

A Bayesian Assessment of the Origins of COVID-19 Using Spatiotemporal & Zoonotic Data

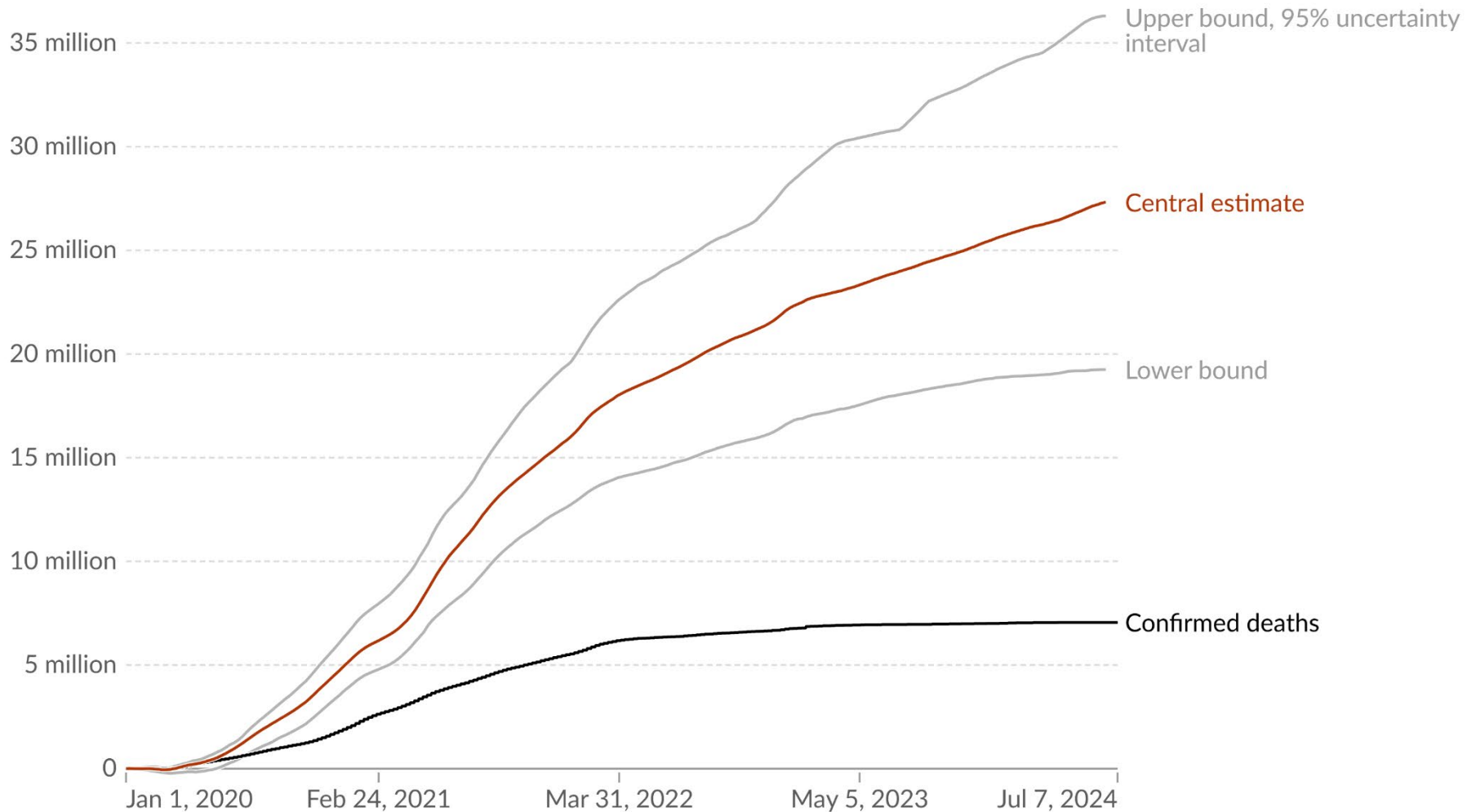
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Dartmouth College

July 2024

Note: This presentation solely reflects the views of the author and should not be interpreted as reflecting the views of any other person or institution.

Estimated cumulative excess deaths during COVID-19, World

For countries that have not reported all-cause mortality data for a given week, an estimate is shown, with uncertainty interval. If reported data is available, that value only is shown. For comparison, cumulative confirmed COVID-19 deaths are shown.





Source: BBC (Jan. 2020)

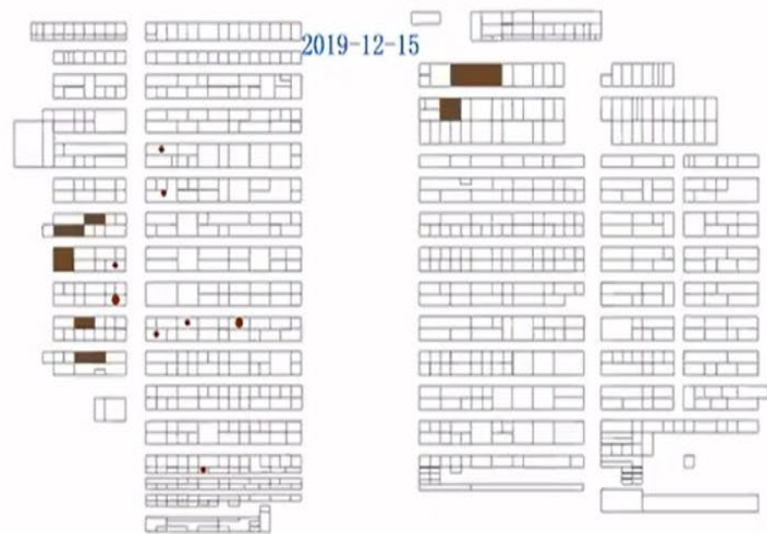


Source: Yahoo News (2020)

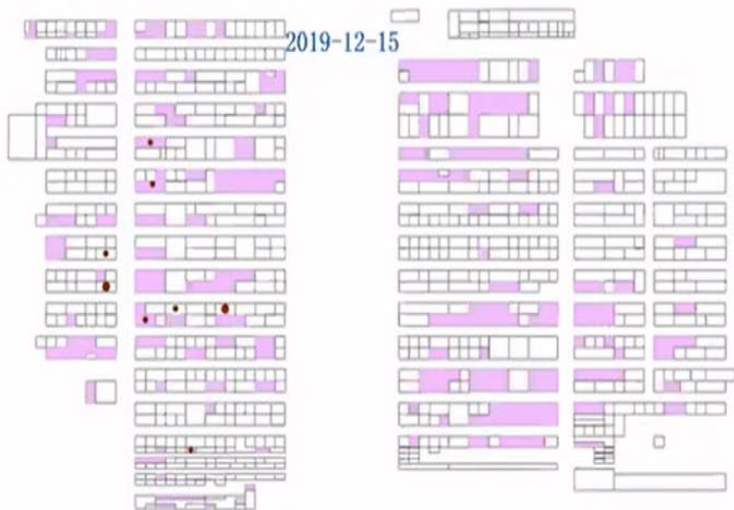




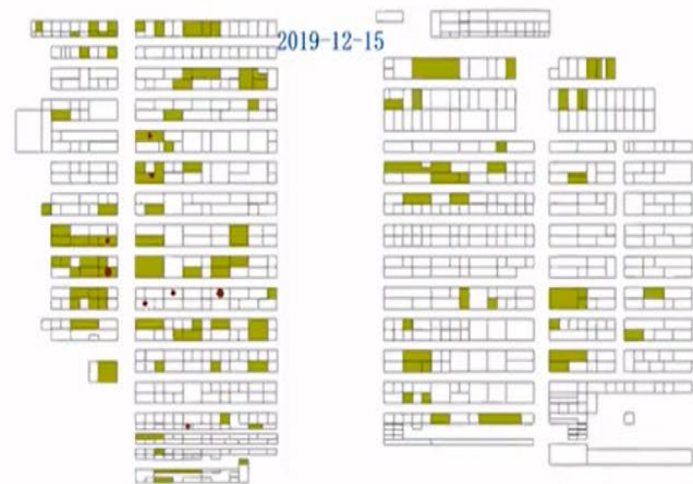
Aquatic products



Wild animal meat



Meat



Poultry

Source: WHO via online seminar by Dr. Marion Koopmans (June 2021)

大众畜牧野味

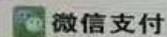


品名	价格	品名	价格	品名	价格	品名	价格	品名	价格	品名	价格		
活孔雀	500/g	活鸭豚		活蝎子	500	狐狸肉	45	活豚鼠	40	鹿 脯	38	鳄鱼尾	45
孔雀肉	350/g	活珍珠鸡		活蜗牛	15	活狼仔	75	活荷兰猪	40	鹿 血	100/g	鳄鱼掌	60
活大雁	120	活贵妃鸡		蜗牛肉	30	狼仔肉	20/45	活藏香猪	30	鹿 筋	100	鳄鱼鞭	40/g
大雁肉	15	鹧 鸪	15/g	蜂 蛹	150	活果子狸	130	活豪猪	45	干鹿筋	150	鳄鱼肚	30
去骨大雁肉	15	土 鸽	18/g	蚕 蛹	15	果子狸肉	70	活湘猪	30	鹿 茸	1500	鳄鱼舌	35
活鸿雁		铁 雀		蚂 蚱	100/g	活刺猬	18	香猪肉	75	鹿里脊	50	鳄鱼肠	30
活火鸡	28	活白鹅		木 虫		刺猬肉	8/g	牦牛肉	30	袋装鹿肉	30	活鳄鱼龟	25
活斗鸡	500/g	香椿鸟	15/g	竹 虫	75	活狗狸獾	25	牦牛掌	45	鹿 鞭	400/g	活山龟	90
活野鸡	60	活鸵鸟	4000/g	活竹鼠	85	活猪狸獾	28	骆驼肉	30	鹿 排	38	活山瑞甲龟	55
野鸡肉	25/g	鸵鸟肉	45	竹鼠肉	75	花猪肉	25	骆驼掌	45	活麂子	55	活水貂	500/g
斑 鸠	18/g	鸵鸟掌	80	活麝香鼠		活石头猪	30	骆驼峰	20	麂子肉	40	活树熊	70
竹 鸡	15/g	鸵鸟肾	45	活青根貂	60	狍子肉	25	活梅花鹿	50	娃娃鱼苗	60/g	带皮乌梢蛇	60
藏 鸡	90/g	鸵鸟蛋	150/g	活海狸鼠	30	杂交野猪肉	15	小活鹿	6000/g	活娃娃鱼	65	去皮乌梢蛇	60
线 鸡		野山羊	40/g	袋鼠肉		野猪肚	120	鹿白条	35	活鳄鱼	40	大蛇条肉	40
育椋鸟	15/g	毛野兔	25	松鼠肉		活野猪	25	冷鲜鹿肉	38	鳄鱼肉	40	活海蛇	220
蜈 蚣	5/g	金 蝉	70	活狐狸	500/g	野猪肉	26	鹿 腿	40	鳄鱼苗	250/g	活虎纹蛙	



活杀现宰 速冻冰鲜 送货上门 代办长途托运

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 建设银行支行 6217002870007563156 邮政 6221885200231709074
 微信：13647233858 支付宝：13647233858



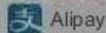
@阎小骏

Source: JustTheNews (Jan. 2020)

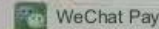
▼ Popular Livestock and Game



Product name	price	Product name	price	Product name	price	Product name	price	Product name	price	Product name	price		
live peacock	500/2	live pig		live scorpion	500	Fox meat	45	live guinea pig	440	Belly	38	Alligator Tail	45
Peacock meat	350/2	live guinea fowl		live snail	15	live wolf cub	75	live guinea pig	440	100 bags of leg blood		Crocodile Hall	60
live wild geese	120	Live royal chicken		snail meat	30	Wolf cub meat 2044		Live Tibetan Pig	30	deer muscle	100	Scipes Whip	40
Wild goose meat	15	partridge	5/2	bee pupa	150	live civet	130	live porcupine	45	Chikasuji	150		30
Boneless bacon	15	Dove	18/2	ant pupa	15	civet meat	70	Live Hunan pig	30	deer antler	1500	crocodile tongue	35
Live swan geese		iron sparrow		ant	100/2	live hedgehog	18	Fragrant Pork	75	Kariji	50	Alligator intestines	30
live turkey	28	live white goose		woodworm		Hedgehog meat	8/2	Yak meat	30	Sagged venison	30	live crocodile turtle water	
live fighting cock	50	toon bird	15/2	bamboo insect	75	live dog badger	25	Yak paw	45	deer whip	4	Live mountain fish	90
live pheasant	60	live ostrich	4000 sq. ft.	live bamboo rat	85	live pig badger	28	camel meat	30	deer steak	38	Live beech turtle	55
pheasant meat	25 pairs	Ostrich meat	45	Bamboo rat meat	75	pork belly	75	camel paw	45	living muntjac	55	live mink	500/2
Ikaruga	18/2	frozen ostrich Palm	80	live muskrat		live stone pig	30	camel hump	20	Reiko meat	40	live koala	70
There are many bamboo sticks		ostrich skin	45	live greenwood snake	60	Roe deer meat	75	live sika deer	50	Salmon fry	60/2	skinned mink	60
Tibetan Chicken	90/2	ostrich Egg	150	live nutria	30	hybrid wild boar	15	small live deer	6000/1	live salamander	65	Red the black snake	60
Line chicken		wild goat	40	Frozen kangaroo meat		wild boar Belly Deer White Strips	35	live crocodile	40	live crocodile	40	Large snake meat	40
Breeding bird	15/and	Hairy Hare	25	squirrel meat		live wild boar	75	Chilled venison	38	crocodile meat	40	live sea snake	220
Centipede	5th floor	golden cicada	70	live fox	500/2	wild boar	26	deer leg	40	crocodile seedlings	250/2	Live tiger palm baby	



Kill alive and kill quickly Frozen Delivery Long-distance shipping agency



Address: No. 7-13, Haifu Street, East District (11th Street), South China Seafood Market, Hankou Railway Station, Wuhan City, Hubei Province

Tel: 027-65658441 13647233858 13907129699 Website www.whdaz.com

Industrial and Commercial Bank of China Harbei Branch 6222083202014342311 Wuhan Agricultural Xinhua Branch 6228480050741706217

China Construction Bank Branch 6217002870007563156 Postal Service 6221885200231709074

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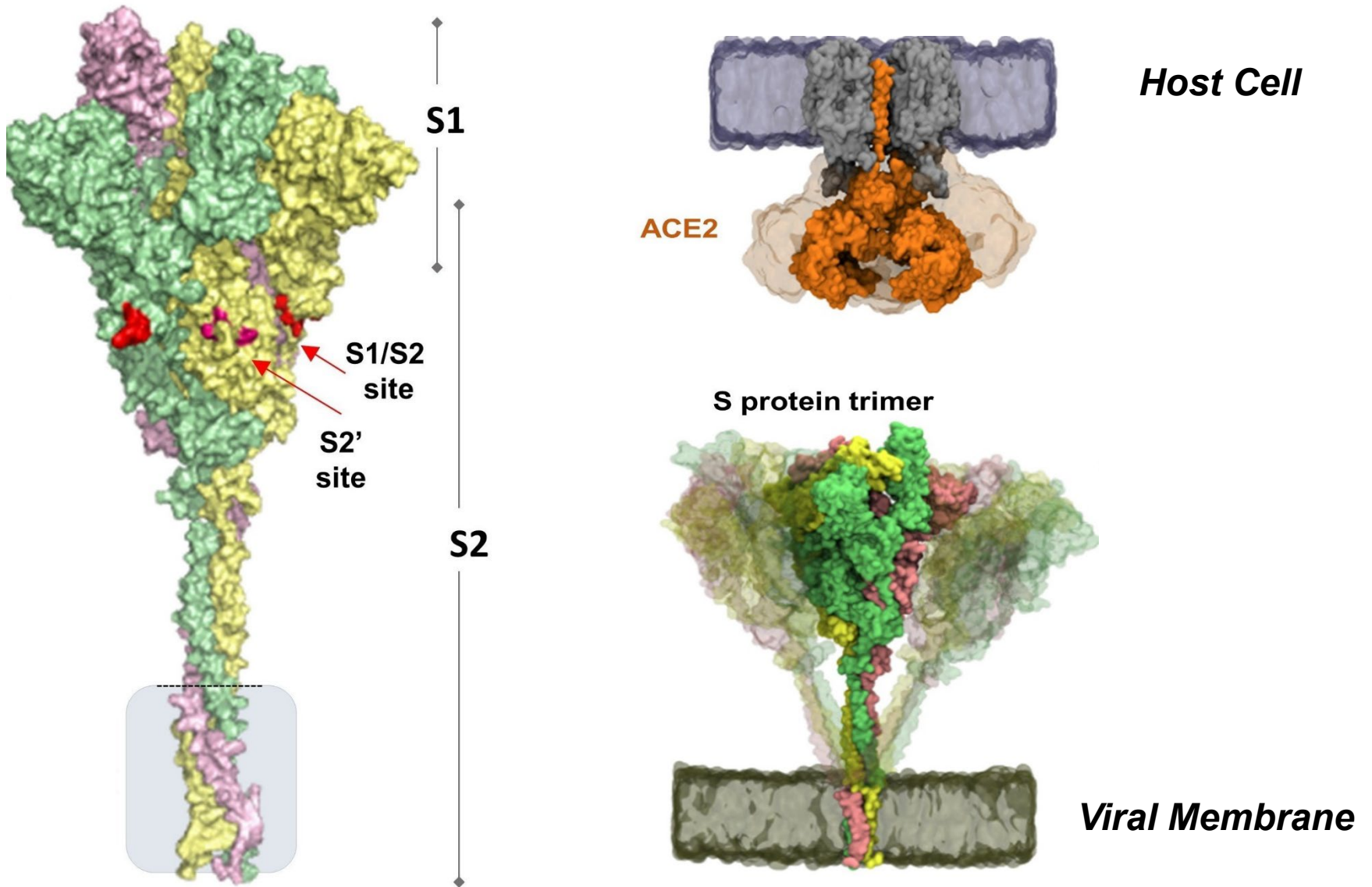
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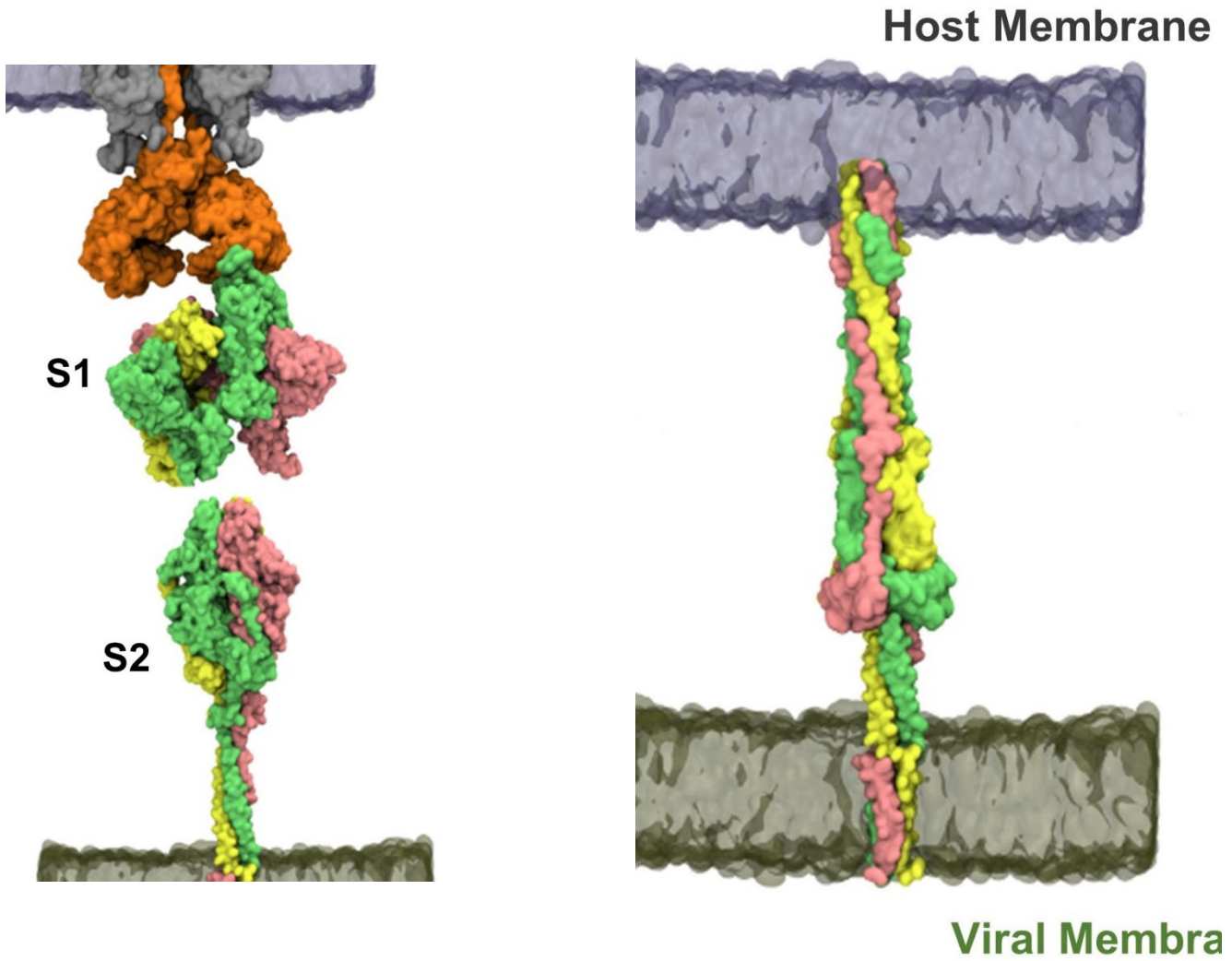
Source: Dr. Edward Holmes (2014)



Source: Kaarina Kauhala (2022)



Source: Raghuvamsi et al. (2021)



Source: Raghuvamsi et al. (2021)

Comparing Genomes of Three Species

<u>Genetic Sequence</u>	<u># Nucleotides</u>	<u>Relative Scale</u>	<u>Relative Size</u>
<i>Homo sapiens</i>	3,000,000,000	Earth to Moon	400,000 km
<i>E. Coli</i> bacteria	4,600,000	San Francisco to Los Angeles	560 km
<i>Sars-Cov-2</i> virus	29,900	Lincoln Memorial to U.S. Capitol	4 km
<i>Spike</i> gene	3,822	Hoover Tower to Green Library	500 m
<i>Furin cleavage</i> site	4	PC keyboard	0.5 m



The 2020 Nobel Prize for Chemistry was awarded to Jennifer Doudna and Emmanuelle Charpentier for the CRISPR/Cas9 gene editing method developed in 2012.

Wuhan Institute of Virology



Source: New York Times (2021)

Two Competing Hypotheses

- **Hypothesis A:** The pandemic was triggered by an accidental lab leak of a bat-related coronavirus.
- **Hypothesis Z:** The pandemic was triggered by a zoonotic spillover from a wild animal that was an intermediate host for a bat-related coronavirus.

Bayesian Analysis

$$POSTERIOR_ODDS_{AZ} = PRIOR_ODDS_{AZ} * BF_1 * BF_2 * BF_3 * BF_4$$

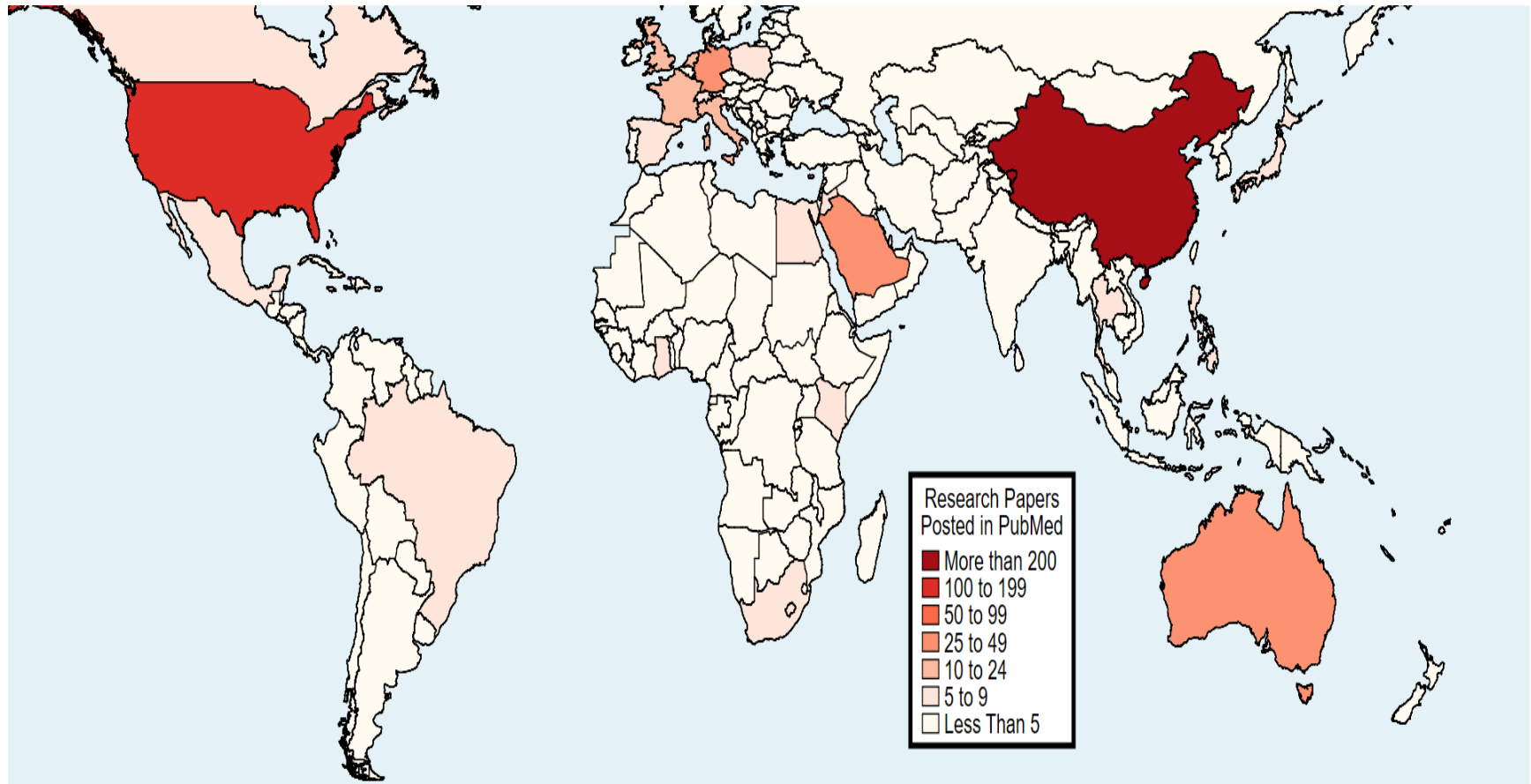
where $BF_i = \text{Marginal Likelihood}_{A_i} / \text{Marginal Likelihood}_{Z_i}$

- **Component #1:** The marginal likelihood that the pandemic outbreak would be observed in PRC under each hypothesis.
- **Component #2:** The marginal likelihood that the pandemic outbreak would be observed in Wuhan, conditional on its occurrence in PRC, under each hypothesis.
- **Component #3:** The marginal likelihood of observing the spatiotemporal pattern of early COVID cases at Huanan Market, conditional on an outbreak in Wuhan, under each hypothesis.
- **Component #4:** The marginal likelihood of observing the pattern of early COVID cases unlinked to Huanan market, conditional on the outbreak occurring in Wuhan, under each hypothesis.

Why Did the Pandemic Start in PRC?

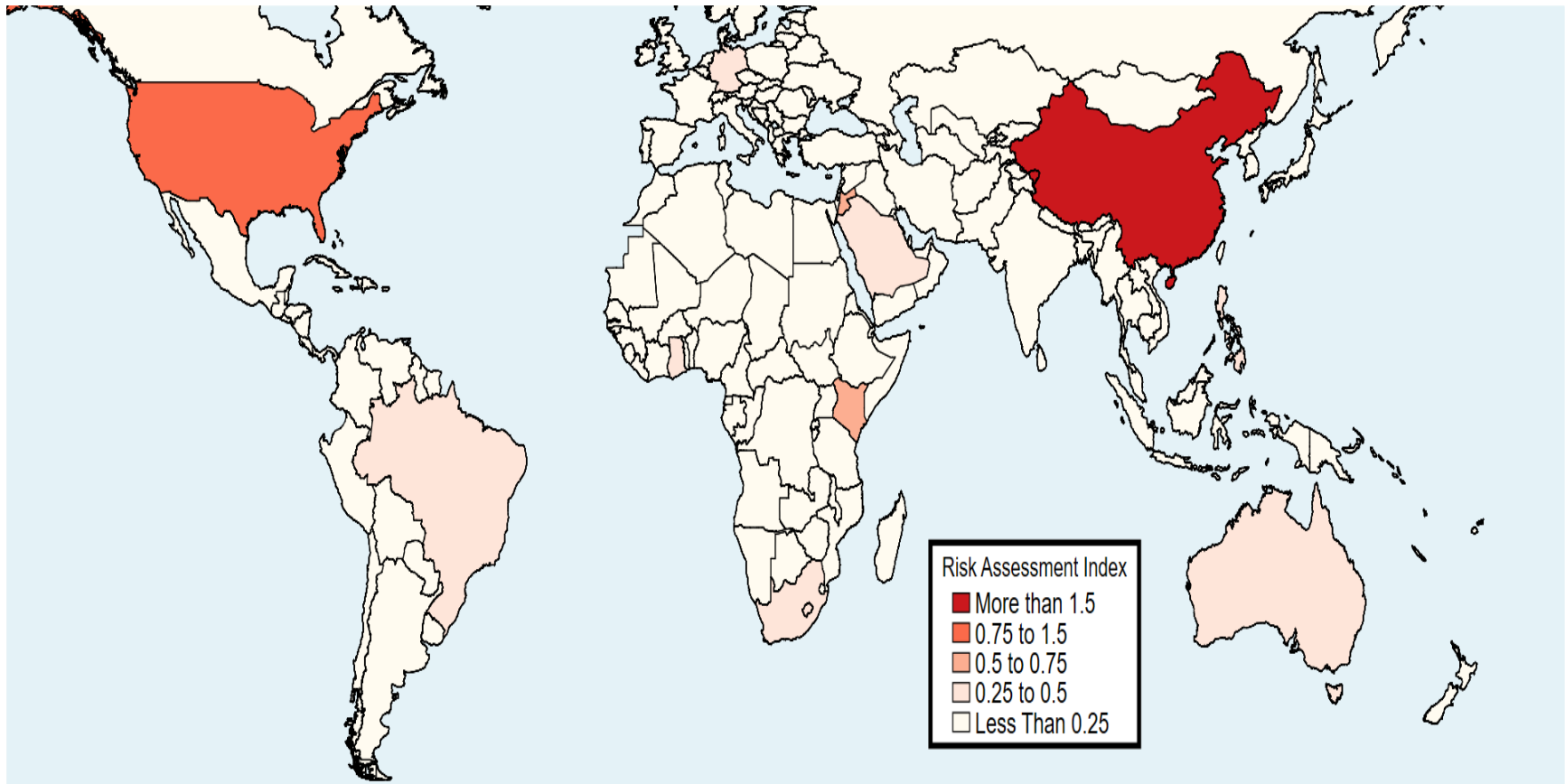
- **Hypothesis A:** Assess the global distribution of research on bat-related coronaviruses as well as cross-country differences in biosafety standards.
- **Hypothesis Z:** Assess the global distribution of bat species identified as hosts of betacoronaviruses, particularly MERS-related and SARS-related viruses.

The Global Distribution of Research on Bat-Related Coronaviruses



Source: Phelps et al. (2019)

The Global Distribution of Risks of Bat-Related Viral Research



Source: Author's calculations

The Global Distribution of Risks of Bat-Related Viral Research

Country	Country-Specific Indicators			Share of Global Total (%)		
	<u>Papers in PubMed</u>	<u>GDP Per Capita (\$)</u>	<u>Risk Index</u>	<u>Papers in PubMed</u>	<u>Risk Index</u>	<u>Non-US Risk</u>
PRC	206	18,465	6.01	33.7	50.3	54.9
USA	129	69,459	1.00	21.1	8.4	---
Kenya	6	5,197	0.62	1.0	5.2	5.7
Jordan	9	9,265	0.52	1.5	4.4	4.8
Ghana	5	6,454	0.42	0.8	3.5	3.8
Saudi Arabia	32	47,298	0.36	5.2	3.1	3.3
Australia	34	57,188	0.32	5.6	2.7	2.9
South Africa	8	14,718	0.29	1.3	2.5	2.7
Philippines	5	9,489	0.28	0.8	2.4	2.6
Germany	32	62,507	0.28	5.2	2.3	2.5

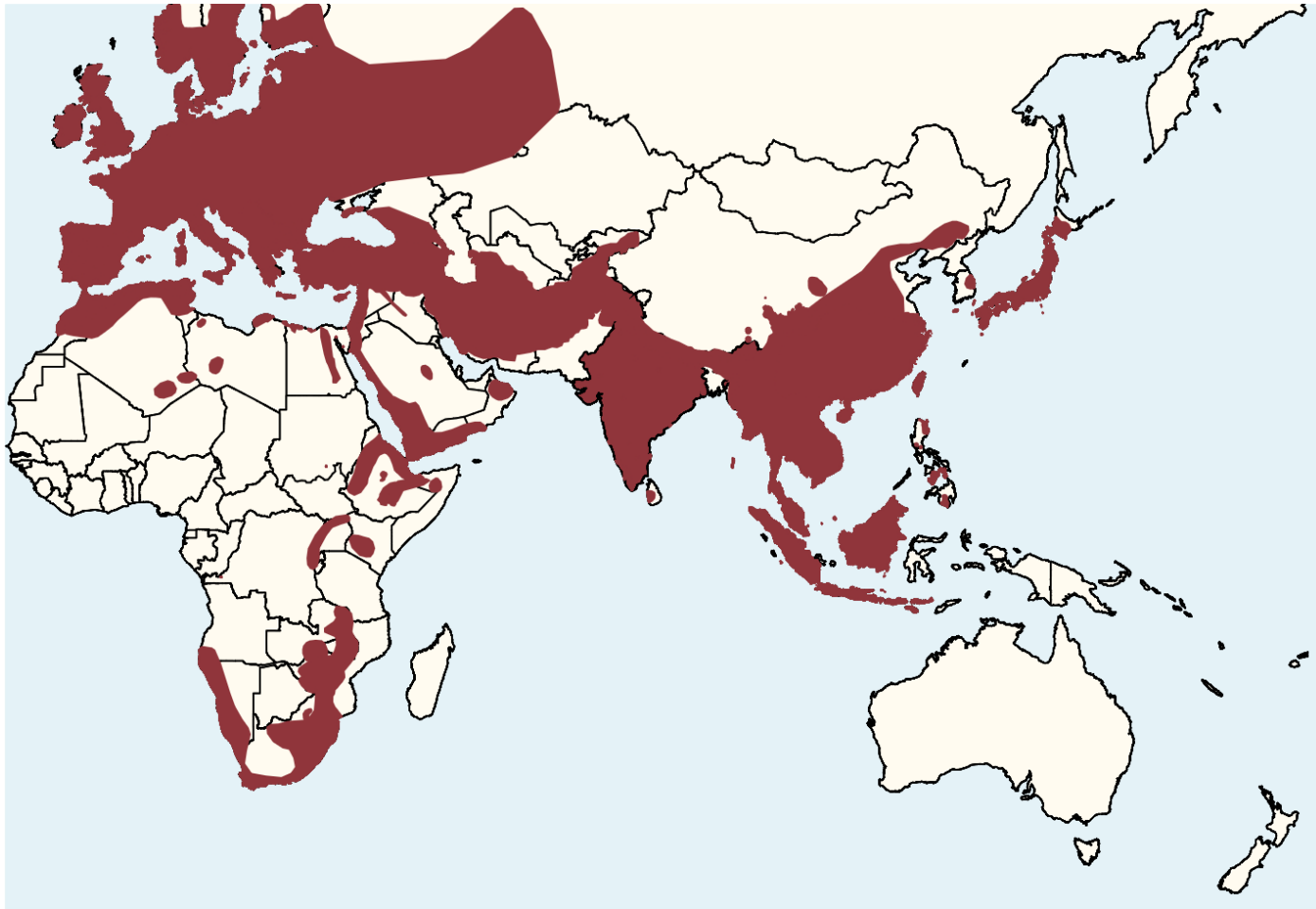
Source: Author's calculations

The Global Distribution of Bat Species with MERS-Related Viruses



Source: Frutos et al. (2021), Wu et al. (2023), IUCN RedList

The Global Distribution of Bat Species with SARS-Related Viruses



Source: Frutos et al. (2021), Wu et al. (2023), IUCN RedList

Assessing the Risk of a Bat-Related Zoonotic Outbreak in PRC

Geographic Range of Bat Host Species	Population in 2019 (millions)		Ratio (%)
	PRC	Total	
All Coronaviruses	1,415.9	7,742.3	18.3
SARS-Related Viruses	1,009.8	5,207.9	19.4
MERS-Related Viruses	1,415.9	7,134.3	19.8

Source: Author's calculations

Why Did the Pandemic Start in Wuhan?

- **Hypothesis A:** Assess the geographic distribution of research on bat-related coronaviruses in PRC.
- **Hypothesis Z:** Assess the geographic distribution of wild and farmed raccoon dogs in PRC.

Bat-Related Viral Research in Wuhan

- During 2011-2013 WIV led expeditions to an abandoned mineshaft in Yunnan province (just a short distance from China's southern border with Laos and Vietnam), where they collected fecal swabs from six species of bats and identified several novel SARS-like virus.
- WIV conducted molecular analysis showing that these viruses were highly similar to the SARS-CoV virus, with nucleotide sequence identity of 95 to 96%.
- WIV researchers used cutting-edge methods to modify viral genomes, produce chimeras and cDNA clones, and compare the *in vitro* efficiency of viral variants using cell cultures.
- WIV's work was generally performed in BSL-2 labs, although one study involving international coauthors was conducted using a BSL-3 lab.
- Wuhan had an agglomeration of other researchers engaged in collecting specimens and molecular analysis of bat-related viruses.

Wild Raccoon Dogs



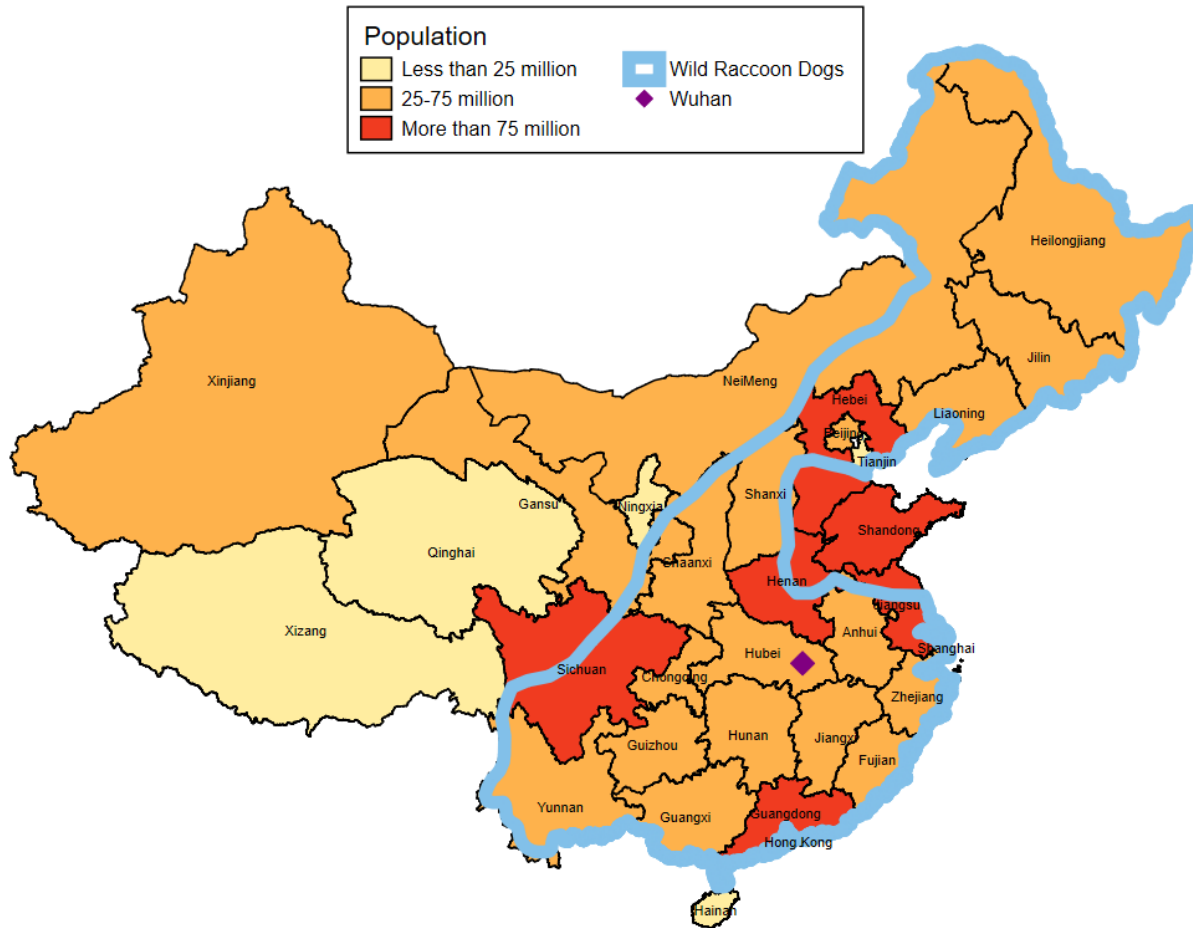
Source: Kaarina Kauhala (2022)

Wild Raccoon Dogs



Source: Kaarina Kauhala (2022)

The Range of Wild Raccoon Dogs in PRC

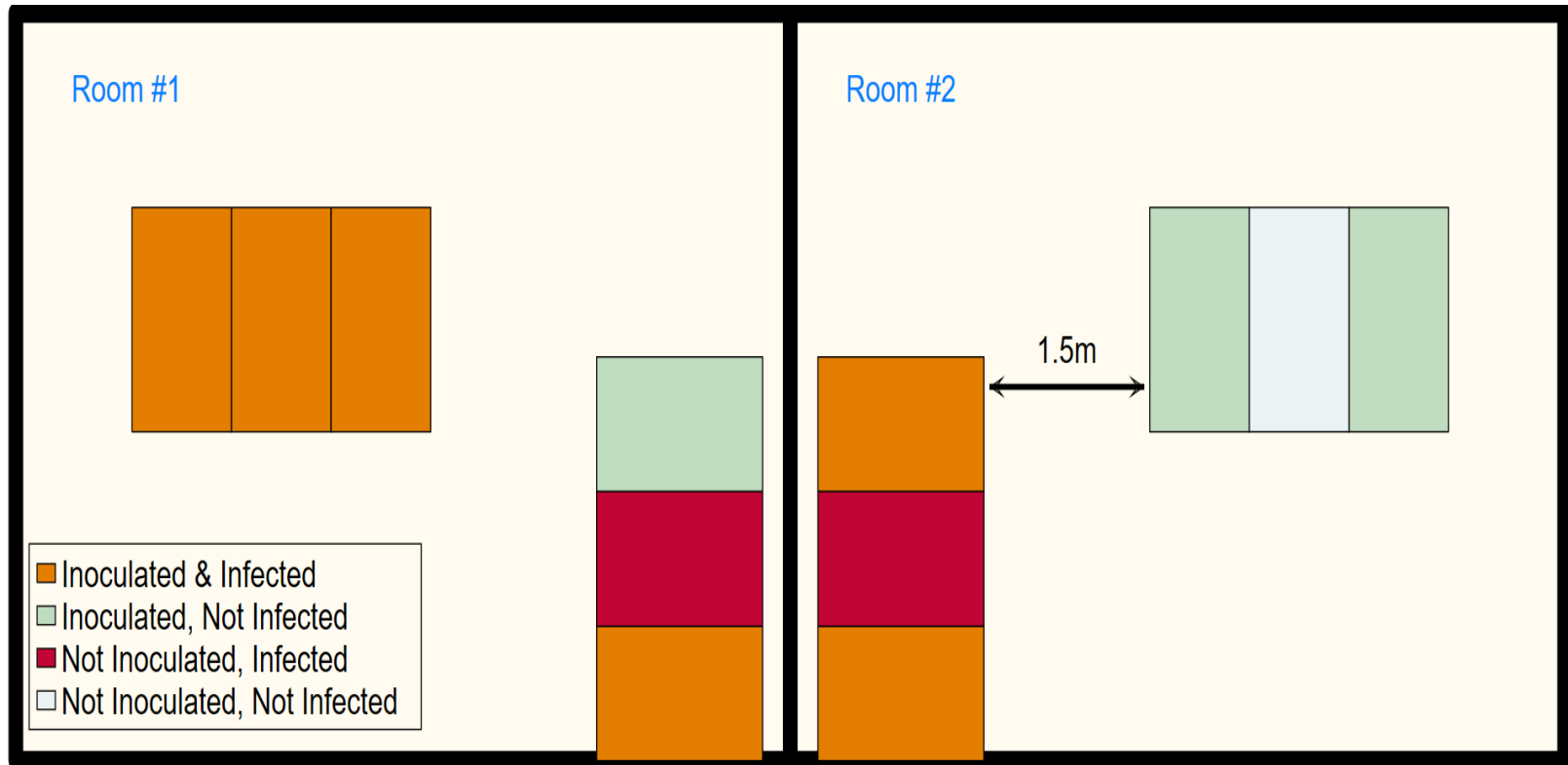


Source: IUCN Redlist data compiled by Kauhala & Saeki (2015)

Friederich Loeffler Laboratory Insel Reims, Germany



SARS-CoV-2 Infection and Transmissibility in Raccoon Dogs



Source: Freuling et al. (2021)

Raccoon Dogs on Fur Farms



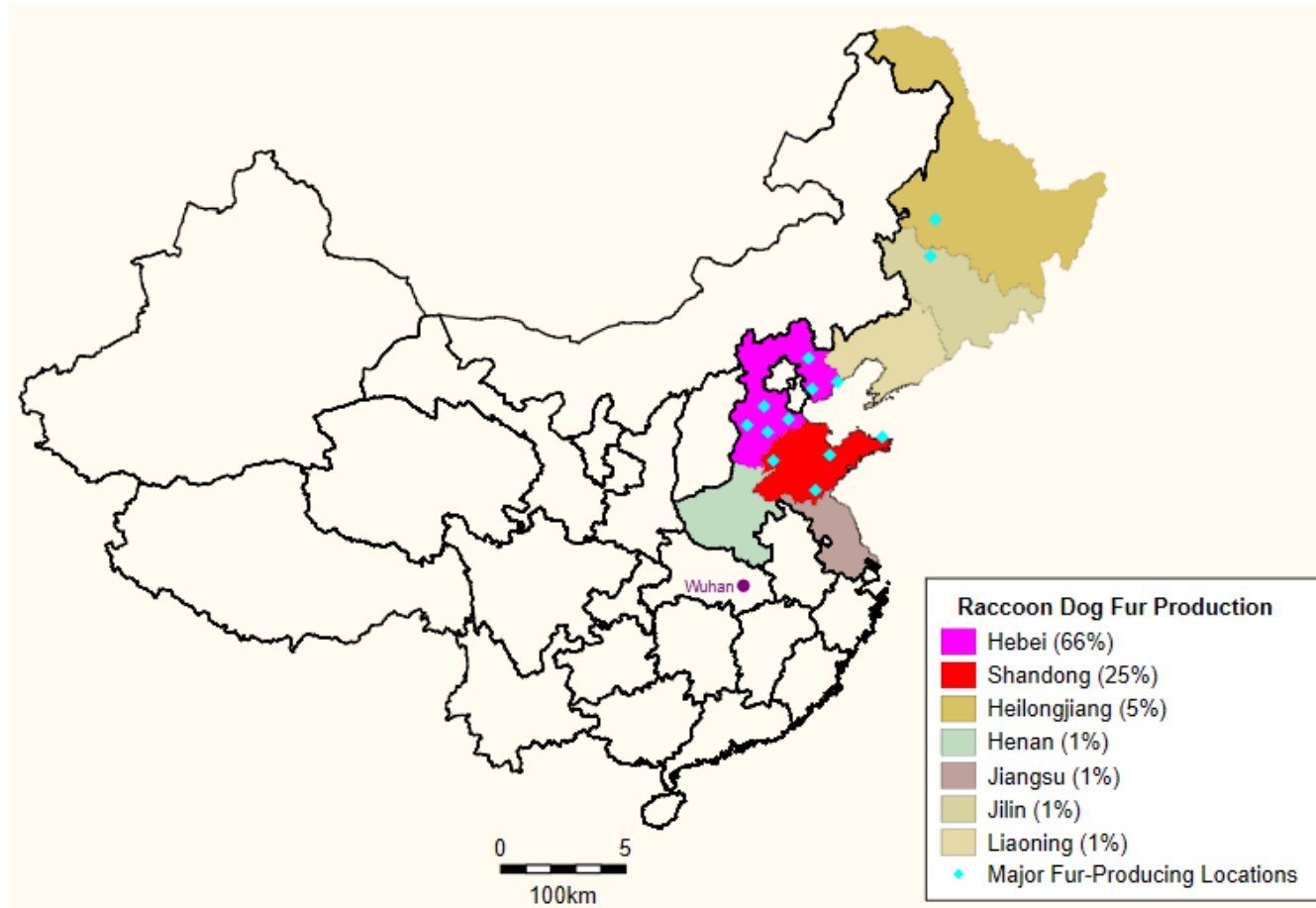
Source: ActAsia (2018)

Raccoon Dogs on Fur Farms



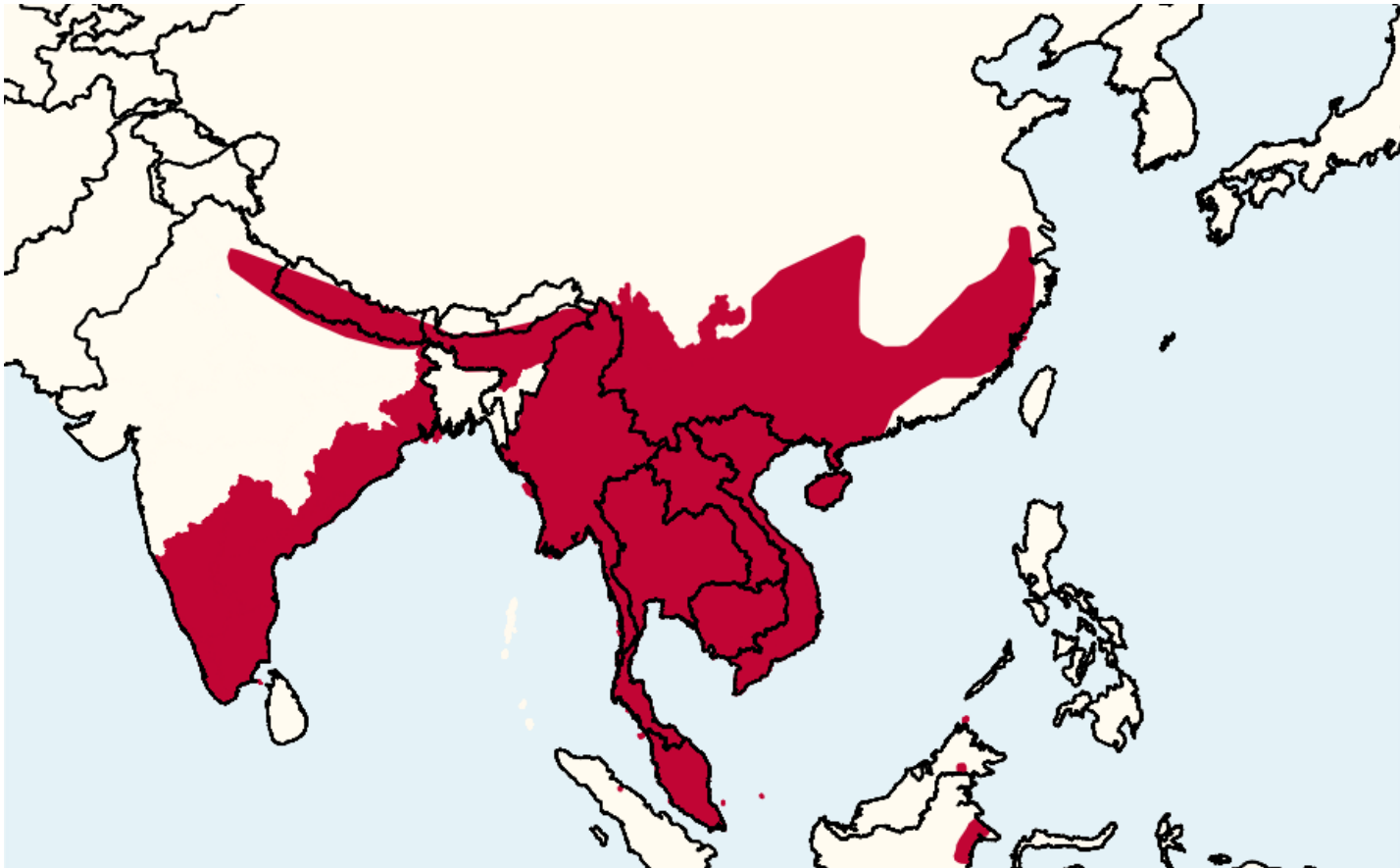
Source: ActAsia (2018)

The Geographical Distribution of Raccoon Dog Fur Farms in PRC



Source: China Leather Industry Association data for 2019

The Distribution of Bat Species with SARS-CoV-2 Related Viruses

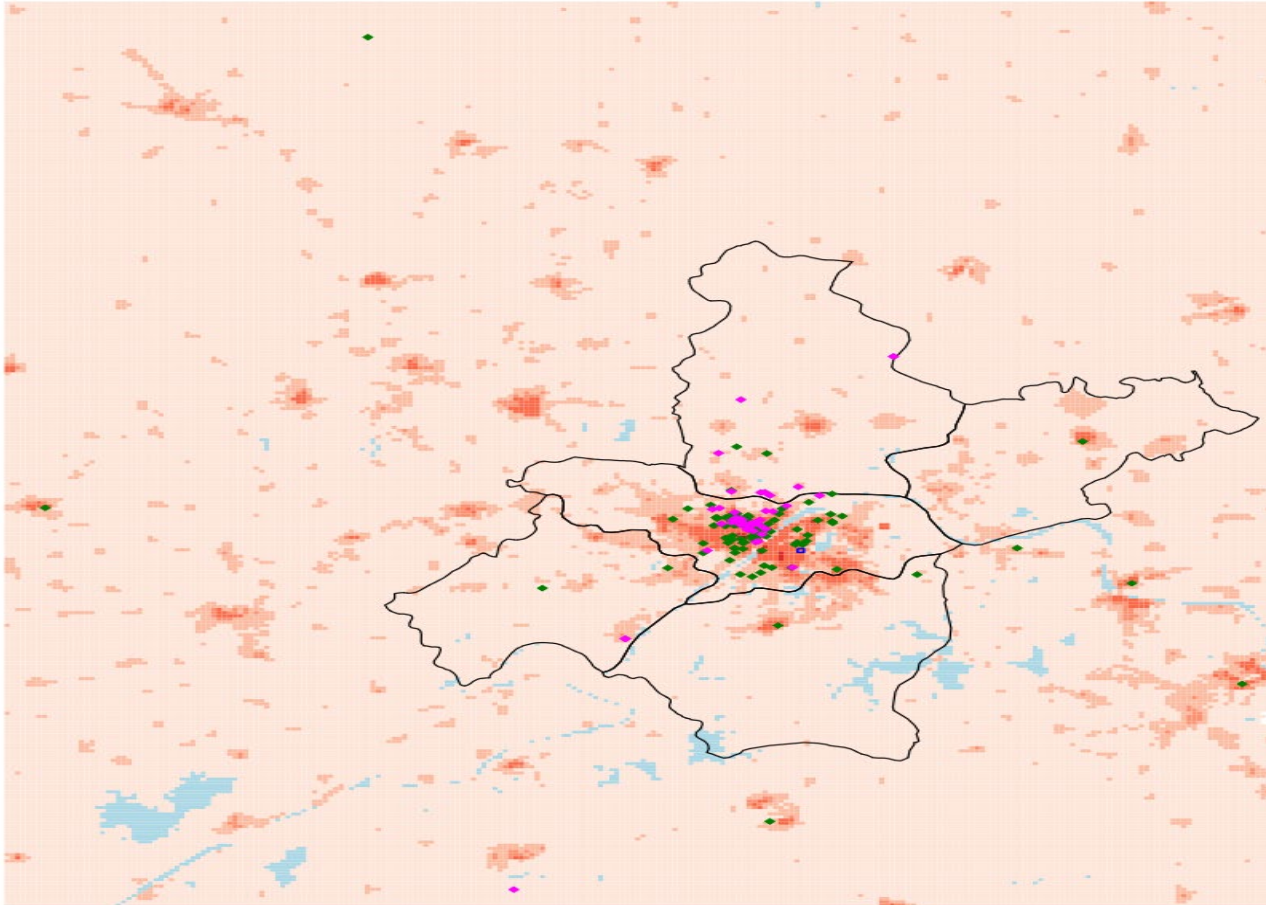


Source: Frutos et al. (2021), Wu et al. (2023), IUCN RedList

What about the Spatiotemporal Pattern of Early Cases in Wuhan?

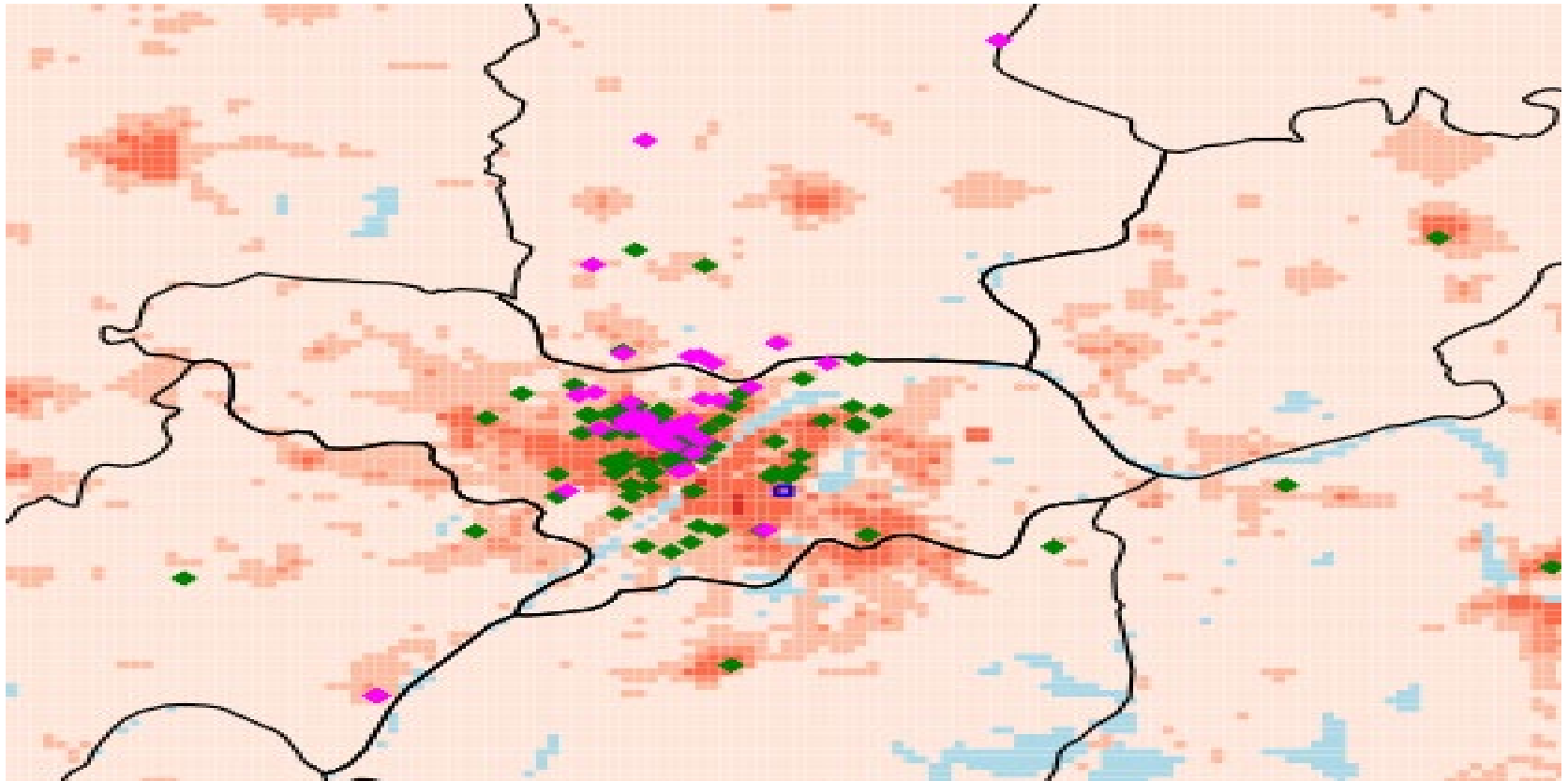
- **Hypothesis A:** Early COVID cases that were unlinked to the Huanan Market would be more frequent on the east bank of the Yangtze River, near the BSL-2 and BSL-3 labs conducting bat viral research.
- **Hypothesis Z:** The distribution of unlinked cases would be roughly similar to the distribution of cases that were linked to the Huanan Market.

The Distribution of Early COVID Cases in the Wuhan Area



Note: magenta = linked cases, green = unlinked cases
Sources: WHO (2021), UN Population Division (2023)

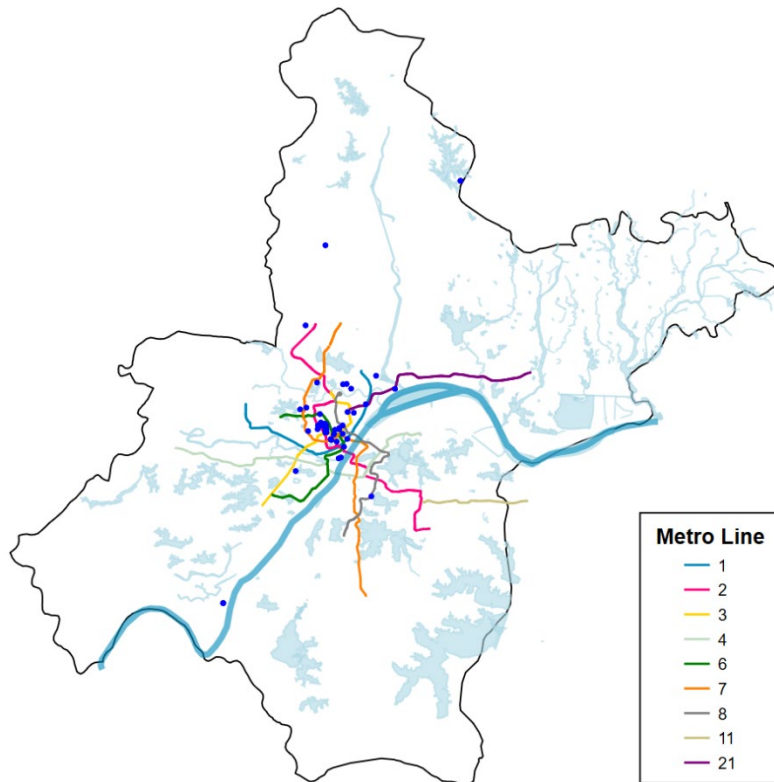
The Distribution of Early COVID Cases in the Central Core of Wuhan



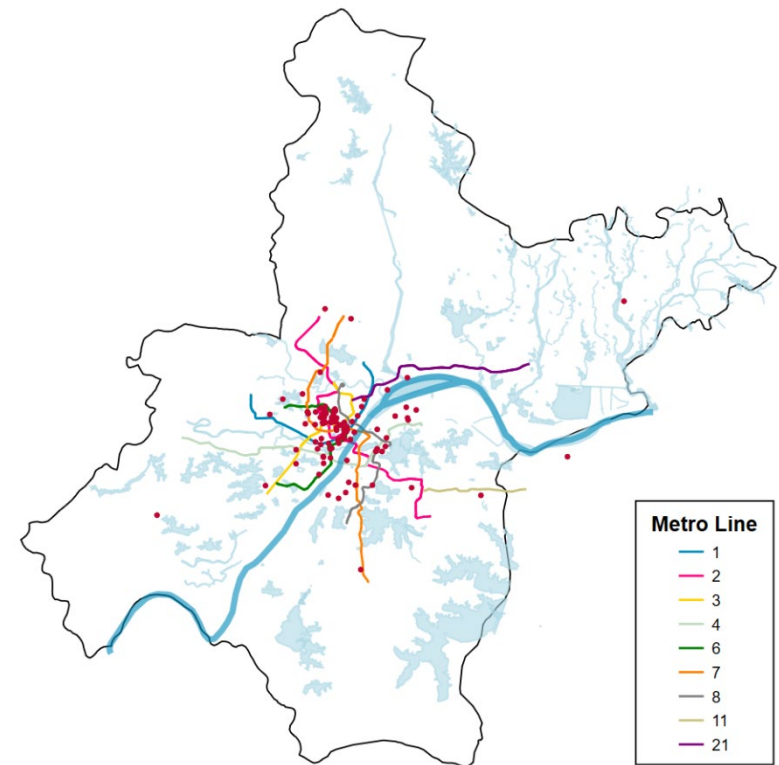
Note: magenta = linked cases, green = unlinked cases
Sources: WHO (2021), UN Population Division (2023)

The Distribution of Early COVID Cases in the Central Core of Wuhan

Cases Linked to Huanan Market



Unlinked Cases



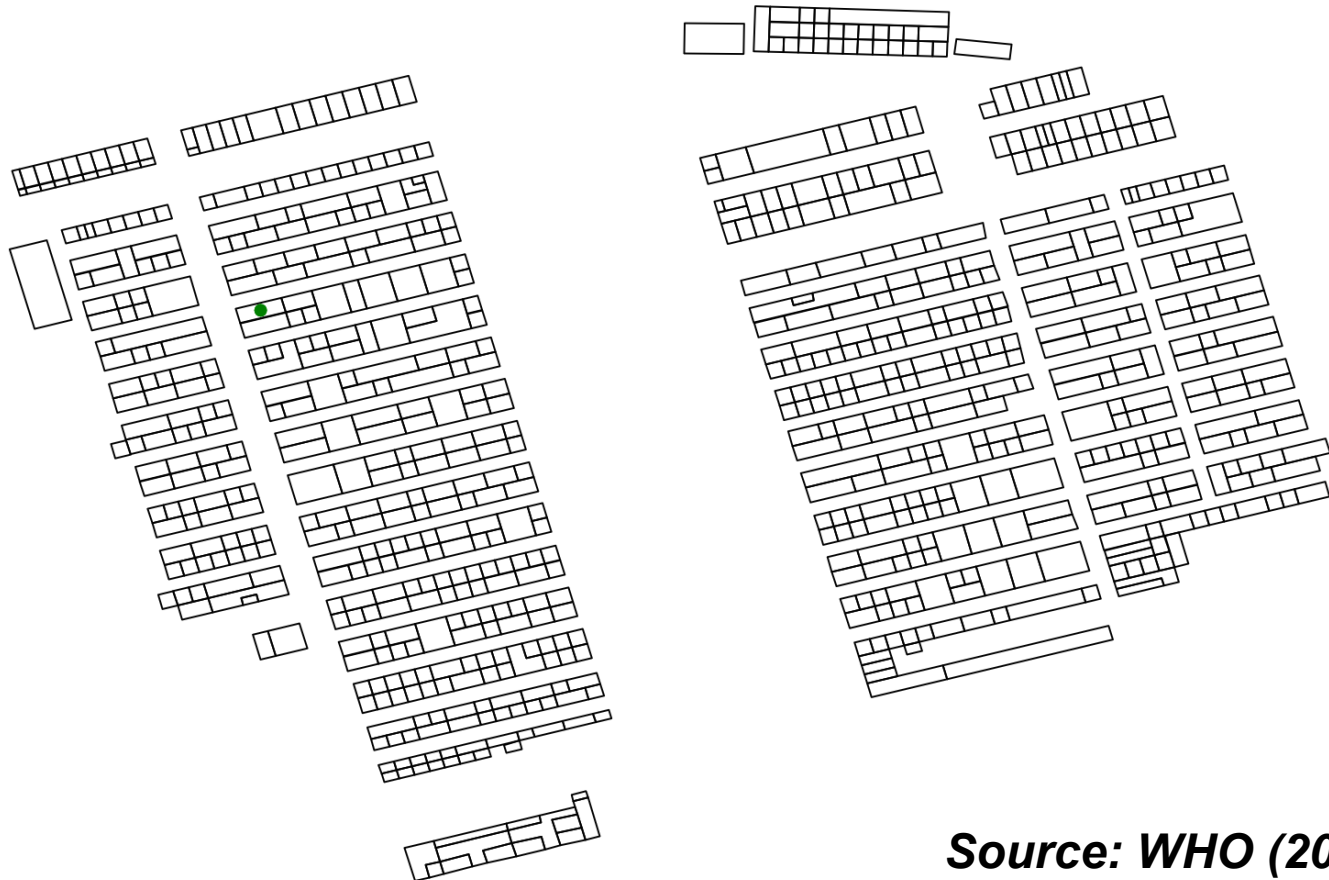
Source: WHO (2021)

What about the Spatiotemporal Pattern of Cases at Huanan Market?

- **Hypothesis A:** Cases where vendors were infected would be strongly linked to prior cases and time of infection, not distance to stalls selling wild mammals.
- **Hypothesis Z:** Cases where vendors were infected would mainly be determined by distance to stalls selling wild animals, not to the spread of infections outside the market.

The Spatiotemporal Pattern of Vendor Cases at Huanan Market

13 December 2019



Source: WHO (2021)

The Spatiotemporal Pattern of Vendor Cases at Huanan Market

20 December 2019



Source: WHO (2021)

The Spatiotemporal Pattern of Vendor Cases at Huanan Market

27 December 2019



Source: WHO (2021)

Kaarina Kauhala (1954-2022)



Source: Helsinki Sanomat (2023)