

Supplementary Table S1: Incidence of NAS (expressed as rate per 1000 live births, ‰) in the nine provinces of Castilla y Leon and the total incidence in the entire region between 2000 and 2019.

Year	Ávila	Burgos	León	Palencia	Salamanca	Segovia	Soria	Valladolid	Zamora	Castilla y león
2000	5,172	1,439	1,563	2,597	2,350	0,000	0,000	2,579	3,247	2,126
2001	0,887	1,123	2,509	1,717	2,023	0,806	1,488	2,803	2,681	1,991
2002	0,890	2,145	1,257	0,838	1,190	1,592	0,000	1,205	4,085	1,492
2003	0,000	1,065	1,236	3,322	2,303	0,000	1,355	0,926	4,122	1,451
2004	0,000	0,337	1,211	0,861	1,118	0,767	1,393	0,909	0,870	0,847
2005	0,756	0,654	0,906	1,633	0,760	0,000	0,000	0,437	1,724	0,721
2006	0,000	0,961	0,304	1,603	2,663	0,000	0,000	1,043	1,681	1,011
2007	0,000	0,000	0,853	1,656	1,083	0,000	0,000	0,633	1,748	0,648
2008	0,000	0,284	0,854	3,130	1,725	0,000	0,000	0,594	1,645	0,845
2009	0,000	0,604	0,861	0,812	1,503	0,000	0,000	0,203	0,869	0,588
2010	0,000	0,595	0,582	0,842	0,382	0,000	0,000	0,588	1,692	0,537
2011	0,000	0,000	0,000	2,445	1,132	0,000	0,000	1,472	0,000	0,655
2012	0,797	0,320	0,625	0,000	1,196	0,000	0,000	0,644	0,000	0,525
2013	0,000	1,000	0,986	1,742	0,442	0,000	0,000	1,622	0,000	0,898
2014	0,000	1,418	1,317	1,695	0,428	0,000	0,000	1,160	2,907	1,062
2015	0,000	0,362	0,330	0,000	0,427	0,000	0,000	0,477	1,032	0,345
2016	1,765	0,752	1,394	1,910	0,000	0,000	0,000	0,248	0,000	0,660
2017	0,000	0,815	0,000	0,929	0,986	0,000	0,000	0,544	2,212	0,580
2018	3,064	0,425	0,760	0,000	1,928	0,000	0,000	0,866	0,000	0,864
2019	0,000	0,000	0,422	0,000	1,552	0,000	0,000	0,608	0,000	0,419
TOTAL	0,614	0,700	0,907	1,424	1,275	0,156	0,220	0,959	1,603	0,912

Supplementary Table S2: Normalized incidence of NAS (expressed as fraction of control \equiv cumulative incidence of NAS for the entire region) in the nine provinces of Castilla y Leon between 2000 and 2019.

Year	Ávila	Burgos	León	Palencia	Salamanca	Segovia	Soria	Valladolid	Zamora	Castilla y león
2000	5,670	1,578	1,713	2,847	2,576	0	0	2,827	3,559	2,330
2001	0,972	1,231	2,751	1,882	2,217	0,884	1,631	3,073	2,939	2,182
2002	0,976	2,351	1,378	0,919	1,304	1,745	0	1,320	4,478	1,635
2003	0	1,167	1,355	3,642	2,525	0	1,485	1,015	4,518	1,591
2004	0	0,369	1,327	0,944	1,226	0,841	1,527	0,996	0,953	0,928
2005	0,829	0,717	0,993	1,790	0,833	0	0	0,479	1,890	0,790
2006	0	1,053	0,333	1,757	2,919	0	0	1,144	1,842	1,109
2007	0	0	0,936	1,815	1,187	0	0	0,694	1,916	0,710
2008	0	0,311	0,937	3,431	1,891	0	0	0,651	1,803	0,926
2009	0	0,662	0,944	0,890	1,648	0	0	0,223	0,952	0,644
2010	0	0,652	0,638	0,923	0,419	0	0	0,645	1,855	0,589
2011	0	0	0	2,680	1,240	0	0	1,613	0	0,717
2012	0,873	0,351	0,685	0	1,311	0	0	0,706	0	0,576
2013	0	1,097	1,080	1,910	0,484	0	0	1,778	0	0,984
2014	0	1,554	1,443	1,858	0,469	0	0	1,271	3,186	1,164
2015	0	0,397	0,362	0	0,468	0	0	0,523	1,131	0,378
2016	1,935	0,825	1,528	2,094	0	0	0	0,272	0	0,723
2017	0	0,894	0	1,019	1,081	0	0	0,597	2,425	0,636
2018	3,359	0,466	0,833	0	2,113	0	0	0,950	0	0,947
2019	0	0	0,463	0	1,701	0	0	0,667	0	0,459
TOTAL	0,673	0,768	0,995	1,561	1,397	0,171	0,241	1,051	1,757	1,000

Supplementary Table S3: Average incidence of NAS in Castilla y León (average \pm S.D. incidence of NAS in the nine provinces), expressed as rate per 1000 live births, ‰ between 2000 and 2019.

Year	Incidence
2000	2,105 \pm 1,614
2001	1,782 \pm 0,768
2002	1,467 \pm 1,140
2003	1,592 \pm 1,409
2004	0,830 \pm 0,432
2005	0,763 \pm 0,611
2006	0,917 \pm 0,937
2007	0,664 \pm 0,719
2008	0,915 \pm 1,067
2009	0,539 \pm 0,525
2010	0,520 \pm 0,539
2011	0,561 \pm 0,908
2012	0,398 \pm 0,440
2013	0,644 \pm 0,716
2014	0,992 \pm 0,984
2015	0,292 \pm 0,344
2016	0,674 \pm 0,809
2017	0,610 \pm 0,737
2018	0,783 \pm 1,067
2019	0,287 \pm 0,526