Supplementary Appendix

Supplement to: Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe Covid-19 in outpatients. N Engl J Med. DOI: 10.1056/NEJMoa2116846

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix to: **Early Outpatient Remdesivir to Prevent Progression to Severe Covid-19**

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Figure S1. Patient Disposition

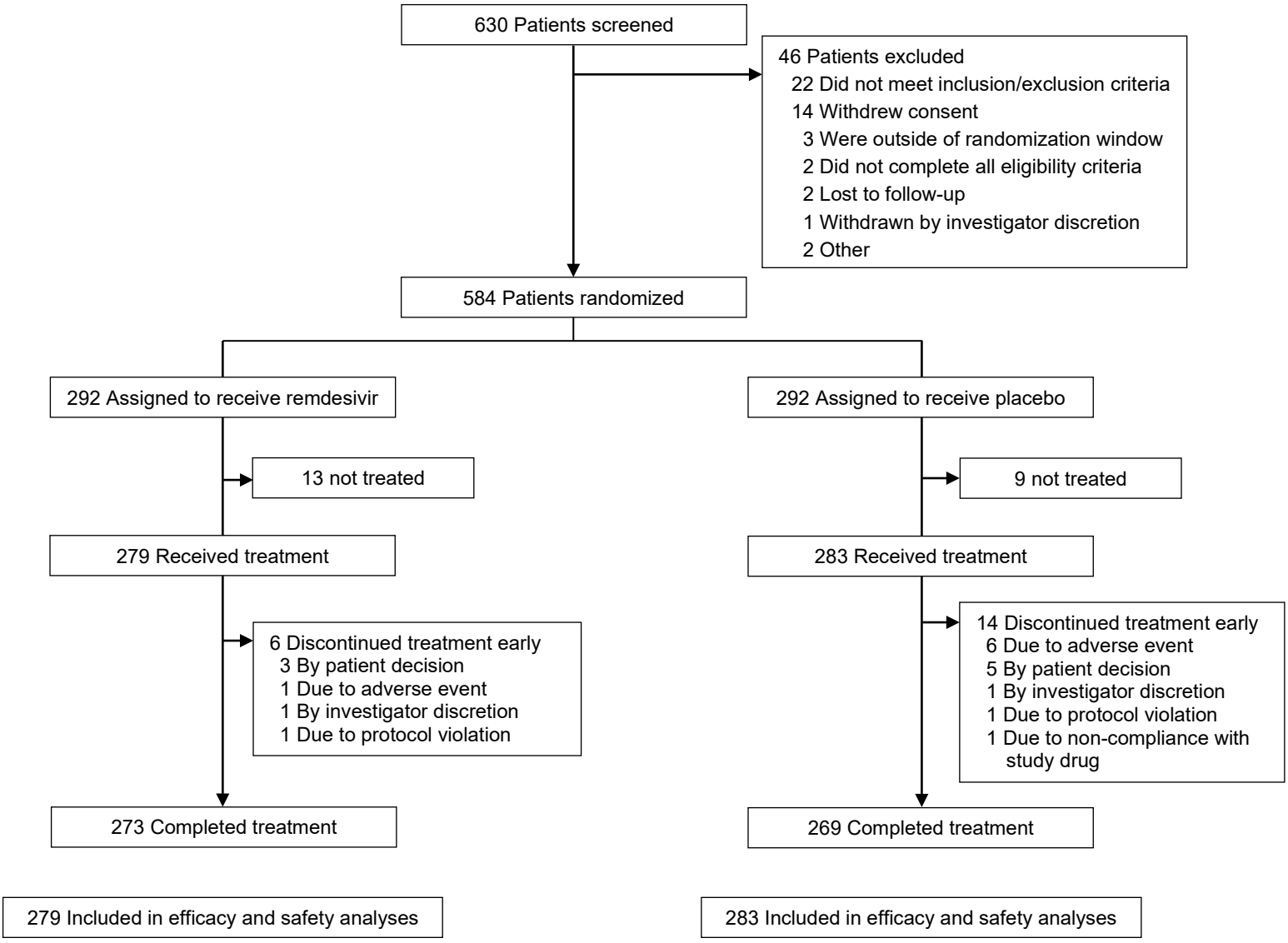
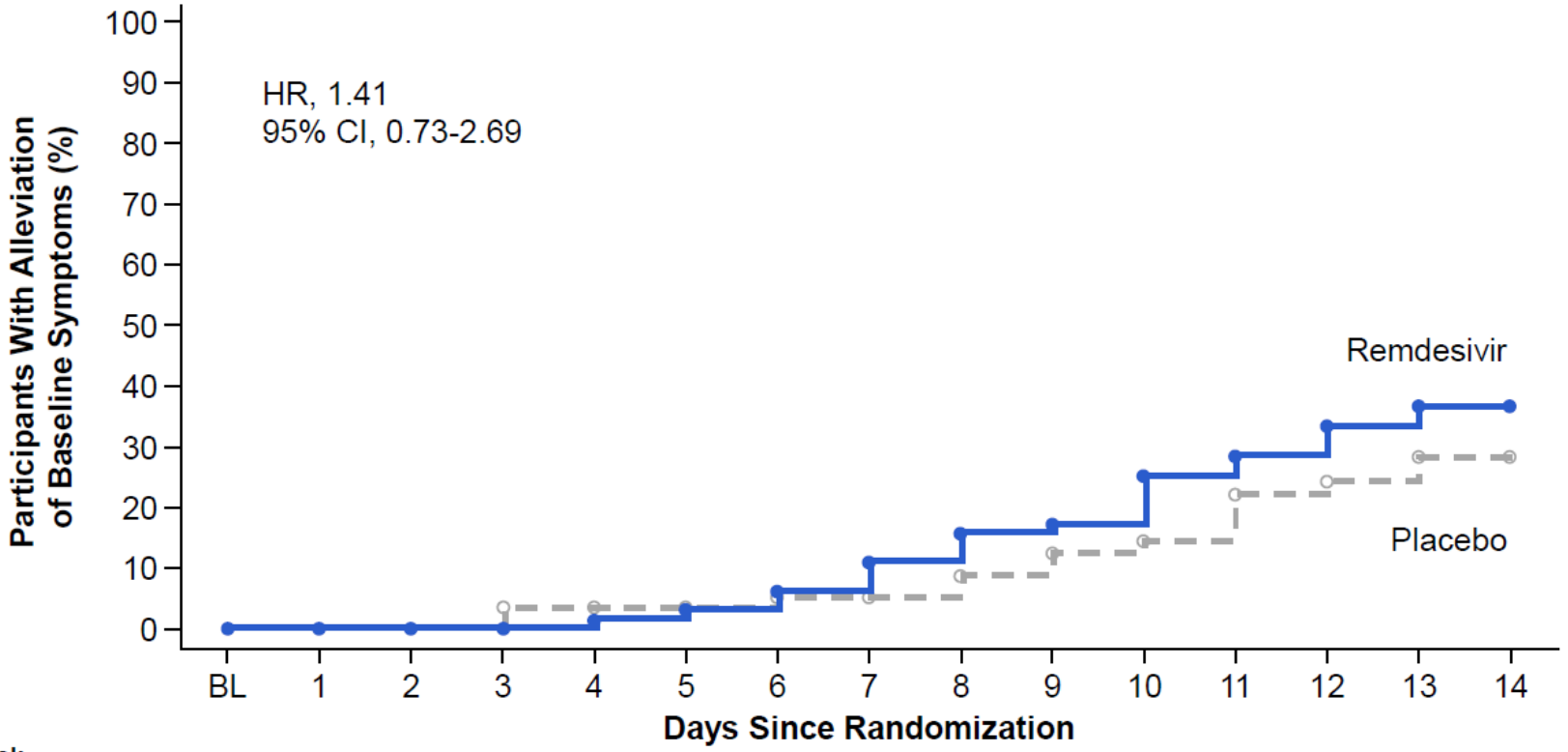


Figure S2. Kaplan-Meier Estimate of Time to Symptom Alleviation as Reported by Covid-19-adapted FLU-PRO Questionnaire

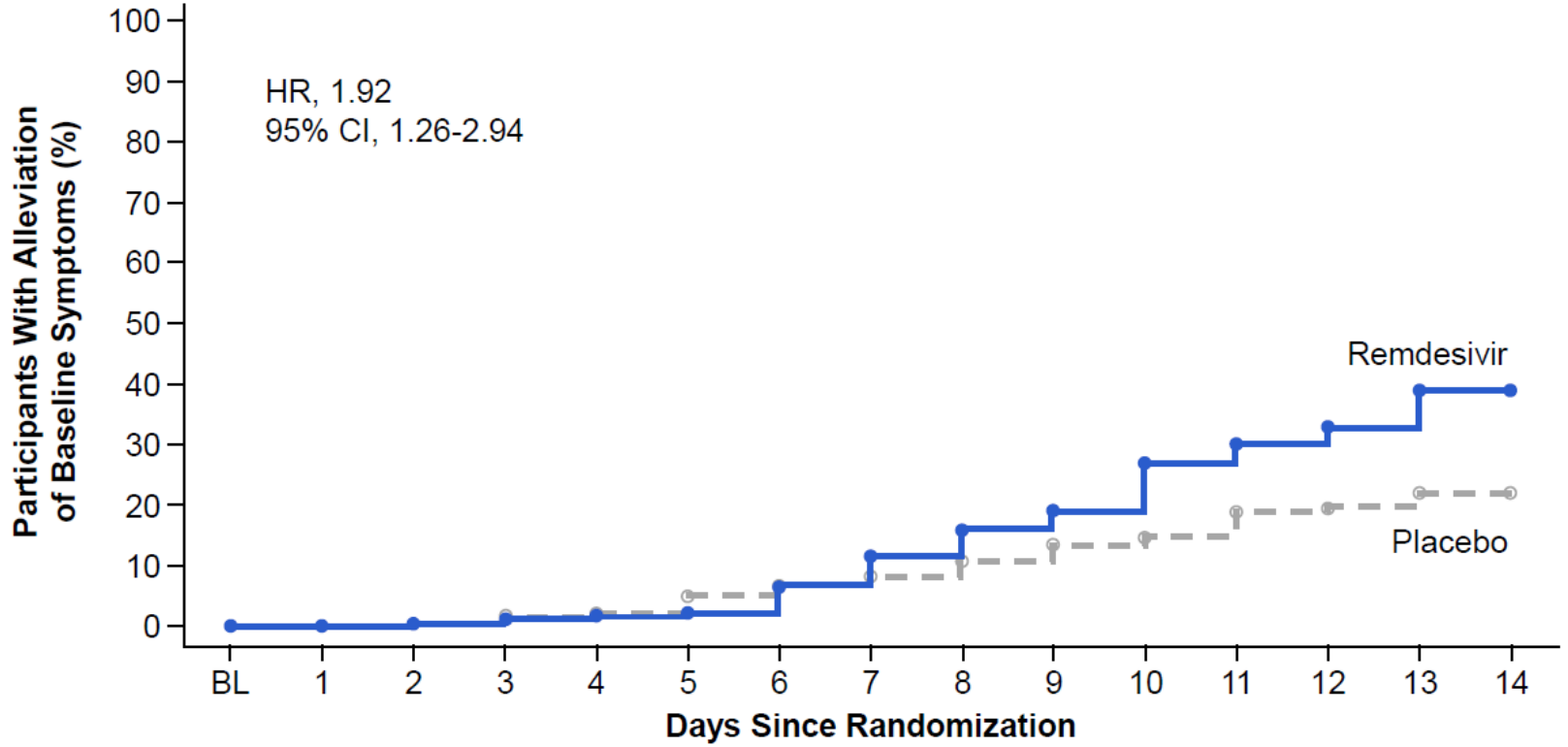
A. Per protocol analysis, including patients who completed the baseline questionnaire before the first treatment dose



No. at risk															
Remdesivir IV for 3 days	66	66	66	66	64	63	62	60	57	53	52	46	44	41	36
Placebo	60	60	60	59	57	57	56	55	52	49	47	44	38	37	32

Hazard Ratio and two-sided 95% CI were estimated using the Cox regression with baseline stratification factors (residence in a skilled nursing facility yes vs no, age <60 vs ≥60 years, and US vs outside US) as covariates.
N represents the number of participants at risk at the beginning of the interval.
BL, baseline; HR, hazard ratio.

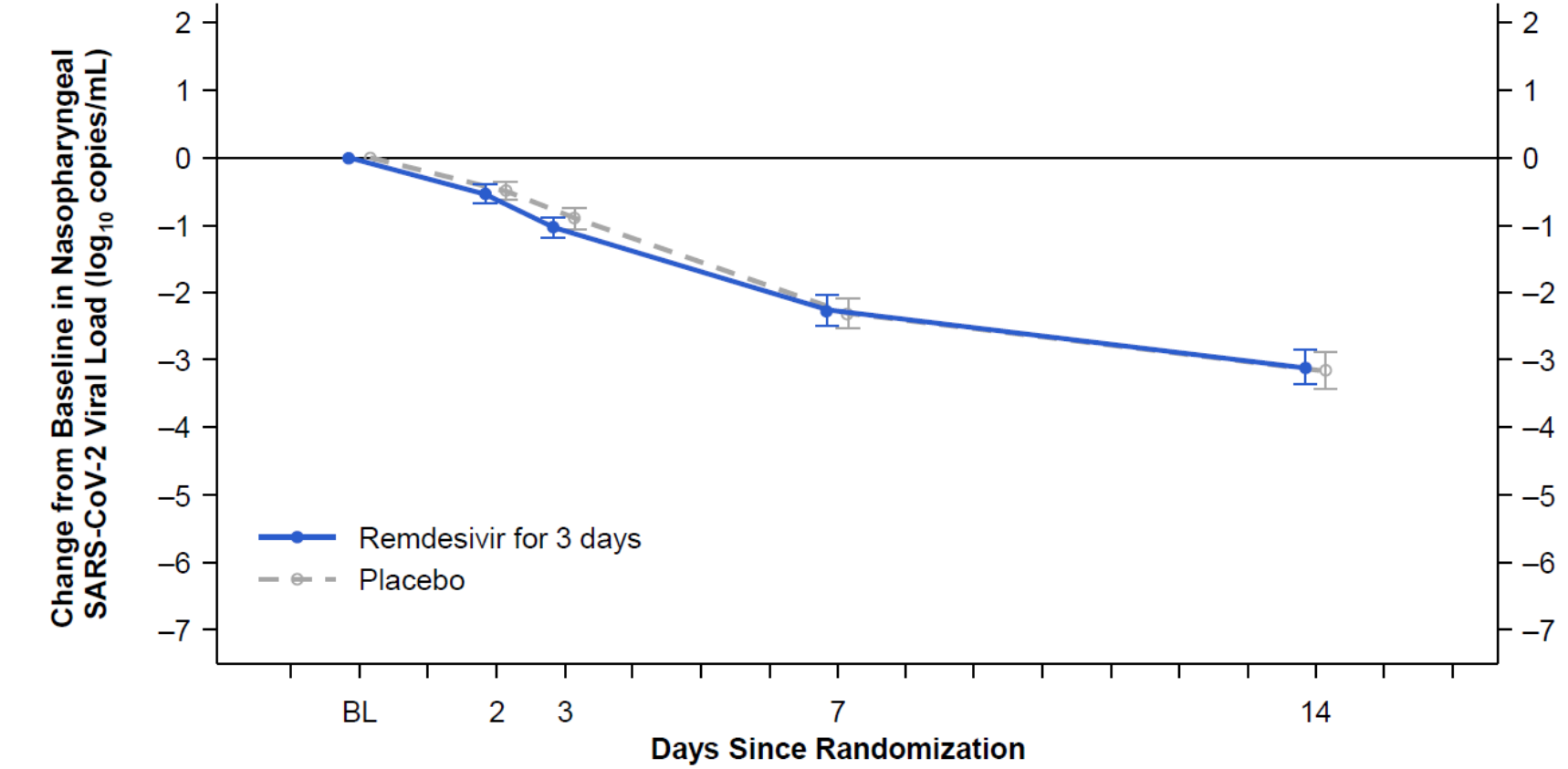
B. Post-hoc analysis, including patients who completed the baseline questionnaire prior to or on the same day as the first treatment dose



No. at risk															
Remdesivir IV for 3 days	169	169	169	167	162	161	159	152	141	133	125	112	106	99	80
Placebo	165	165	165	162	156	154	149	145	138	132	127	123	112	109	93

Participants who had baseline symptoms scored as 1 or higher and did not have alleviation were censored at the last assessment day.
Hazard ratio and two-sided 95% CI were estimated using the Cox regression with baseline stratification factors (residence in a skilled nursing facility yes vs no, age <60 vs ≥60 years, and US vs outside US) as covariates.
N represents the number of participants at risk at the beginning of the interval.
BL, baseline; HR, hazard ratio.

Figure S3. Mean (95% CI) Change from Baseline in Nasopharyngeal SARS-CoV-2 Viral Load by Visit Day.



Remdesivir IV for 3 days	215	195	195	192	184
Placebo	213	192	187	190	169

Table S1. Patient demographics, hospitalization data, and outcomes over the course of available follow-up

Patient	Treatment	Age	Sex	Day of hospitalization (from time of randomization)	Reason for hospitalization	Covid-19 related Yes/no	ICU Yes/no	Outcome (transfer/discharged/death)
Remdesivir group								
1	Remdesivir	81	F	3	Respiratory failure	Yes	Unknown	Discharged
2	Remdesivir	40	M	2	Pneumonia	Yes	Yes	Discharged
3	Remdesivir	60	F	8	Atrial fibrillation	No	Yes	Discharged
4	Remdesivir	71	M	7	Cardiac failure congestive, Atrial fibrillation	No	Yes	Discharged
5	Remdesivir	49	M	4	Angina pectoris	No	No	Discharged
Placebo group								
6	Placebo	53	F	2	Covid-19 pneumonia	Yes	Yes	Discharged
7	Placebo	62	F	3	Pneumonia	Yes	No	Discharged
8	Placebo	71	M	9	Covid-19 pneumonia	Yes	Yes	Discharged
9	Placebo	50	M	3	Hypoxia	Yes	No	Discharged
10	Placebo	68	M	14	Pneumonia	Yes	No	Discharged
11	Placebo	66	M	7	Fibrin D-dimer increased	Yes	No	Discharged
12	Placebo	68	M	2	Acute respiratory failure, Covid-19 pneumonia	Yes	No	Discharged
13	Placebo	57	M	7	Covid-19 pneumonia	Yes	No	Discharged
14	Placebo	63	F	7	Covid-19 pneumonia	Yes	No	Discharged
15	Placebo	69	M	7	Covid-19	Yes	Yes	Death at study day 59

16	Placebo	74	F	2	Covid-19 pneumonia	Yes	No	Transferred
17	Placebo	60	F	1	Dyspnea	Yes	No	Discharged
18	Placebo	54	M	2	Covid-19	Yes	No	Discharged
19	Placebo	55	M	6	Covid-19 pneumonia, Respiratory failure	Yes	No	Discharged
20	Placebo	56	F	3	Hypoxia, Pneumonia	Yes	No	Discharged
21	Placebo	63	F	21	Lumbar vertebral fracture, road traffic accident	No	No	Discharged
22	Placebo	56	M	26	Angina pectoris	No	Unknown	Discharged
23	Placebo	48	F	19	Acute myocardial infarction	No	No	Discharged

Shaded rows indicate non-Covid-19-related hospitalizations.

Table S2. Representativeness of Study Participants

Category	
Disease, problem, or condition under investigation	Covid-19 in high-risk, non-hospitalized patients.
Special considerations related to:	
Sex and gender	Male patients have a significantly higher risk of Covid-19 disease progression.[1]
Age	Older adults aged 60 years or greater are at higher risk of severe illness due to Covid-19.[2,3]
Race or ethnic group	Covid-19 does not generally impact racial or ethnic groups differently, but due to systemic health and social inequities, some racial and ethnic minorities, such as Hispanic/Latinx and Black persons in the United States, are at increased risk for Covid-19.[2] This trial is noteworthy for high enrollment among Hispanic/Latinx and American Indian/Alaskan Native population relative to the general population of the US.
Geography	Covid-19 is a global pandemic.
Other considerations	The risk of severe Covid-19 increases as the number of underlying medical conditions increases in a person.[3]
Overall representativeness of this trial	The patient population enrolled was balanced between male and female sex. About one third (30%) of patients were over the age of 60. No patients under the age of 12 were enrolled. Relative to the general United States population, of 562 patients, a higher proportion of patients with Hispanic/Latinx ethnicity (235, 44%) and American Indian or Alaskan Native race were enrolled (36, 7%), and a lower proportion of Black (42, 8%) or Asian race (13, 2%) were enrolled. Most patients enrolled (94%) were from the United States. Patients with severe renal disease and patients who were not vaccinated were excluded from enrollment. A lower proportion of patients who were immunocompromised (23, 5%) and patients with active cancer (30, 4%) were enrolled. Although the pediatric population does not generally contain high-risk patients, and vaccinated individuals have low rates of hospitalization, the lack of these patients in the study population precludes generalizability to these groups. All patient characteristics described here were self-reported by patients and collected at screening and were entered into the electronic database.

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3. Assessing Risk Factors for Severe COVID-19 Illness. Atlanta, GA; Centers for Disease Control and Prevention., November 2020. (https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/assessing-risk-factors.html).