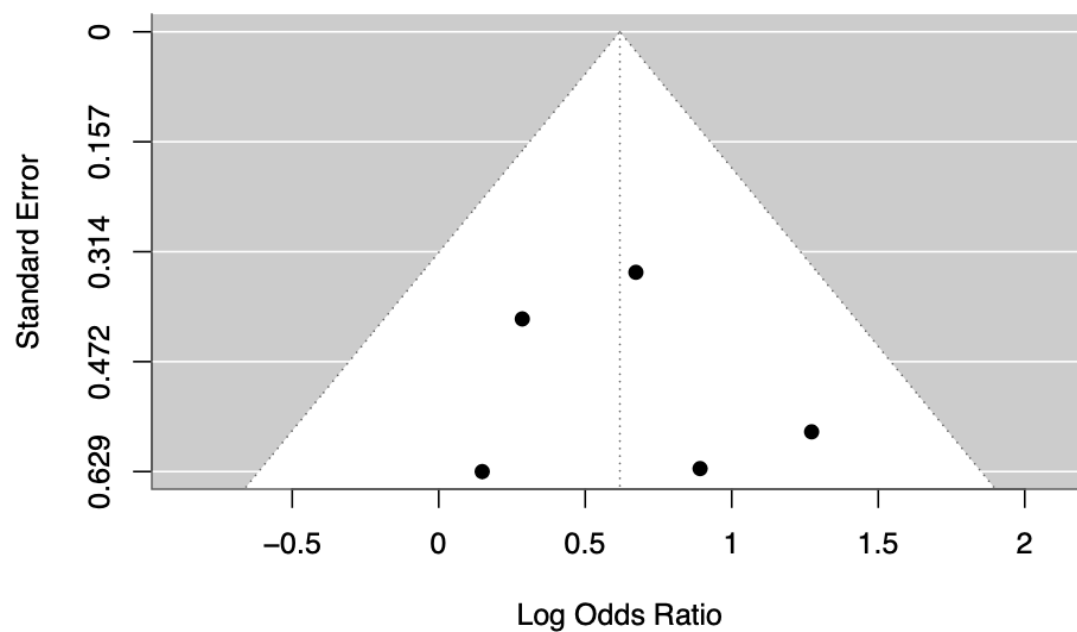
**Analysis – Melanoma Prognosis (Mitotic Rate and Vitamin D level):**

**Test for Funnel Plot Asymmetry:  $p = 0.34$**



**Analysis – Melanoma Prognosis (Tumor thickness and Vitamin D Deficiency):**

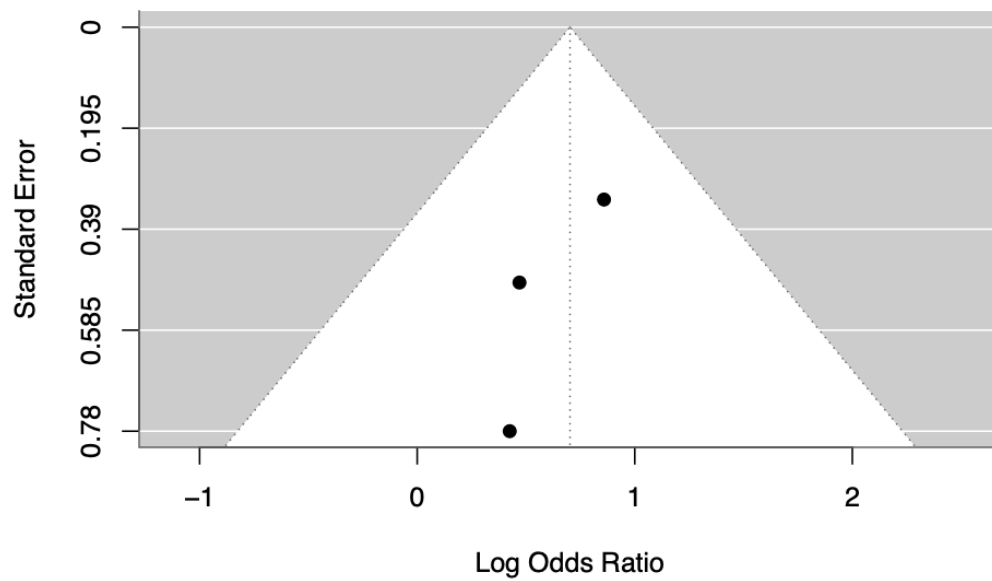
**Test for Funnel Plot Asymmetry:  $p = 0.74$**





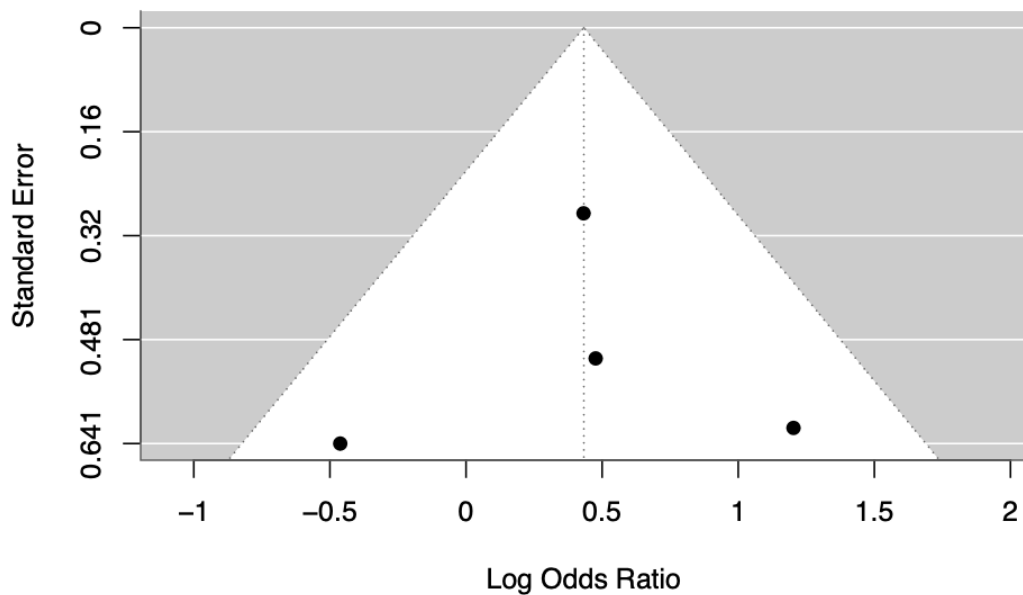
**Analysis – Melanoma Prognosis (Mitotic Rate and Vitamin D Deficiency):**

**Test for Funnel Plot Asymmetry:  $p = 0.52$**



**Analysis – Melanoma Prognosis (Tumor stage and Vitamin D Deficiency):**

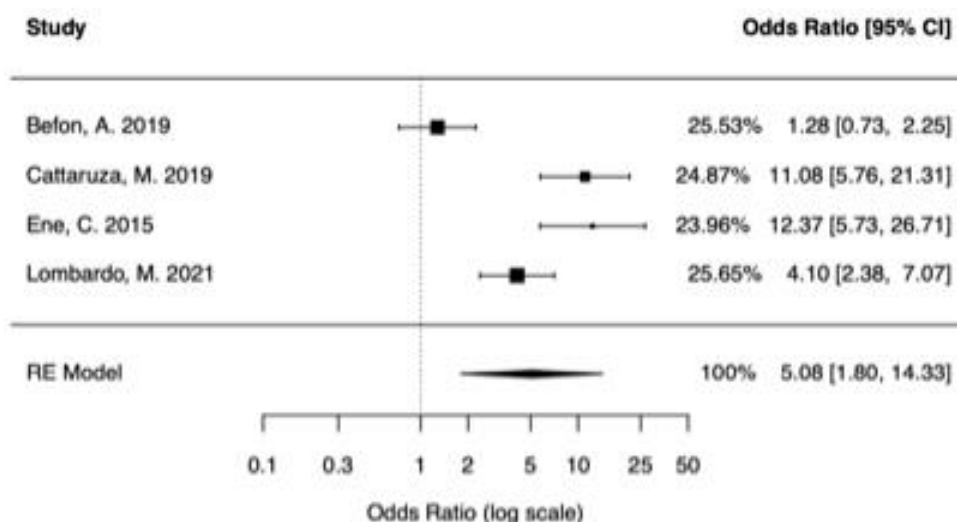
**Test for Funnel Plot Asymmetry:  $p = 0.91$**



### 3) Sensitivity Analyses:

#### Melanoma Risk (Odds Ratio):

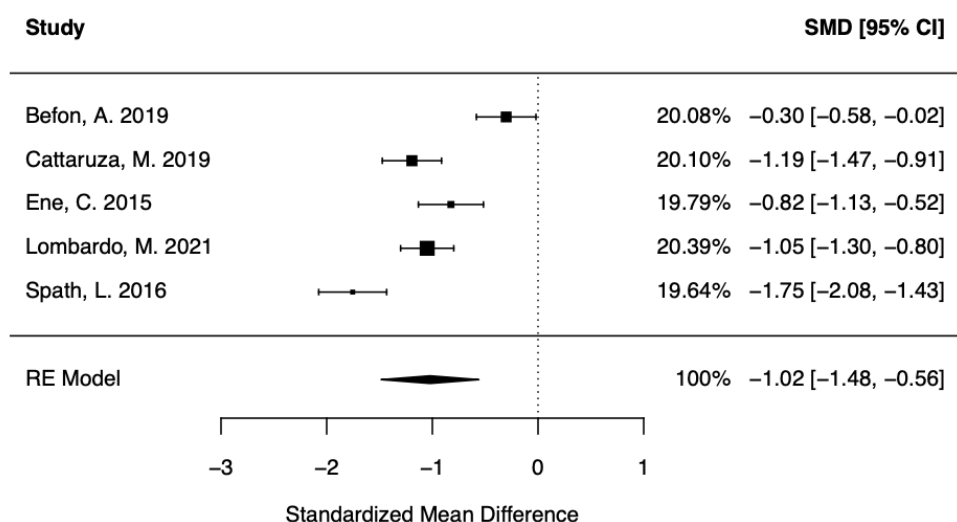
Moderator Analyses for geographic region (moderator) was significant ( $p=0.03$ ).



Forest Plot: Melanoma Risk and Vitamin D Deficiency – Subgroup analyses: Southern European studies ( $p=0.01$ ),  $I^2: 91\%$ ,  $Q = 33.12$ ,  $p < 0.0001$

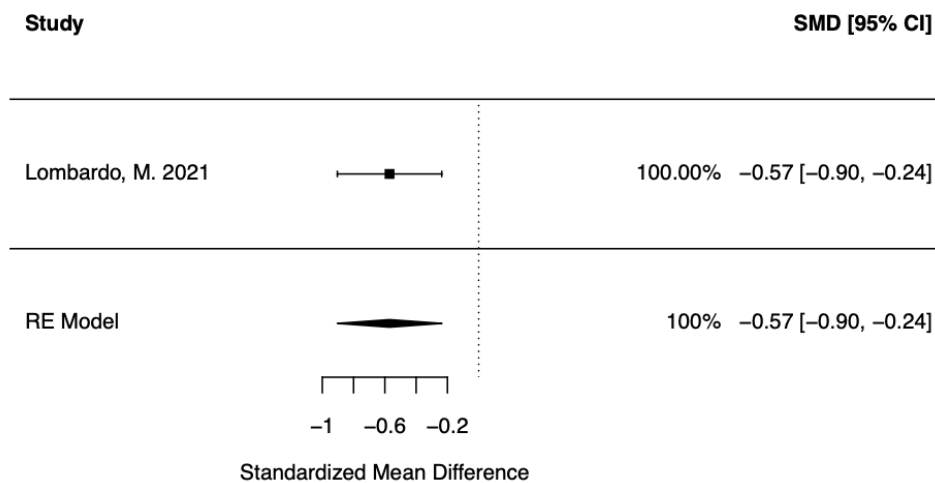
#### Melanoma Risk (standardized mean difference):

Moderator Analyses for geographic region (moderator) was significant ( $p=0.001$ ).



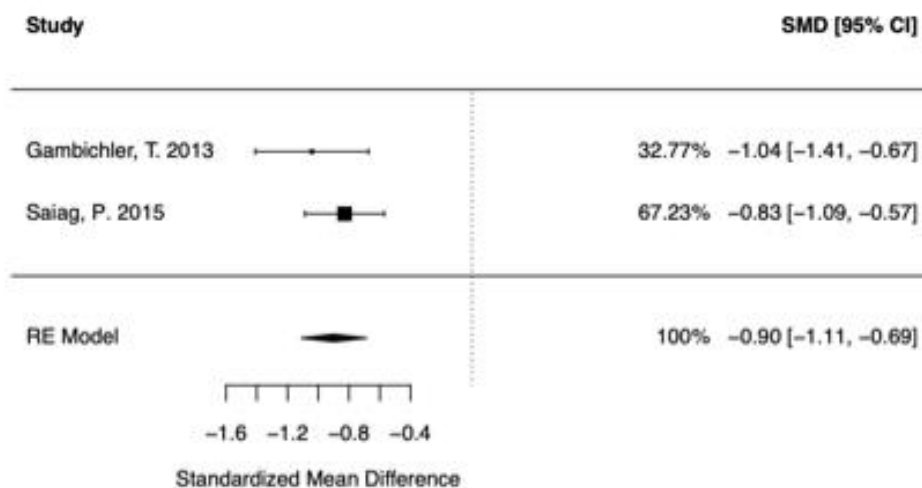
Forest Plot: Melanoma Risk and Vitamin D Deficiency – Subgroup analyses: Southern European studies ( $p < 0.0001$ ),  $I^2: 92.3\%$ ,  $Q = 48$ ,  $p < 0.0001$

Melanoma Prognosis - (standardized mean difference and mitotic rate):  
 Moderator Analyses for geographic region (moderator) was significant ( $p = 0.02$ ).



Forest Plot: Melanoma Prognosis (mitotic rate) and Vitamin D levels - Subgroup analyses:  
 Southern European studies ( $p=0.008$ ), Heterogeneity tests not possible due to  $n = 1$  study.

Melanoma Prognosis - (standardized mean difference and melanoma stage):  
 Moderator Analyses for geographic region (moderator) was significant ( $p = 0.001$ ).



Forest Plot: Melanoma Prognosis (melanoma stage) and Vitamin D levels – Subgroup  
 analyses: Central European studies ( $p = 0.006$ ),  $I^2: 0\%$ ,  $Q = 0.86$ ,  $p = 0.35$