



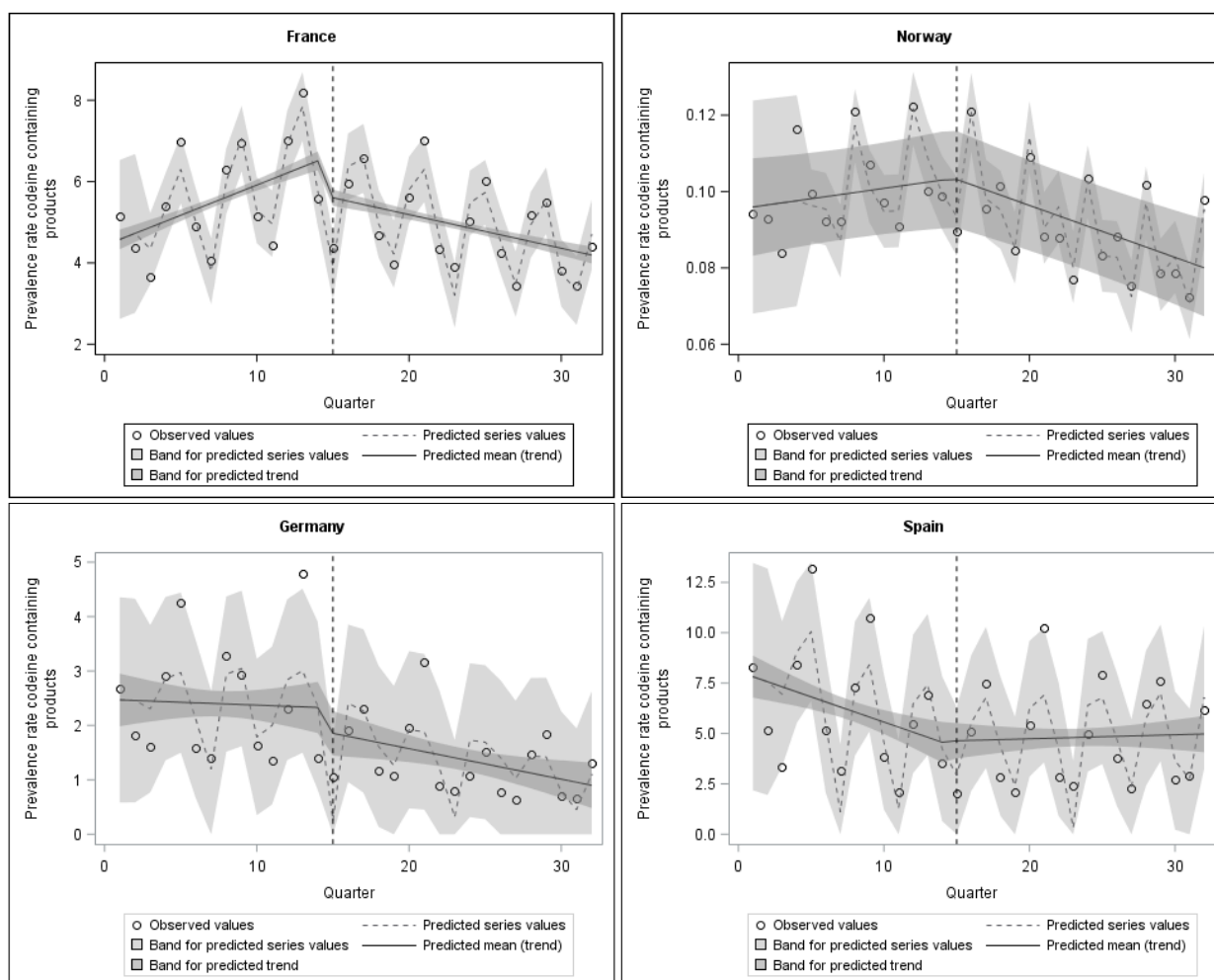
Annex B

This annex B describes the prevalence of use of codeine, alternative analgesics and antitussives before and after both codeine referrals for pain relief and cough or cold indications in the population between 12 and 18 years of age for each of the participating cohorts.

1. Referral on pain relief indication (June 2013)

1.1. Use of codeine containing products

Figure 1.1 Quarterly (n=32) trends in codeine containing products in France, Norway, Germany, Spain and United Kingdom between 1 January 2010 and 31 December 2017



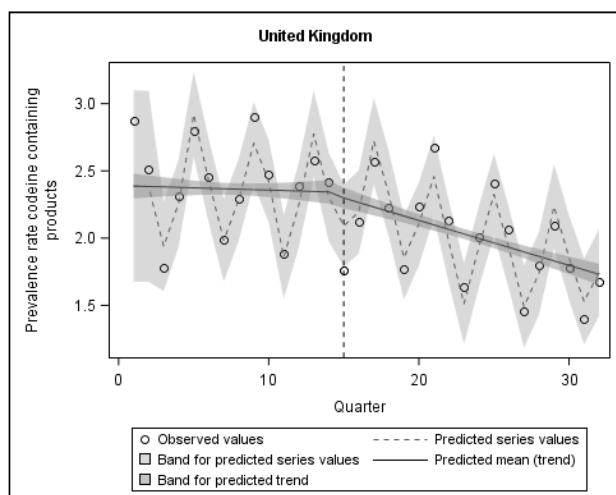
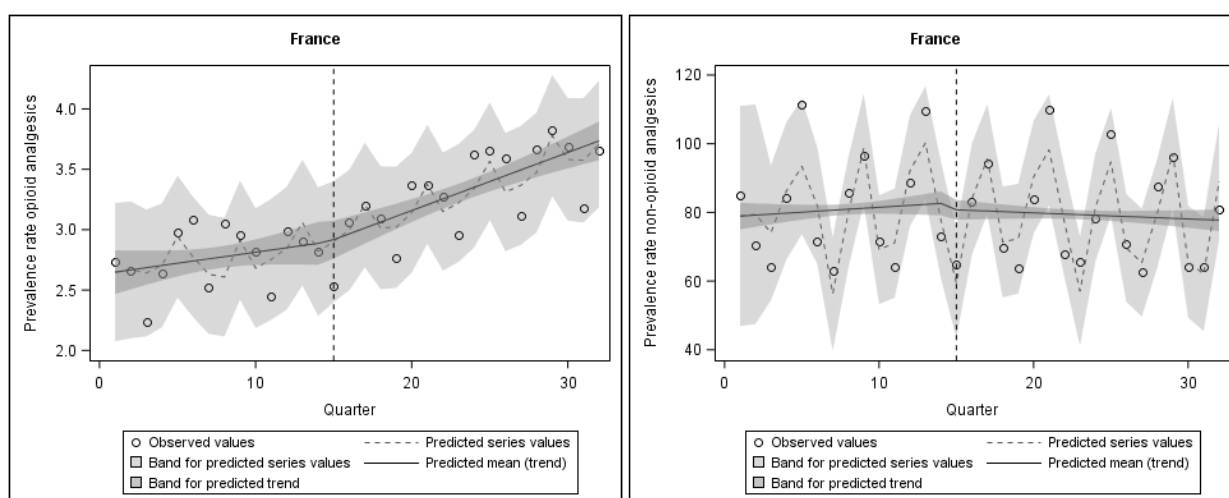


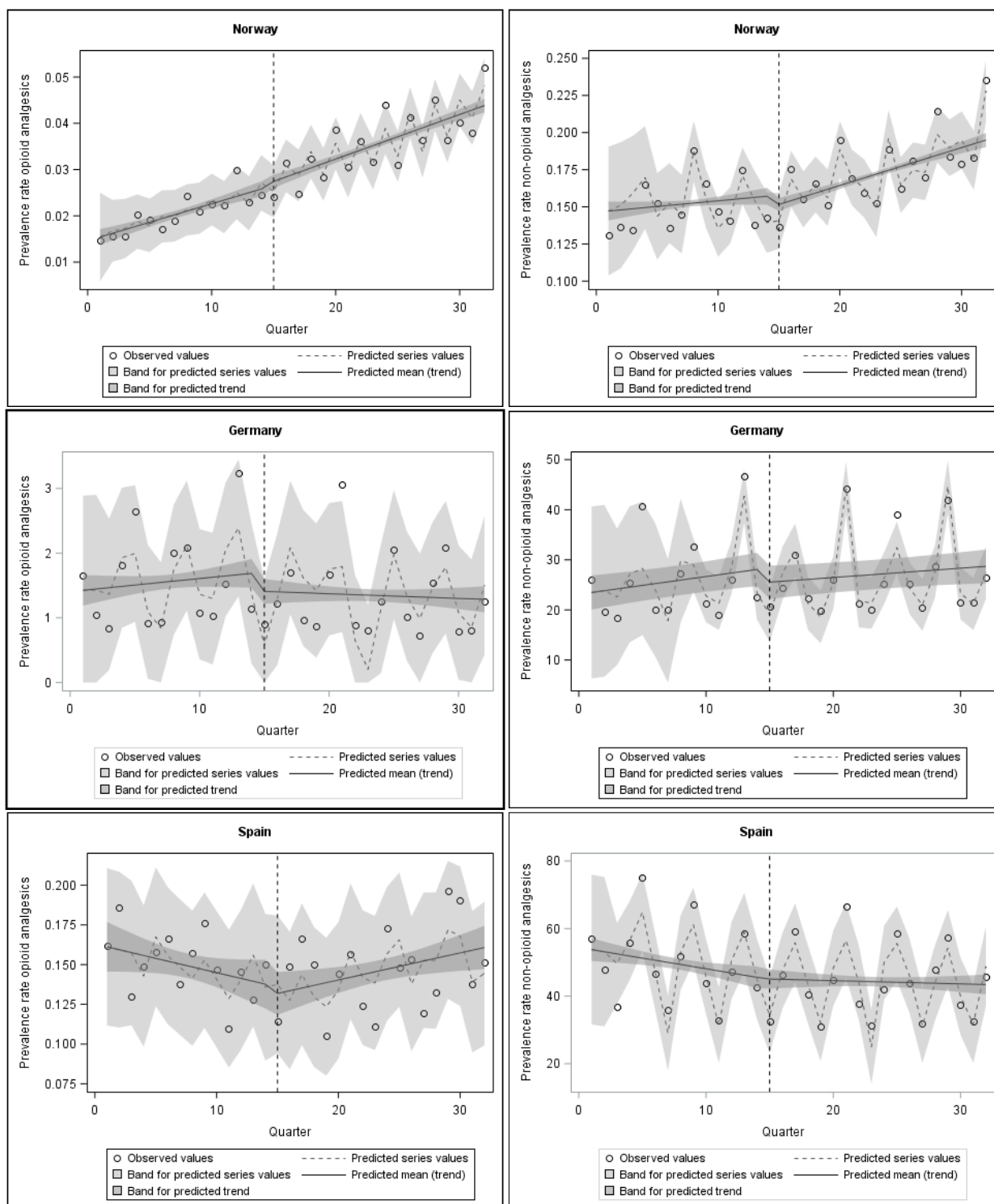
Table 1.1 Results of interruption time series analysing for trends in codeine containing products in population between 12 and 18 years of age after the pain referral (June 2013) in France, Norway, Germany, Spain and United Kingdom

	Pre-intervention trend and p-value		Change in level immediate after regulatory measure and p-value after June 2013		Change in trend postintervention compared with the baseline prescribing trend and p-value	
	Change	p-value	Change	p-value	Change	p-value
France	0.1485	< .0001	-0.8234	< .0001	-0.2314	< .0001
Norway	0.0005	0.1228	0.0015	0.5486	-0.0019	0.0003
Germany	-0.0107	0.7336	-0.4186	0.2201	-0.0455	0.2155
Spain	-0.2505	0.0009	0.0570	0.9371	0.2702	0.0016
United Kingdom	-0.0033	0.5706	-0.0116	0.8541	-0.0300	0.0001

1.2. Use of alternative treatments

Figure 1.2 Quarterly (n=32) trends in alternative medicines in France, Norway, Germany, Spain and United Kingdom between 1 January 2010 and 31 December 2017





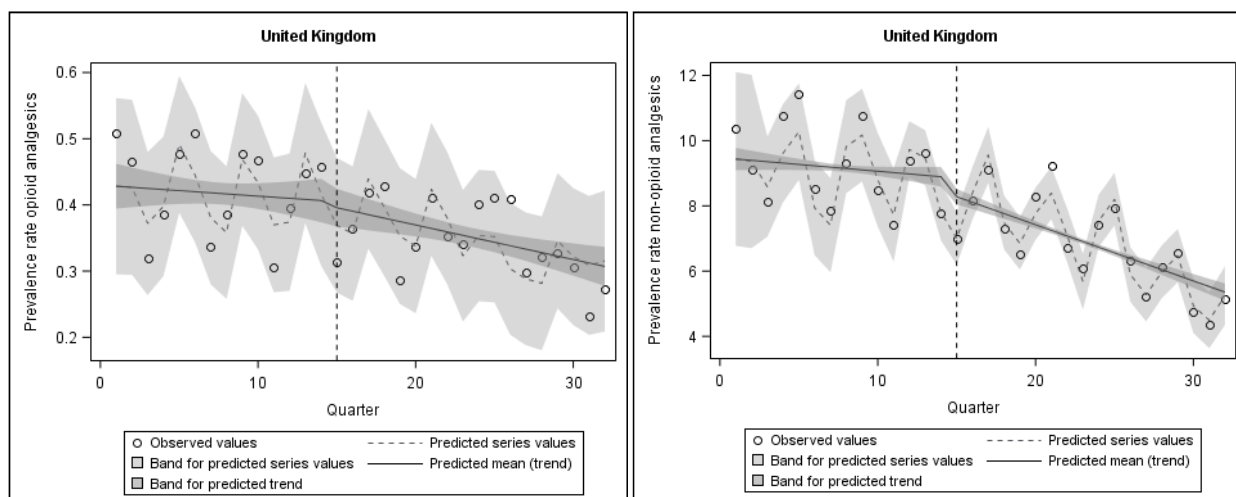


Table 1.2 Results of interruption time series analysing for trends in alternative medicine in population between 12 and 18 years of age after the pain referral (June 2013) in France, Norway, Germany, Spain and United Kingdom

	Pre-intervention trend and p-value		Change in level immediate after regulatory measure and p-value after June 2013		Change in trend postintervention compared with the baseline prescribing trend and p-value	
	Change	p-value	Change	p-value	Change	p-value
Opioid Analgesics						
France	0.0183	0.1278	-0.0171	0.8926	0.0298	0.0362
Norway	0.0008	<.0001	0.0007	0.5597	0.0002	0.1923
Germany	0.0201	0.1944	-0.2721	0.1010	-0.0273	0.1198
Spain	-0.0018	0.0848	-0.0075	0.4940	0.0035	0.0057
United Kingdom	-0.0016	0.4528	-0.0057	0.8080	-0.0035	0.1680
Non-Opioid Analgesics						
France	0.2829	0.2635	-1.6858	0.5180	-0.4599	0.0938
Norway	0.0007	0.0775	-0.0080	0.0724	0.0017	0.0002
Germany	0.3532	0.0051	-2.7184	0.0172	-0.1677	0.2585
Spain	-0.6293	0.0073	-0.4233	0.8554	0.5337	0.0408
United Kingdom	-0.0417	0.0761	-0.4418	0.0591	-0.1302	<.0001

2. Referral on cough or cold indications (June 2015)

As codeine containing products are not authorised in Norway for cough or cold indications, Norwegian data are not included in this section.

2.1. Use of codeine containing products

Figure 2.1 Quarterly (n=32) trends in codeine containing products in France, Germany, Spain and United Kingdom between 1 January 2010 and 31 December 2017

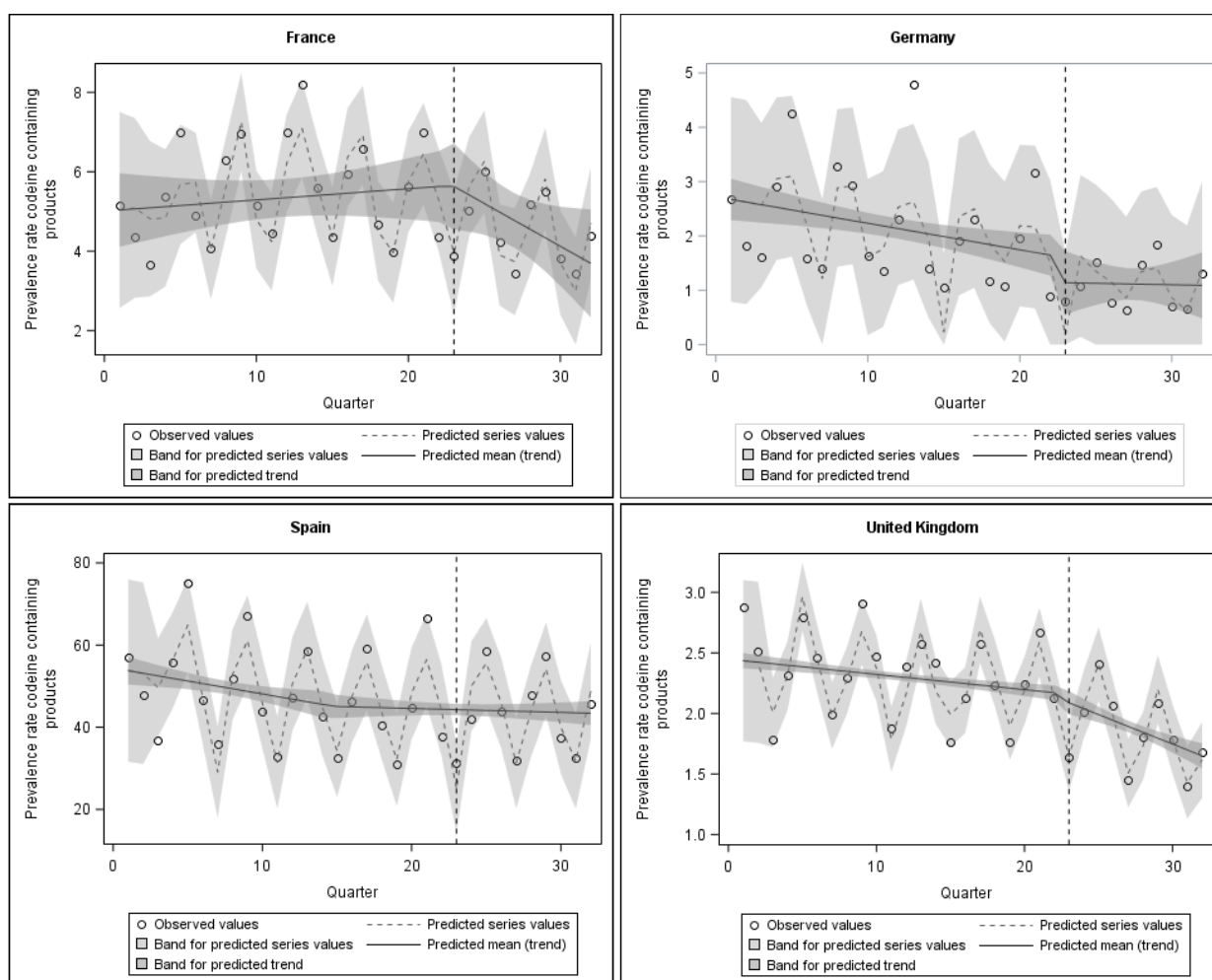
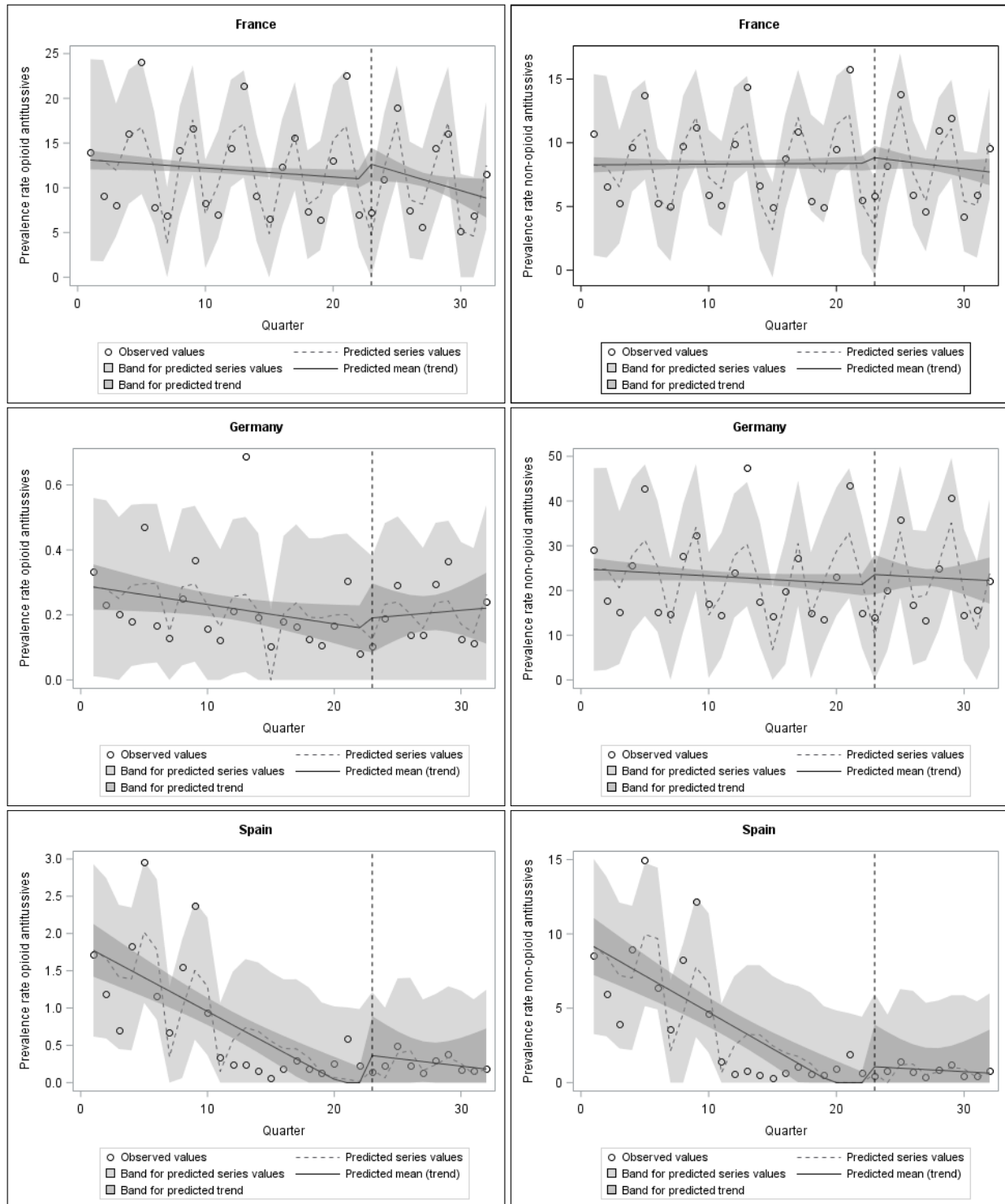


Table 2.1 Results of interruption time series analysing for trends in codeine containing products in population between 12 and 18 years of age after the cough and cold referral (April 2015) in France, Germany, Spain and United Kingdom

	Pre-intervention trend and p-value		Change in level immediate after regulatory measure and p-value after June 2013		Change in trend postintervention compared with the baseline prescribing trend and p-value	
	Change	p-value	Change	p-value	Change	p-value
France	0.0282	0.4217	0.2165	0.7025	-0.2433	0.0453
Germany	-0.0488	0.0035	-0.5026	0.2200	0.0434	0.4535
Spain	-0.1136	0.0261	0.3133	0.7463	0.1179	0.4340
United Kingdom	-0.0126	<.0001	-0.0334	0.6179	-0.0362	0.0008

2.2. Use of alternative treatments

Figure 2.2 Quarterly (n=32) trends in alternative medicine in France, Germany, Spain and United Kingdom between 1 January 2010 until 31 December 2017



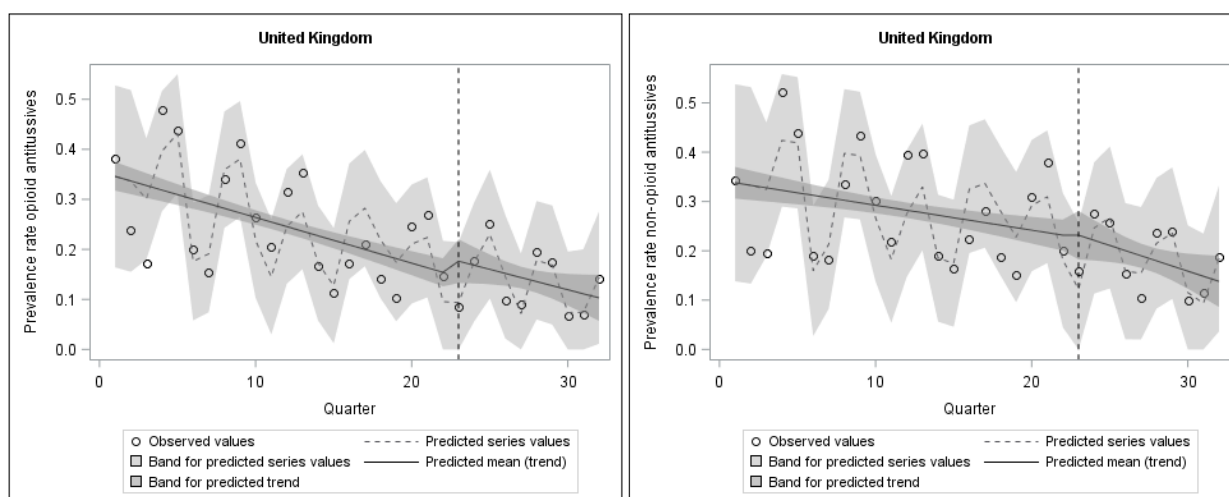


Table 2.2 Results of interruption time series analysing for trends in alternative medicine in population between 12 and 18 years of age after the cough and cold referral (April 2015) in France, Germany, Spain and United Kingdom

	Pre-intervention trend and p-value		Change in level immediate after regulatory measure and p-value after June 2013		Change in trend postintervention compared with the baseline prescribing trend and p-value	
	Change	p-value	Change	p-value	Change	p-value
Opioid Antitussives						
France	-0.0994	0.0270	2.0336	0.1325	-0.3210	0.1103
Germany	-0.0059	0.0420	0.0273	0.7099	0.0092	0.3750
Spain	-0.0910	<.0001	0.5201	0.1535	0.0709	0.1791
United Kingdom	-0.0091	<.0001	0.0303	0.3222	0.0009	0.8214
Non-Opioid Antitussives						
France	0.0056	0.8113	0.5618	0.3922	-0.1299	0.1795
Germany	-0.1610	0.1227	2.3820	0.4520	0.0141	0.9759
Spain	-0.4906	<.0001	2.2642	0.2398	0.4432	0.1199
United Kingdom	-0.0050	0.0005	0.0103	0.7622	-0.0053	0.2781