

## Supplementary Material

## Appendix 1: Summary of balance for models (a), (b) and (c) using propensity score matching with Optimal Full Matching in VACCINATION subset

## Model (a)

```
Call:
matchit(formula = VACCINATION ~ SEX + AGE + INPATIENT + VARIANT +
  HCQ + AZ_only + IVM + DIABETE + HBP + OBESITY + ASTHMA +
  COPD + CANCER + IMMUNODEFICIENCY + AutoImmuneDiseases + ChronicCardiacDiseases,
  data = wrk_matchit, method = "full", distance = "glm")

Summary of Balance for Matched Data:
```

	Means Treated	Means Control	Std. Mean Diff.	Var. Ratio	eCDF Mean	eCDF Max	Std. Pair Dist.
distance	0.2264	0.2263	0.0004	1.0031	0.0002	0.0028	0.0007
SEX	0.5334	0.5505	-0.0342	.	0.0171	0.0171	0.3571
AGE1	0.4487	0.4407	0.0161	.	0.0080	0.0080	0.1556
AGE2	0.3894	0.3858	0.0072	.	0.0035	0.0035	0.1963
AGE3	0.1563	0.1680	-0.0323	.	0.0117	0.0117	0.1612
AGE4	0.0056	0.0055	0.0026	.	0.0002	0.0002	0.0533
INPATIENT	0.0636	0.0798	-0.0668	.	0.0163	0.0163	0.3067
VARIANT1	0.1568	0.1467	0.0278	.	0.0101	0.0101	0.2124
VARIANT2	0.0127	0.0146	-0.0165	.	0.0019	0.0019	0.1356
VARIANT4	0.6379	0.6298	0.0169	.	0.0081	0.0081	0.0356
VARIANT5	0.0414	0.0482	-0.0341	.	0.0068	0.0068	0.1661
VARIANTNA	0.1511	0.1607	-0.0267	.	0.0096	0.0096	0.1637
HCQ	0.7679	0.7635	0.0105	.	0.0044	0.0044	0.2213
AZ_only	0.0537	0.0592	-0.0247	.	0.0056	0.0056	0.2576
IVM	0.1874	0.1866	0.0019	.	0.0008	0.0008	0.1212
DIABETE	0.0918	0.1135	-0.0751	.	0.0217	0.0217	0.2258
HBP	0.1893	0.2087	-0.0496	.	0.0194	0.0194	0.2092
OBESITY	0.1963	0.1958	0.0013	.	0.0005	0.0005	0.2519
ASTHMA	0.0866	0.0999	-0.0471	.	0.0133	0.0133	0.1841
COPD	0.0146	0.0202	-0.0467	.	0.0056	0.0056	0.1630
CANCER	0.0683	0.0662	0.0083	.	0.0021	0.0021	0.1536
IMMUNODEFICIENCY	0.0292	0.0362	-0.0416	.	0.0070	0.0070	0.1559
AutoImmuneDiseases	0.0725	0.0707	0.0070	.	0.0018	0.0018	0.2054
ChronicCardiacDiseases	0.0447	0.0510	-0.0305	.	0.0063	0.0063	0.1446

```
Sample Sizes:
      Control Treated
All      13939.    2124
Matched (ESS) 2275.69 2124
Matched      13939.    2124
Unmatched     0.        0
```

## Model (b)

```
Call:
matchit(formula = VACCINATION ~ SEX + AGE + INPATIENT + VARIANT +
  HCQ + AZ_only + IVM + DIABETE + HBP + OBESITY, data = wrk_matchit,
  method = "full", distance = "glm")

Summary of Balance for Matched Data:
```

	Means Treated	Means Control	Std. Mean Diff.	Var. Ratio	eCDF Mean	eCDF Max	Std. Pair Dist.
distance	0.2243	0.2243	-0.0003	0.9997	0.0003	0.0112	0.0007
SEX	0.5334	0.5339	-0.0009	.	0.0005	0.0005	0.1971
AGE1	0.4487	0.4221	0.0534	.	0.0265	0.0265	0.1018
AGE2	0.3894	0.3974	-0.0165	.	0.0081	0.0081	0.1390
AGE3	0.1563	0.1729	-0.0458	.	0.0166	0.0166	0.1184
AGE4	0.0056	0.0075	-0.0248	.	0.0019	0.0019	0.0495
INPATIENT	0.0636	0.0938	-0.1239	.	0.0302	0.0302	0.2376
VARIANT1	0.1568	0.1413	0.0426	.	0.0155	0.0155	0.1504
VARIANT2	0.0127	0.0179	-0.0460	.	0.0052	0.0052	0.1294
VARIANT4	0.6379	0.6327	0.0110	.	0.0053	0.0053	0.0230
VARIANT5	0.0414	0.0424	-0.0048	.	0.0010	0.0010	0.1344
VARIANTNA	0.1511	0.1658	-0.0409	.	0.0147	0.0147	0.1078
HCQ	0.7679	0.7584	0.0226	.	0.0095	0.0095	0.1081
AZ_only	0.0537	0.0590	-0.0234	.	0.0053	0.0053	0.2024
IVM	0.1874	0.1890	-0.0041	.	0.0016	0.0016	0.0801
DIABETE	0.0918	0.1043	-0.0434	.	0.0125	0.0125	0.1503
HBP	0.1893	0.2118	-0.0575	.	0.0225	0.0225	0.1372
OBESITY	0.1963	0.2119	-0.0392	.	0.0156	0.0156	0.2080

```
Sample Sizes:
      Control Treated
All      13939.    2124
Matched (ESS) 2186.2 2124
Matched      13939.    2124
Unmatched     0.        0
Discarded     0.        0
```

Model (c)

Summary of Balance for Matched Data:

	Means Treated	Means Control	Std. Mean Diff.	Var. Ratio	eCDF Mean	eCDF Max	Std. Pair	Dist.
distance	0.2226	0.2226	-0.0001	0.9995	0.0002	0.0014		0.0004
SEX	0.5334	0.5313	0.0042	.	0.0021	0.0021		0.1299
AGE1	0.4487	0.4495	-0.0016	.	0.0008	0.0008		0.0289
AGE2	0.3894	0.3846	0.0098	.	0.0048	0.0048		0.0349
AGE3	0.1563	0.1567	-0.0010	.	0.0004	0.0004		0.0102
AGE4	0.0056	0.0093	-0.0481	.	0.0036	0.0036		0.0411
INPATIENT	0.0636	0.0702	-0.0274	.	0.0067	0.0067		0.0552
VARIANT1	0.1568	0.1560	0.0020	.	0.0007	0.0007		0.0409
VARIANT2	0.0127	0.0123	0.0033	.	0.0004	0.0004		0.0556
VARIANT4	0.6379	0.6380	-0.0001	.	0.0000	0.0000		0.0024
VARIANT5	0.0414	0.0442	-0.0138	.	0.0028	0.0028		0.0330
VARIANTNA	0.1511	0.1495	0.0047	.	0.0017	0.0017		0.0094
HCQ	0.7679	0.7641	0.0089	.	0.0038	0.0038		0.0358
AZ_only	0.0537	0.0540	-0.0015	.	0.0003	0.0003		0.0642
IVM	0.1874	0.1889	-0.0038	.	0.0015	0.0015		0.0249

Sample Sizes:

	Control	Treated
All	13939.	2124
Matched (ESS)	1960.97	2124
Matched	13939.	2124
Unmatched	0.	0
Discarded	0.	0

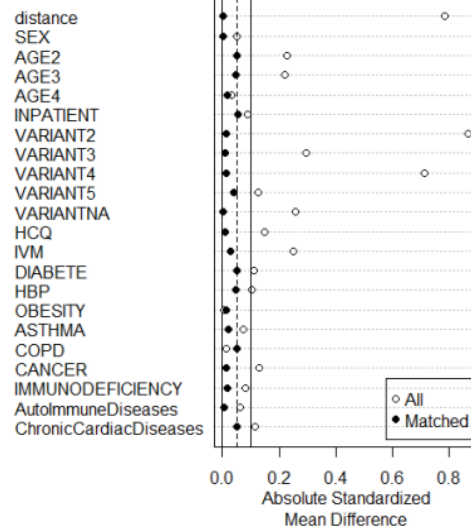
**Appendix 2a:** Sensitivity analysis, model (a) for age ≥ 50 years, propensity score matching with Optimal Full Matching in VACCINATION subset.

Call:

```
glm(formula = Status_56.EFS ~ VACCINATION + SEX + AGE + INPATIENT +
  VARIANT + HCQ + IVM + DIABETE + OBESITY + HBP + ASTHMA +
  COPD + CANCER + IMMUNODEFICIENCY + AutoImmuneDiseases + ChronicCardiacDiseases,
  family = quasibinomial(), data = m.data, weights = weights)
```

Coefficients:

	OR	2.5 %	97.5 %	Pr(> t )
(Intercept)	0.0157	0.0051	0.0423	7.72e-15 ***
VACCINATION	0.3350	0.1832	0.5719	0.000153 ***
SEX	0.5559	0.4664	0.6582	2.33e-11 ***
AGE3	1.7306	1.2311	2.4369	0.001628 **
AGE4	3.1246	1.3209	6.8633	0.006350 **
INPATIENT	16.5176	12.0103	22.9515	< 2e-16 ***
VARIANT3	0.6571	0.2646	1.8569	0.392563
VARIANT4	0.7203	0.3012	1.9802	0.489175
VARIANT5	0.4906	0.1707	1.5302	0.198046
VARIANTNA	0.3759	0.1359	1.1409	0.068265 .
HCQ	0.8119	0.5461	1.2122	0.305335
IVM	3.0269	2.0467	4.4997	3.58e-08 ***
DIABETE	0.9292	0.6441	1.3276	0.690326
OBESITY	2.1014	1.5031	2.9273	1.24e-05 ***
HBP	1.2878	0.9231	1.7950	0.135712
ASTHMA	0.6765	0.3117	1.3136	0.282132
COPD	0.9412	0.3779	2.0614	0.887535
CANCER	1.0398	0.6629	1.5912	0.860862
IMMUNODEFICIENCY	1.2236	0.5844	2.3312	0.564164
AutoImmuneDiseases	0.5505	0.2684	1.0260	0.078339 .
ChronicCardiacDiseases	0.7232	0.4546	1.1219	0.158774

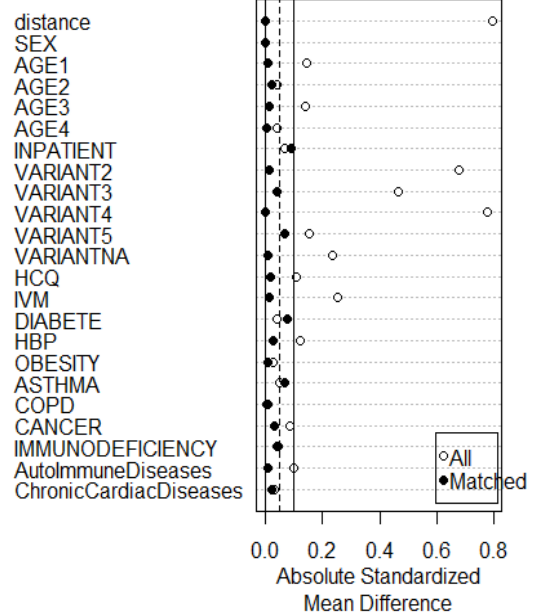


**Appendix 2b:** Sensitivity analysis, model (a) for women, propensity score matching with Optimal Full Matching in VACCINATION subset.

```
Call:
glm(formula = Status_56.EFS ~ VACCINATION + AGE + INPATIENT +
  VARIANT + HCQ + IVM + DIABETE + OBESITY + HBP + ASTHMA +
  COPD + CANCER + IMMUNODEFICIENCY + AutoImmuneDiseases + ChronicCardiacDiseases,
  family = quasibinomial(), data = m.data, weights = weights)
```

Coefficients:

	OR	2.5 %	97.5 %	Pr(> t )
(Intercept)	0.0006	0.0001	0.0023	< 2e-16 ***
VACCINATION	0.4720	0.2380	0.8547	0.020398 *
AGE2	11.0950	5.0389	30.0162	7.37e-08 ***
AGE3	10.6561	4.5926	29.7764	4.45e-07 ***
AGE4	41.8733	14.2031	138.5101	7.89e-11 ***
INPATIENT	17.6688	12.3020	25.6125	< 2e-16 ***
VARIANT3	3.3394	1.2744	11.4200	0.027314 *
VARIANT4	2.1314	0.8368	7.1685	0.157060
VARIANT5	0.1384	0.0065	0.9916	0.086194 .
VARIANTNA	0.3624	0.0906	1.5240	0.145967
HCQ	0.5370	0.3589	0.8059	0.002563 **
IVM	0.8622	0.5653	1.3058	0.487140
DIABETE	1.6067	1.0229	2.4970	0.036995 *
OBESITY	1.1401	0.7494	1.7102	0.532618
HBP	1.2453	0.8282	1.8643	0.288655
ASTHMA	0.1642	0.0524	0.3912	0.000315 ***
COPD	1.7105	0.6168	4.0684	0.258317
CANCER	0.5411	0.3015	0.9179	0.029848 *
IMMUNODEFICIENCY	0.8188	0.3127	1.8107	0.650708
AutoImmuneDiseases	0.8270	0.4709	1.3774	0.485810
ChronicCardiacDiseases	0.3031	0.1199	0.6729	0.006096 **

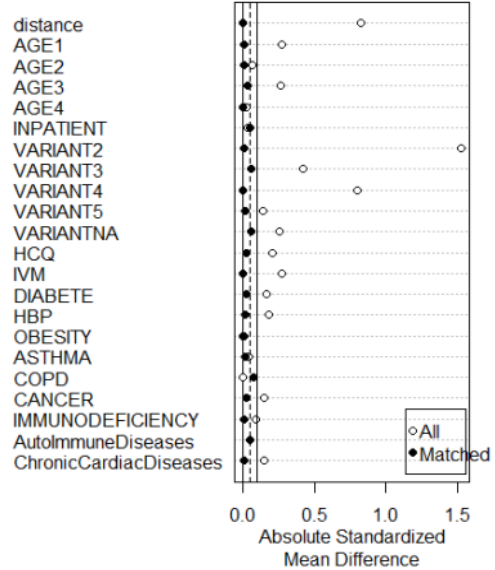


Appendix 2c: Sensitivity analysis, model (a) for men, propensity score matching with Optimal Full Matching in VACCINATION subset.

```
Call:
glm(formula = Status_56.EFS ~ VACCINATION + AGE + INPATIENT +
  VARIANT + HCQ + IVM + DIABETE + OBESITY + HBP + ASTHMA +
  COPD + CANCER + IMMUNODEFICIENCY + AutoImmuneDiseases + ChronicCardiacDiseases,
  family = quasibinomial(), data = m.data, weights = weights)
```

Coefficients:

	OR	2.5 %	97.5 %	Pr(> t )
(Intercept)	0.0005	0.0000	0.0043	2.00e-08 ***
VACCINATION	0.2218	0.1072	0.4178	1.26e-05 ***
AGE2	4.4217	2.3098	9.3446	2.56e-05 ***
AGE3	16.2282	8.4932	34.3257	3.27e-15 ***
AGE4	218.4149	70.8905	686.6068	< 2e-16 ***
INPATIENT	13.2182	9.6861	18.1703	< 2e-16 ***
VARIANT3	3.5436	0.4068	150.7884	0.34207
VARIANT4	6.3459	0.7383	269.0154	0.16394
VARIANT5	6.5661	0.7215	283.4540	0.16244
VARIANTNA	3.8529	0.4360	164.8666	0.31318
HCQ	0.5627	0.3841	0.8256	0.00321 **
IVM	3.6219	2.4611	5.3546	8.82e-11 ***
DIABETE	0.3118	0.1990	0.4766	1.65e-07 ***
OBESITY	2.2559	1.6039	3.1621	2.59e-06 ***
HBP	1.9252	1.3987	2.6520	5.95e-05 ***
ASTHMA	0.4570	0.1818	1.0255	0.07462 .
COPD	1.0358	0.5219	1.9407	0.91613
CANCER	1.2086	0.7230	1.9660	0.45679
IMMUNODEFICIENCY	0.2080	0.0594	0.5356	0.00404 **
AutoImmuneDiseases	0.0955	0.0036	0.5220	0.03731 *
ChronicCardiacDiseases	0.4561	0.2706	0.7430	0.00227 **



Appendix 3: R version 4.3.1 line commands to run Propensity Score Matching and the multivariate logistic regression

(0) download the publically available IHU-Méditerranée dataset from : [Dryad | Data -- Monocentric retrospective cohort of 30,423 COVID-19 patients \(datadryad.org\)](https://datadryad.org/dataset/doi:10.26502/ami.936500151)

(1) transform the dataset in a .csv (coma separated variable) file (named here: cohort\_entry\_status\_ok\_2\_mod.csv) and add 4 binary variables that list for every patient whether an event (ICU transfer or DEATH) occurred at 42,56,90 and 640 days after presentation (here we have named these additional variables Status\_42.EFS, Status\_56.EFS, Status\_90.EFS and Status\_640.EFS).

(2) launch the R software (version 4.3.1) interactive windows

(3) install package from a selected CRAN mirror using the interactive menu “Packages” and then “Install packages”

(4) activate interactively at the prompt the packages needed :

```
setwd("C:/Users/Valer/Desktop/IHU rétrospective cohort/Calculs stat")
```

```
library(coxphf)
```

```
library(survival)
```

```
library(MatchIt)
```

```
library(optmatch)
```

```
library(survey)
```

```
library(quickmatch)
```

```
library("marginaleffects")
```

```
library(ipw)
```

```
library(adjustedCurves)
```

```
cohort_entry_status_2_ok <- read.csv(file="cohort_entry_status_ok_2_mod.csv", header=TRUE, sep=',')
```

```
nrow(cohort_entry_status_2_ok)
```

```
wrk_vaccination_cohort <- subset(cohort_entry_status_2_ok, VACCINATION == 1 | VACCINATION == 0)
```

```
nrow(wrk_vaccination_cohort)
```

```
[1] 16063
```

```
ADDING AZ - HCQ - IVM
```

```
wrk_vaccination_cohort$AZ <- as.numeric(as.character(wrk_vaccination_cohort$AZ))
```

```
wrk_vaccination_cohort$HCQ <- as.numeric(as.character(wrk_vaccination_cohort$HCQ))
```

```
wrk_vaccination_cohort$IVM <- as.numeric(as.character(wrk_vaccination_cohort$IVM))
```

```
wrk_vaccination_cohort$AZ_only <- (wrk_vaccination_cohort$AZ - wrk_vaccination_cohort$HCQ - wrk_vaccination_cohort$IVM)
```

```
wrk_vaccination_cohort$AZ_only <- ifelse(wrk_vaccination_cohort$AZ_only == "-1", "0", wrk_vaccination_cohort$AZ_only)
```

```
wrk_vaccination_cohort$AZ_only <- ifelse(wrk_vaccination_cohort$AZ_only == "-2", "0",
wrk_vaccination_cohort$AZ_only)
```

```
wrk_vaccination_cohort$AZ_only <- as.numeric(as.character(wrk_vaccination_cohort$AZ_only))
```

```
wrk_vaccination_cohort[wrk_vaccination_cohort == 'NULL'] <- 'NA'
```

```
wrk_vaccination_cohort$VARIANT_int <- as.numeric(as.character(wrk_vaccination_cohort$VARIANT_int))
```

```
wrk_vaccination_cohort$VACCINATION <- as.numeric(as.character(wrk_vaccination_cohort$VACCINATION))
```

```
wrk_vaccination_cohort$DIABETE <- as.numeric(as.character(wrk_vaccination_cohort$DIABETE))
```

```
wrk_vaccination_cohort$HBP <- as.numeric(as.character(wrk_vaccination_cohort$HBP))
```

```
wrk_vaccination_cohort$OBESITY <- as.numeric(as.character(wrk_vaccination_cohort$OBESITY))
```

```
wrk_vaccination_cohort$ASTHMA <- as.numeric(as.character(wrk_vaccination_cohort$ASTHMA))
```

```
wrk_vaccination_cohort$COPD <- as.numeric(as.character(wrk_vaccination_cohort$COPD))
```

```
wrk_vaccination_cohort$CANCER <- as.numeric(as.character(wrk_vaccination_cohort$CANCER))
```

```
wrk_vaccination_cohort$IMMUNODEFICIENCY <-
```

```
as.numeric(as.character(wrk_vaccination_cohort$IMMUNODEFICIENCY))
```

```
wrk_vaccination_cohort$AutoImmuneDiseases <-
```

```
as.numeric(as.character(wrk_vaccination_cohort$AutoImmuneDiseases))
```

```
wrk_vaccination_cohort$ChronicCardiacDiseases <-
```

```
as.numeric(as.character(wrk_vaccination_cohort$ChronicCardiacDiseases))
```

```
wrk_vaccination_cohort$VARIANT_int[is.na(wrk_vaccination_cohort$VARIANT_int)] <-
```

```
mean(wrk_vaccination_cohort$VARIANT_int, na.rm=TRUE)
```

```
wrk_vaccination_cohort$VACCINATION[is.na(wrk_vaccination_cohort$VACCINATION)] <-
```

```
mean(wrk_vaccination_cohort$VACCINATION, na.rm=TRUE)
```

```
wrk_vaccination_cohort$DIABETE[is.na(wrk_vaccination_cohort$DIABETE)] <-
```

```
mean(wrk_vaccination_cohort$DIABETE, na.rm=TRUE)
```

```
wrk_vaccination_cohort$HBP[is.na(wrk_vaccination_cohort$HBP)] <- mean(wrk_vaccination_cohort$HBP,
na.rm=TRUE)
```

```
wrk_vaccination_cohort$OBESITY[is.na(wrk_vaccination_cohort$OBESITY)] <-
```

```
mean(wrk_vaccination_cohort$OBESITY, na.rm=TRUE)
```

```
wrk_vaccination_cohort$ASTHMA[is.na(wrk_vaccination_cohort$ASTHMA)] <-
```

```
mean(wrk_vaccination_cohort$ASTHMA, na.rm=TRUE)
```

```
wrk_vaccination_cohort$COPD[is.na(wrk_vaccination_cohort$COPD)] <- mean(wrk_vaccination_cohort$COPD,
na.rm=TRUE)
```

```

wrk_vaccination_cohort$CANCER[is.na(wrk_vaccination_cohort$CANCER)] <-
mean(wrk_vaccination_cohort$CANCER, na.rm=TRUE)
wrk_vaccination_cohort$IMMUNODEFICIENCY[is.na(wrk_vaccination_cohort$IMMUNODEFICIENCY)] <-
mean(wrk_vaccination_cohort$IMMUNODEFICIENCY, na.rm=TRUE)
wrk_vaccination_cohort$ChronicCardiacDiseases[is.na(wrk_vaccination_cohort$ChronicCardiacDiseases)] <-
mean(wrk_vaccination_cohort$ChronicCardiacDiseases, na.rm=TRUE)
wrk_vaccination_cohort$AutoImmuneDiseases[is.na(wrk_vaccination_cohort$AutoImmuneDiseases)] <-
mean(wrk_vaccination_cohort$AutoImmuneDiseases, na.rm=TRUE)

str(wrk_vaccination_cohort)

wrk_vaccination_cohort$SEX <- ifelse(wrk_vaccination_cohort$SEX == "1", "0", wrk_vaccination_cohort$SEX)

wrk_vaccination_cohort$SEX <- ifelse(wrk_vaccination_cohort$SEX == "2", "1", wrk_vaccination_cohort$SEX)

wrk_vaccination_cohort$VARIANT <- ifelse(wrk_vaccination_cohort$VARIANT == "3", "1",
wrk_vaccination_cohort$VARIANT)

wrk_matchit <- subset(wrk_vaccination_cohort,
select=c(HCQ,SEX,AGE,INPATIENT,PERIOD,VARIANT,AZ_only,IVM,VACCINATION,DIABETE,HBP,OBE
SITY,ASTHMA,COPD,CANCER,IMMUNODEFICIENCY,AutoImmuneDiseases,ChronicCardiacDiseases,Status_
42.EFS,Status_56.EFS,Status_90.EFS,Status_700.EFS))

wrk_matchit$HCQ <- as.numeric(as.character(wrk_matchit$HCQ))
wrk_matchit$AGE <- as.character(as.integer(wrk_matchit$AGE))
wrk_matchit$PERIOD <- as.character(as.integer(wrk_matchit$PERIOD))
wrk_matchit$SEX <- as.numeric(as.character(wrk_matchit$SEX))

str(wrk_matchit)

m.check_balance <- matchit(VACCINATION ~ SEX + AGE + INPATIENT + HCQ + AZ_only + IVM +
DIABETE + HBP + OBESITY + ASTHMA + COPD + CANCER + IMMUNODEFICIENCY +
AutoImmuneDiseases + ChronicCardiacDiseases, data = wrk_matchit, method = NULL, distance = "glm")

m.get_balance <- matchit(VACCINATION ~ SEX + AGE + INPATIENT + VARIANT + HCQ + AZ_only + IVM
+ DIABETE + HBP + OBESITY + ASTHMA + COPD + CANCER + IMMUNODEFICIENCY +
AutoImmuneDiseases + ChronicCardiacDiseases, data = wrk_matchit, method = "full", distance = "glm")

```

```
summary(m.get_balance)
```

```
plot(summary(m.get_balance))
```

```
plot(m.get_balance, type = "density", interactive = FALSE, which.xs = "PERIOD")
```

```
plot(m.get_balance, type = "density", interactive = FALSE, which.xs = "HCQ")
```

```
plot(m.get_balance, type = "density", interactive = FALSE, which.xs = "AGE")
```

```
m.data <- match.data(m.get_balance)
```

```
m.fit.logis <- glm(Status_56.EFS ~ VACCINATION *(SEX + AGE + INPATIENT + VARIANT + HCQ +  
AZ_only + IVM + DIABETE + OBESITY + HBP + ASTHMA + COPD + CANCER + IMMUNODEFICIENCY +  
AutoImmuneDiseases + ChronicCardiacDiseases), data = m.data, weights = weights, family = quasibinomial())
```

Odds Ratio :

```
avg_comparisons(m.fit.logis, variables = "VACCINATION", vcov = ~subclass, newdata = subset(m.data,  
VACCINATION == 1), wts = "weights", comparison = "lnoravg", transform = "exp")
```

```
summary(m.fit.logis)
```

```
lreg.or <- exp(cbind(OR = coef(m.fit.logis), confint(m.fit.logis)))
```

```
round(lreg.or, digits=4)
```

```
m.fit.logis <- glm(Status_56.EFS ~ VACCINATION + SEX + AGE + INPATIENT + VARIANT + HCQ +  
AZ_onky + IVM + DIABETE + OBESITY + HBP + ASTHMA + COPD + CANCER + IMMUNODEFICIENCY +  
AutoImmuneDiseases + ChronicCardiacDiseases, data = m.data, weights = weights, family = quasibinomial())
```

```
summary(m.fit.logis)
```

```
lreg.or <- exp(cbind(OR = coef(m.fit.logis), confint(m.fit.logis)))
```

```
round(lreg.or, digits=4)
```