

Original Research

Changes in human effective population size overlap the beginning and end of a critical time in European medieval history, also characterized by the Black Death epidemic

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Supplementary Materials

Supplementary Text S1

Historical note about Black Death in Europe

New findings related to the ancient and modern DNA of *Yersinia pestis*, the bacterium that causes the plague, have provided insight into the spread of the Black Death from Asia to Europe [1–3]. Specifically, the disease is believed to have originated in Kyrgyzstan, where it is endemic in rodents [4].

Plague can be transmitted to various hosts, rodents and humans by a vector, the flea. When a flea sucks blood from an infected rodent, some of the bacteria settle in the flea's proventriculus where they multiply, preventing the flea from getting proper nourishment. The flea does not get infected, rather it becomes a healthy carrier. When the rodent dies, infected fleas seek out other hosts, including humans, regurgitating the plague carrying bacteria into their tissue [5].

The Black Death, one of the deadliest pandemics recorded in human history, arrived in Europe from Crimea in 1347 [6], possibly brought there by Tartars along the Silk Road. According to the Sicilian chronicler Michele da Piazza, who witnessed the Black Death, the disease was brought to Europe by Genoese galleys that had fled from Kaffa. It is

believed that the Tartars besieging the city, deliberately infected their Genoese enemies with plague by throwing infected dead bodies within the city walls as a form of biological warfare that was the first in human history. Within five years, chroniclers of the time reported unprecedented mortality in Europe, the Middle East, and North Africa.

If scholars now agree that the plague represented the most devastating epidemic ever to hit Europe in Medieval and Early Modern times, still many doubts remain about the forms it took, the timing of its transmission, the symptoms and the mortality levels it provoked. Shrewsbury [7] argues, for example, that in its first appearance in the mid-14th century it did not cause more than 20% of the deaths and that in England mortality was around 5%. However, it has been shown that in Cambridgeshire mortality reached 75%, while in mountainous and less densely populated Wales mortality reached much lower levels [8]. In Italy, Dubois suggests a population loss of about 55% in Albi between 1343 and 1357, while Comba [9] suggests that in that same period losses in the Susa Valley ranged between 20 and 55%. In the case of Florence and its countryside, the plague would have reduced the population between 62.9% and 67.5% [10]. The data, therefore, varies considerably from zone to zone, moreover, estimates are also difficult because the size of local and regional populations prior to 1347 are not known. The subsequent cycles of plague, on the other hand, caused, in general terms, fewer victims and took on different connotations. However, because they mainly decimated children and young individuals that were born between two plague cycles and that were thus not immunized, the cyclical recurrence of outbreaks strongly compromised population recovery and growth.

Finally, as our analyses show, from the 17th century European populations started growing again. Recent studies based on written and archaeological sources indicate that starting from the 17th century European population survival increased quite significantly compared to previous historical periods [11], challenging the traditional idea that mortality started sharply declining only after the Industrial Revolution [12]. This was possibly due to a changing human response to infectious diseases, including *Yersinia pestis*, provoked by genetic variations around immune-related genes triggered by centuries of plague epidemics, as evidenced by a very recent study on ancient DNA [13]. These first results need to be further investigated, nonetheless, it is interesting that different sources converge to the same trends.

Our analysis of populations in the 1000 Genomes repository reveals a significant demographic decline in Europe at the turn of the 14th century that lasted until at least the 16th century. We also discuss the bottleneck in the extra-European population and its peaks, although there is less or no historical data on the plague in China, South East Asia, Africa and America.

Supplementary Figures

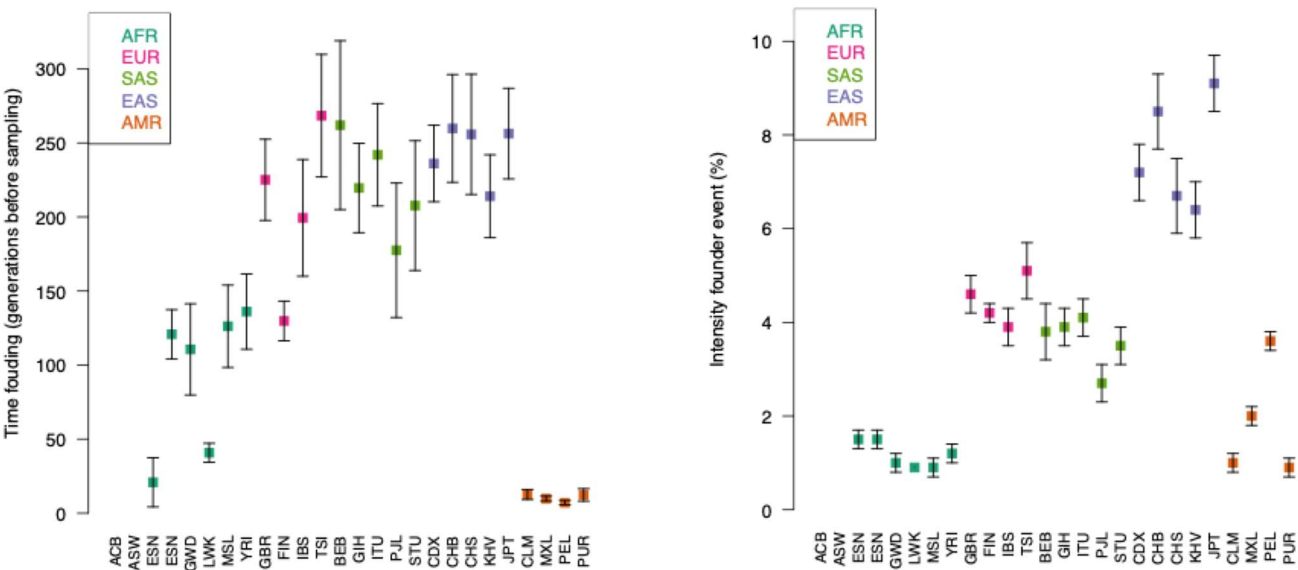


Figure S1 ASCEND analysis. On the left side is reported the timing of the bottleneck, on the right side is reported the intensity of the bottleneck (I_f), which is calculated as $I_f = D_f/2N_f$, where D_f is the duration of the bottleneck and N_f is the size of the founding population. With the exception of the Americans and two African populations (ESN and LWK), there is no evidence of a founding event in the last 50 generations. East Asian and South Asians show similar timing of the founder effect (244 and 221 generations ago respectively). European populations show a higher variability in the timing of the founding event, with TSI having the older event (268 generations ago) and FIN having the most recent one (129 generations ago). As for the intensity, Africans show the lowest levels of bottleneck intensity whereas East Asians show the highest ones.

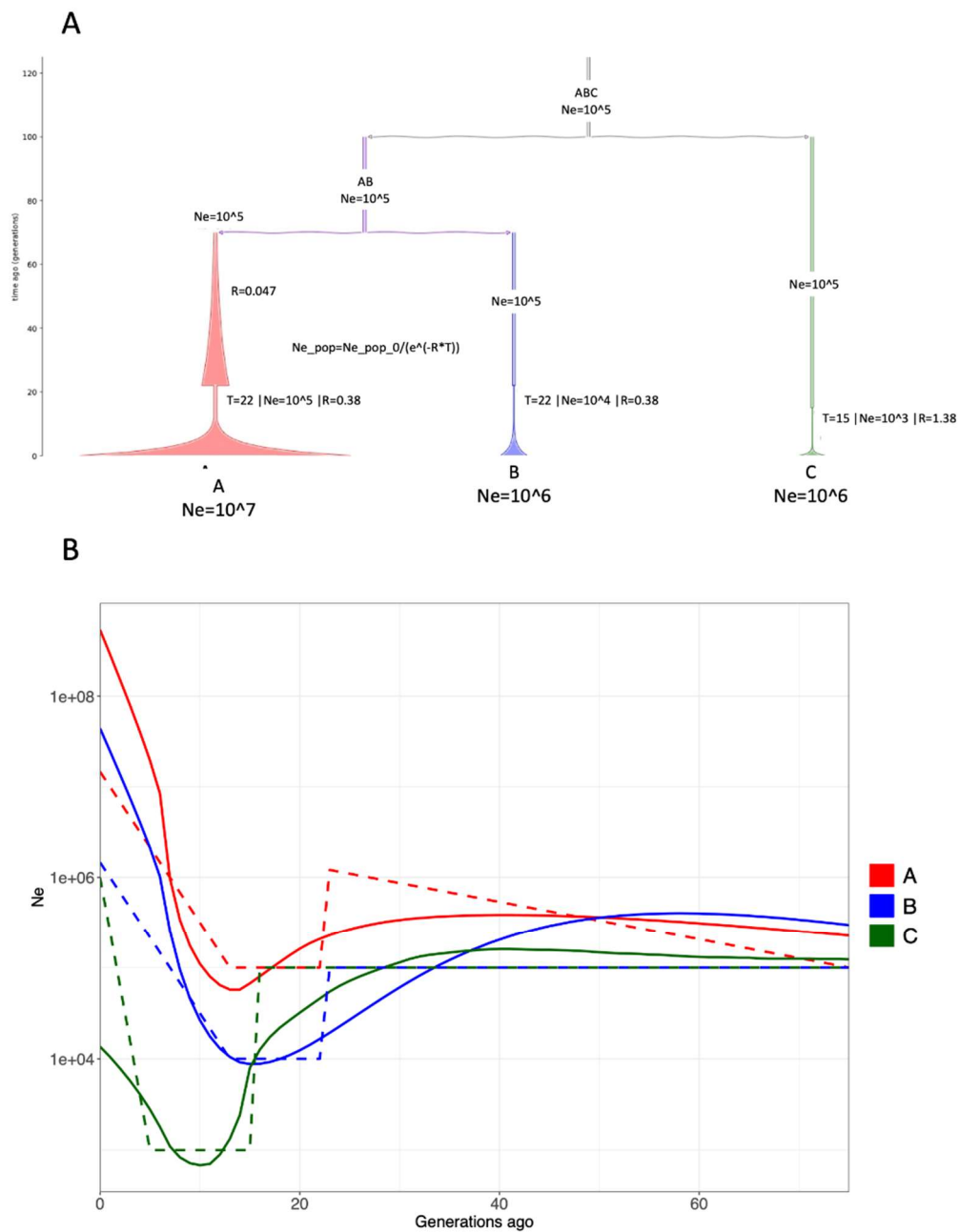


Figure S2 Coalescent simulations. (A). Simulation scheme used for msprime. (B) IBDNe curves (continuous lines) and simulated demographics (dashed lines), for estimate Ne using IBDNe we used a sample size of 100 simulated individuals. Based on simulation results we observe that peak detections are related and possibly biased by the demographic dynamics of the bottlenecks (Ne before and after the bottleneck, intensity of the bottleneck and recovery) and before the simulated peak (start of the bottleneck). Depending on demography, valleys detections seem less prone to this bias, being always later than the simulated recovery and reliable independently from demography. We could speculate that the real peaks and valleys should be always included between the estimated peaks and valleys intervals.

Supplementary Tables

Table S1 Populations sample used in the analysis.

Superpopulation	Population	Description	Outliers	Retained individuals
AFR	ACB	African Caribbean in Barbados	4	94
AFR	ASW	African Ancestry in SW USA	5	56
AFR	ESN	Esan in Nigeria	4	95
AFR	GWD	Gambian in Western Division – Mandinka	3	111
AFR	LWK	Luhya in Webuye, Kenya	5	94
AFR	MSL	Mende in Sierra Leone	6	81
AFR	YRI	Yoruba in Ibadan, Nigeria	12	103
AMR	CLM	Colombian in Medellín, Colombia	9	94
AMR	MXL	Mexican Ancestry in Los Angeles, CA USA	0	64
AMR	PEL	Peruvian in Lima Peru	6	81
AMR	PUR	Puerto Rican in Puerto Rico	3	101
EAS	CDX	Chinese Dai in Xishuangbanna, China	2	91
EAS	CHB	Han Chinese in Beijing, China	1	103
EAS	CHS	Han Chinese South	9	105
EAS	JPT	Japanese in Tokyo, Japan	0	104
EAS	KHV	Kinh in Ho Chi Minh City, Vietnam	0	99
EUR	CEU	Utah residents (CEPH)	13	95
EUR	FIN	Finnish in Finland	1	99
EUR	GBR	British From England and Scotland	4	87
EUR	IBS	Iberian Populations in Spain	2	108
EUR	TSI	Toscani in Italy	2	105
SAS	BEB	Bengali in Bangladesh	4	84
SAS	GIH	Gujarati Indians in Houston, Texas, USA	4	95
SAS	ITU	Indian Telugu in the U.K	27	72
SAS	PJL	Punjabi in Lahore, Pakistan	4	92
SAS	STU	Sri Lankan Tamil in the UK	7	95
Total			137	2408

Table S2 Results of ASCEND for all the populations included in the present study.

Region	Population	Tf	Tf_SE	Tf_CI_95high	Tf_CI_95low	If	If_SE	If_CI_95high	If_CI_95low	NRMSD
AFR	ACB	0	0	0	0	-2075.2	563.4	-3179.5	-970.9	1.17605733
AFR	ASW	0	0	0	0	-2232.4	490.7	-3194.2	-1270.6	0.70082389
AFR	ESN	120.8	8.3	104.6	137.1	1.5	0.1	1.3	1.6	0.02961718
AFR	GWD	110.6	15.4	80.4	140.8	1	0.1	0.9	1.1	0.04702696
AFR	LWK	40.8	3.2	34.5	47	0.9	0	0.8	1	0.04014475
AFR	MSL	126.2	13.9	98.9	153.5	0.9	0.1	0.8	1	0.04423023
AFR	YRI	136.1	12.7	111.3	160.9	1.2	0.1	1	1.4	0.03984009
AMR	CLM	12.6	1.7	9.3	15.8	1	0.1	0.9	1.1	0.10010957
AMR	MXL	9.8	0.8	8.3	11.3	2	0.1	1.8	2.1	0.09025837
AMR	PEL	7	0.7	5.6	8.3	3.6	0.1	3.4	3.8	0.10499635
AMR	PUR	12.3	2.1	8.2	16.4	0.9	0.1	0.8	1	0.07255546
EAS	CDX	236.1	12.9	210.9	261.4	7.2	0.3	6.7	7.7	0.01726212
EAS	CHB	259.8	18.2	224	295.5	8.5	0.4	7.7	9.3	0.01581755
EAS	CHS	255.8	20.3	216	295.6	6.7	0.4	6	7.4	0.01905817
EAS	KHV	214	14	186.6	241.3	6.4	0.3	5.8	6.9	0.01870887
EAS	JPT	256.3	15.3	226.3	286.2	9.1	0.3	8.4	9.7	0.01591675
EUR	GBR	225.1	13.7	198.2	252	4.6	0.2	4.2	5	0.02255326
EUR	FIN	129.8	6.7	116.6	142.9	4.2	0.1	4	4.5	0.02413292
EUR	IBS	199.4	19.7	160.9	237.9	3.9	0.2	3.5	4.2	0.02207384
EUR	TSI	268.4	20.7	227.8	308.9	5.1	0.3	4.6	5.6	0.01855824
SAS	BEB	262	28.5	206.2	317.9	3.8	0.3	3.3	4.3	0.02316224
SAS	GIH	219.6	15.1	190.1	249.1	3.9	0.2	3.6	4.3	0.02590092
SAS	ITU	242	17.3	208.1	276	4.1	0.2	3.6	4.6	0.02152826
SAS	PJL	177.5	22.7	133	222	2.7	0.2	2.2	3.1	0.03390385
SAS	STU	207.7	21.9	164.7	250.7	3.5	0.2	3.2	3.9	0.02840135

Tf = time of the founder event; Tf_SE = time of the founder event standard deviation; Tf_CI_95 high = time of the founder event upper bound; Tf_CI_95low = time of the founder event lower bound; If = Intensity bottleneck; If_SE = Intensity bottleneck standard deviation; If_CI_95high = Intensity bottleneck upper bound; If_CI_95low = Intensity bottleneck lower bound; NRMSD = root-mean-square deviation.

Table S3 Full data on Ne and Nc for the analyzed populations. (See attached Excel table).**Table S4** Estimation of bottleneck size and intensity estimated between the most recent Ne peaks and valleys.

Region	Population	Ne at second most recent Peak or Valley	Duration	Ne at most recent Peak or Valley	Change of Ne	Intensity (Change per generations)
AFR	ACB	3.73E+06	17	2.25E+04	-99%	-5.8%
AFR	ASW	7.89E+05	NA	NA	NA	NA
AFR	ESN	1.60E+05	35	1.21E+04	-92%	-2.6%
AFR	GWD	9.14E+04	19	8.70E+04	-5%	-0.3%
AFR	LWK	7.22E+03	50	6.03E+04	735%	14.7%
AFR	MSL	9.56E+04	45	1.91E+04	-80%	-1.8%
AFR	YRI	5.42E+05	23	1.39E+05	-74%	-3.2%
AMR	CLM	1.52E+05	25	2.20E+03	-99%	-3.9%
AMR	MXL	1.68E+05	41	3.04E+04	-82%	-2.0%
AMR	PEL	3.49E+05	10	1.82E+05	-48%	-4.8%
AMR	PUR	66100	31	1450	-98%	-3.2%
EAS	CDX	5.20E+04	15	1.11E+04	-79%	-5.2%
EAS	CHB	NA	NA	NA	NA	NA
EAS	CHS	NA	NA	NA	NA	NA
EAS	KHV	5.58E+05	9	4.23E+05	-24%	-2.7%
EAS	JPT	3.58E+07	10	8.54E+06	-76%	-7.6%
EUR	GBR	1.67E+05	40	3.32E+04	-80%	-2.0%
EUR	FIN	NA	NA	8220	NA	NA
EUR	IBS	1.50E+06	11	1.95E+05	-87%	-7.9%
EUR	TSI	158000	47	35100	-78%	-1.7%
SAS	BEB	2.83E+06	NA	NA	NA	NA
SAS	GIH	5.26E+04	8	3.28E+04	-38%	-4.7%
SAS	ITU	6.08E+05	NA	NA	NA	NA
SAS	PJL	1.98E+04	19	2.01E+05	915%	48.2%
SAS	STU	1.00E+05	53	1.52E+04	-85%	-1.6%

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