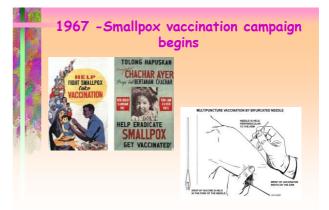


"The conquest of tuberculosis" Selman Waksman, 1964

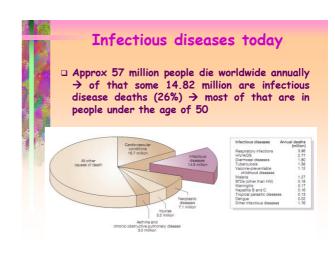
"But most important, the ancient foe of man, known as consumption, the great white plague, tuberculosis, or by whatever other name, is on the way to being reduced to a minor ailment of man. The future appears bright indeed, and the complete eradication of this disease is in sight."

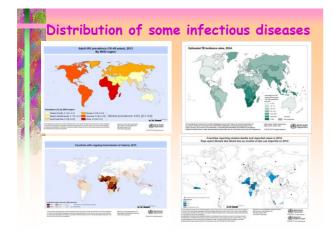
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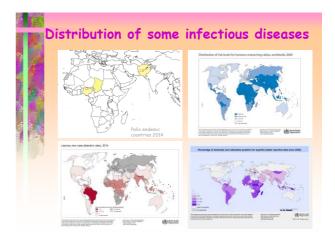


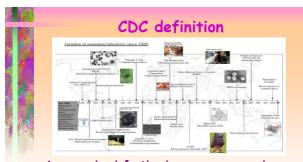










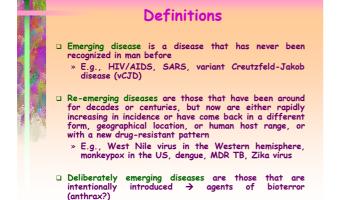


An emerging infection is a new, reemerging or drug-resistant infection whose incidence in humans has increased within the past three decades or whose incidence threatens to increase in the near future





10



WHY??

□ Emergence of infectious disease results from dynamic interactions between rapidly evolving infectious agents and changes in the environment and in host behaviour that provide such agents with favourable new ecological niches



- Microbial adaptation and change
- □ Breakdown of public health measures



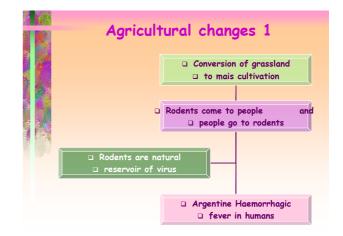


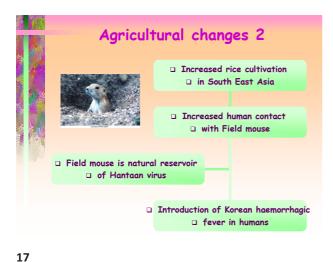


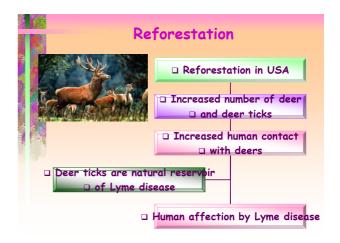


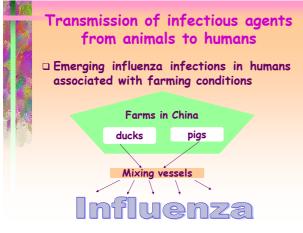
Agricultural changes

- Increased possibility for agents to breach species barrier between animals and humans because of:
 - » animal displacement in search of food after deforestation
 - » animals forced into closer human contact
 - or » humans penetrating modifying unpopulated regions and coming closer to animal reservoirs or vectors











Global warming

Elevated rainfall

- » creates new breeding habitats for mosquitoes
- » decreases salinity which can increase toxic bacteria
- » increases vegetation which raises rodents
- » amplifies runoff into drinking reservoirs
- Higher ocean temperatures increase Vibrio parahaemolyticus growing in shellfish
- Some soil pathogens are carried by dry dusty winds (Coccidiodes)



- Environmental changes and agricultural development
- Changes in human demographics and behaviour
- International travel and commerce
- Technology and industry
- D Microbial adaptation and change
- □ Breakdown of public health measures

21

Human demograp	hic and behaviour
 Population growth and migration Urban decay Use of high-density facilities (e.g., prisons, day care) Economic impoverishment War or civil conflict Famine 	 Sexual behaviour Drug use Diet Outdoor recreation



14

Urbanization

- Increased population density in urban areas
- Basic services may be strained or unavailable in inner city slums or in shanty towns on the periphery
 - » clean water supplies
 - » sanitary conditions
 - » sewage disposal
 - » adequate housing
 - » ...

25





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Urbanization

- □ Fast paced lifestyles and more stress
- Elderly population increased
- Increase in children in daycare: working women with kids under 5 was 30% in 1970, 75% in 2000
- Increase in high-density facilities (such as prisons, daycare, homeless shelters, etc.)



Poverty, Neglect

- Poor populations major reservoir and source of continued transmission
- Malnutrition
- □ Substandard housing → indoor air pollution (>10% preventable ill health)
- Increase in the number of homeless people in large cities

War and famine

Closely linked

- Famine may also be caused by social, economic and political forces, weather emergencies and diseases
- □ World refugees 2014: nearly 22 millions
- □ Forced onto new areas where they are exposed to new microbes from vectors and people

Refugee

□ Who, owing to wellfounded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country; or who, not having a nationality and being outside the country of his former habitual residence as a result of serious events, is unable or, owing to such fear, is unwilling to return to it.

Geneve Convention (art. 1) - 1951

29

Human behaviour

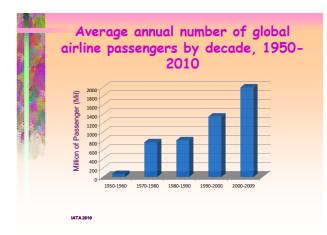
- Unsafe sexual practices
- » HIV, gonorrhoea, syphilis, hepatitis
- High-risk behaviour
- » drug use
- Outdoor activity



□ Breakdown of public health measures

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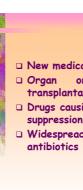




Recently importing into the US: Infectious diseases Animals West Nile fever □ 47,000 mammals West Nile fever
 Dengue fever
 Yellow fever
 Mayaro fever
 Chikungunya
 Epidemic polyarthritis
 SARS
 Influenza
 Lassa fever
 Monkeypox
 CJD/BSE
 HIV/AIDS
 Cholera □ 379,000 birds 2 million reptiles and poisonous snakes
 49 million amphibians □ 223 million fish Mosquitoes Aedes albopictus HTV/AIDS
Cholera
E. coli 0157
E. coli 0104:H4
Malaria
Leishmaniasis
Chagas disease
Cyclospora
Zika Ochlerotatus (A. Finlaya) togoi Ochlerotatus (A. Finlaya) japonicus Aedes bahamensis Culex biscayensis







Health care

New medical devices 🗆 Organ 🛛 or tissue transplantation

- Drugs causing immune suppression
- Widespread use of

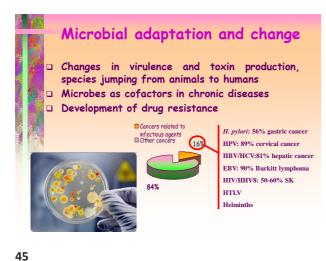


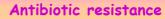
42

- Health care
- People living longer, but with weaker immune systems
 - Blood and organ transplantation may transmit infections
 - Concentrating effect of blood and nosocomial infections
- New diagnostic technology leads to identification of previously unknown microbes for known diseases
 - » Helicobacter pylori and peptic ulcer
 - » Human herpes virus 6 and roseola infantum
 - » ...



□ Breakdown of public health measures





- Antibiotic-resistant bacteria are emerging from the environment in response to the wide distribution of antimicrobials
- Selection for antibiotic-resistant bacteria and drug-resistant parasites have become common, generated by the wide and often unsuitable use of antimicrobial drugs

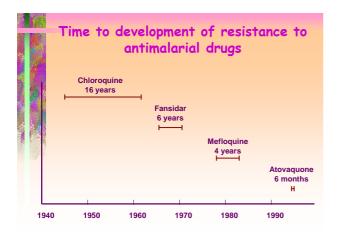
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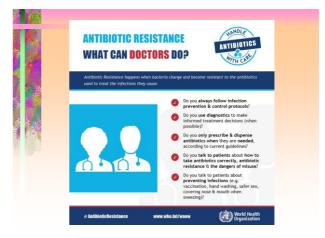


http://www.who.int/who-campaigns/world-antibiotic-awareness-week

An example

□ The use of unsupervised prophylactic tetracycline administration to 100,000 pilgrims en route to Mecca from Indonesia is thought to have been significantly responsible for the fact that 50% of cholera strains in that country are now tetracycline resistant







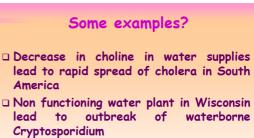
- Environmental changes and agricultural development
- Changes in human demographics and behaviour
- International travel and commerce
- Technology and industry
- D Microbial adaptation and change
- □ Breakdown of public health measures



» Infectious disease specialists

Possible reasons

- Lack of funding
- Poor prioritization of health funds
- Misplaced in curative rather than preventive infrastructure
- Failure to develop adequate health delivery systems



- Inadequate vaccinations and diphtheria in former USSR independent countries
- Discontinued mosquito control efforts and dengue and malaria re-emergence

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February 28, 2003

- Carlo Urbani, medical doctor for WHO, worrying it could be avian flu, reports the case of atypical pneumonia to the Pacific Regional Office of WHO and starts alert on the new illness
- He will die in Bangkok on March 29, killed by the same disease he had discovered







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SARS

Severe Acute Respiratory Syndrome

WHO definition

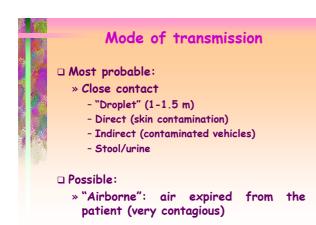
» acute disease of unknown aetiology whose main symptoms are high fever, cough, shortness of breath or breathing difficulties, which develops in subjects who have had very close contact with other cases



SARS-CoV

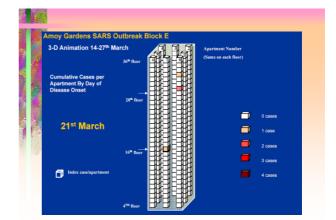
- Infects mammalian and birds
- Viral replication inside epithelial cells of respiratory and enteral tract and macrophages
- In man they produce only pathological damages on respiratory (cold), enteric and (rarely) neurological systems

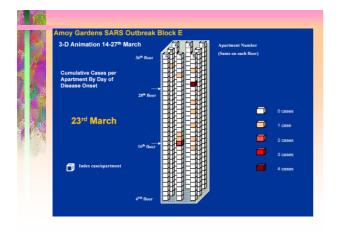


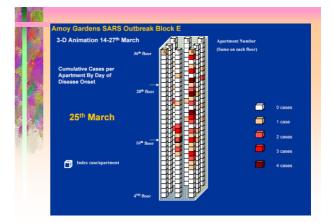


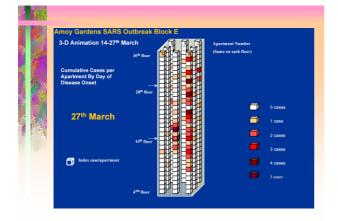


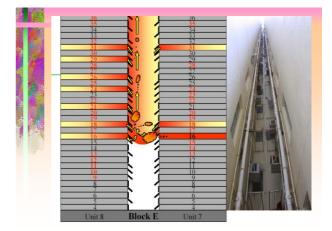


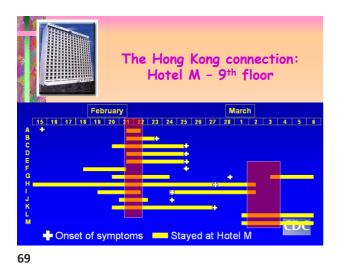


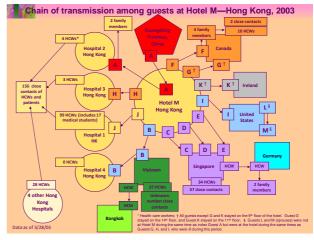




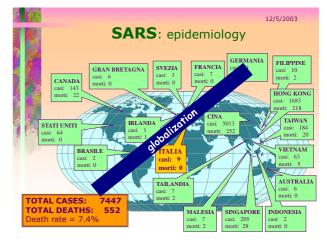


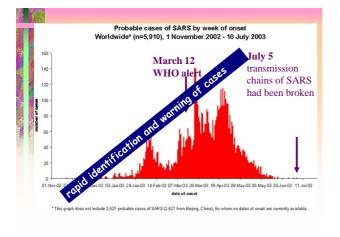


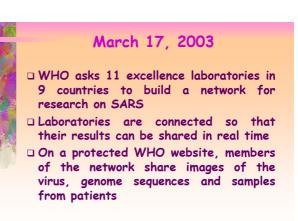


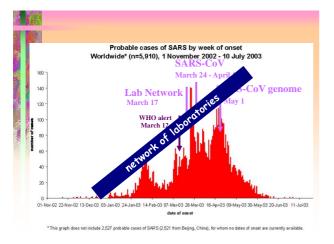












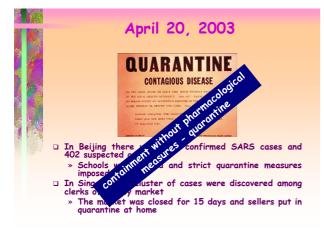




- social distancing measures
- quarantine
- isolation and treatment of ill persons

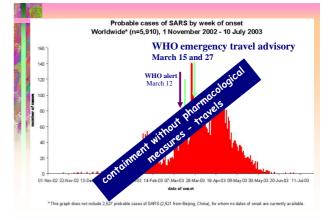








Ho AS, et al Annals Internal Medicine 2003; 139: 564-7





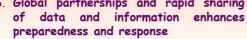


SARS Worldwide \$40-50 bn

ian Ru (H5N: \$25-30 bri

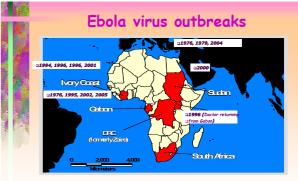




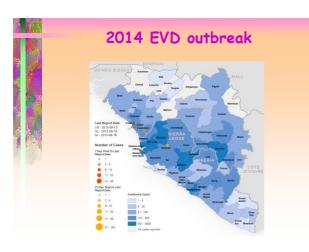






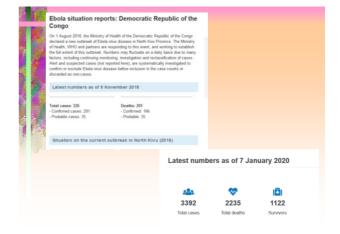


Ebola was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo Since then, outbreaks have appeared sporadically in Africa



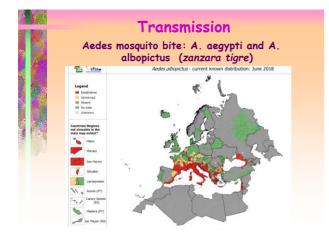


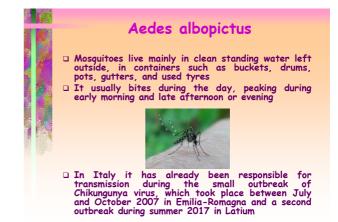


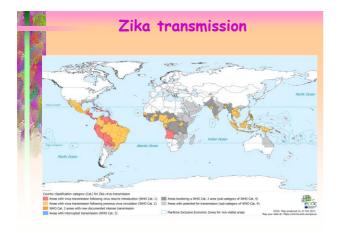








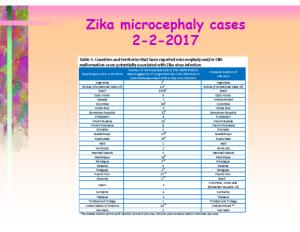








Also possible are miscarriages and stillbirths

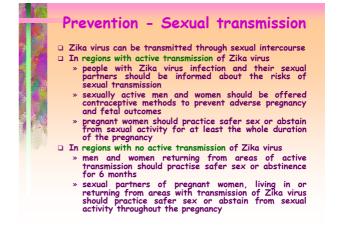




 using insect repellent containing DEET, IR3535 or icaridin







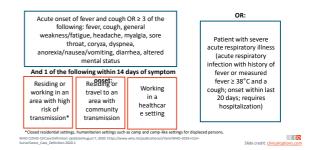
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WHO: Suspect Case Definition



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WHO: Probable Case Definition

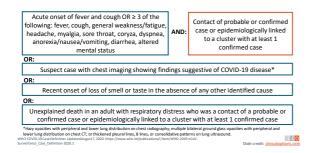
<u>https://coronavirus.jhu.edu/map.html</u>
 <u>http://opendatadpc.maps.arcgis.com/apps/ops</u>

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s-cov-2-dashboard

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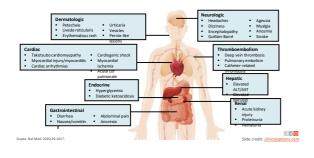
https://www.epicentro.iss.it/en/coronavirus/sar



Headache Congestion or runny nose, new loss of taste or Cough, sore throat smell "Symptoms may appear 2-14 days Shortness of breath after exposure to or difficulty breathing Fatigue, muscle or body aches, the virus" fever or chills Nausea or vomiting, diarrhea C C O Slide credit: clinical

Primary Symptoms of COVID-19

Extrapulmonary Manifestations of COVID-19: Which of These Return or Last?

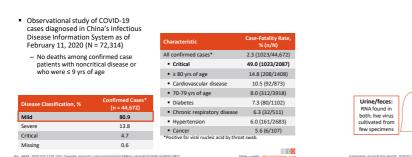


NIH Guidelines: Defining a COVID-19 Severity Spectrum

Asymptomatic or	
presymptomatic infection	 Positive test for SARS-CoV-2 but no symptoms
Mild illness	 Varied symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain) but no shortness of breath, dyspnea, abnormal imaging
Moderate illness	 SpO₂ ≥ 94% and lower respiratory disease evidenced by clinical assessment or imaging
Severe illness	 SpO₂ < 94%, PaO₂/FiO₂ < 300, respiratory rate > 30 breaths/min, or lung infiltrates > 50%
Critical illness	 Respiratory failure, septic shock, and/or multiorgan dysfunction

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JAMA. 2020;32

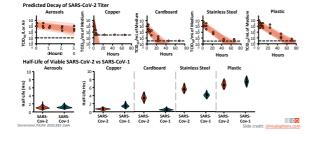
COVID-19 Severity in Mainland China

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Proposed Routes of SARS-CoV-2 Transmission



SARS-CoV-2: Aerosol and Surface Viability



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Rapid Inactivation of SARS-CoV-2 Aerosols in Sunlight

In vitro simulations suggest a 90% loss of infectivity in 8-19 min for SARS-CoV-2 aerosols exposed to mid to high intensity sunlight

Suspension Matrix at 20°C	Simulated Sunlight	Tests, n	Mean k _{infectivity} , min ^{.1} (SD)	Mean Decay Rate, %/min (SD)
Simulated saliva	None	18	0.008 (0.011)	0.8 (1.1)
	Mid intensity	3	0.121 (0.017)	11.4 (1.5)
	High intensity	8	0.306 (0.097)	26.1 (7.1)
Culture medium	None	16	0.013 (0.012)	1.2 (1.2)
	Mid intensity	4	0.169 (0.062)	15.4 (5.3)
	High intensity	7	0.182 (0.041)	16.6 (3.3)
Results pooled across te	sts of varying relative hun	nidity as this f	actor not found to significa	ntly affect viral decay.
·	sts of varying relative hun	nidity as this f	actor not found to significa	ntly affect viral deca
Results pooled across te	÷ ,		0.182 (0.041)	16.6 (3.3)

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Key Considerations on Modes of SARS-CoV-2 Transmission

- Person-to-person considered predominant mode of transmission, likely via respiratory droplets from coughing, sneezing, or talking^[1,2]

 - High-level viral shedding evident in upper respiratory tract^[3,4]
 - Airborne transmission suggested by multiple studies, but frequency unclear in absence of aerosol-generating procedures in healthcare settings^[2]
- Virus rarely cultured in respiratory samples > 9 days after symptom onset, especially in patients with mild disease^[5]
- Multiple studies describe a correlation between reduced infectivity with reases in viral loads and rises in neutralizing antibodies^[5]
- ACOG: "Data indicate that vertical transmission appears to be uncommon"^[6]

https://www.cdc.gov/coronavirus/2019-ncov/prevent.getting-sick/how-covid-spreads.html
 WHO. Scientific Brief. July 9, 2020.3. Wolfel. Nature. 2020;581:465.4. Zou. NEIM. 2020;382:1177.
 S. WHO. Scientific Brief. June 17. 2020.6. ACOG. COVID-197405 for Obstatrician-Greecolousts. Obst.

C C 🖸 Slide credit: clinical

Timing of SARS-CoV-2 Transmission **Based on Symptoms**

- Prospective study of lab-confirmed COVID-19 cases (n = 100) and their close contacts (n = 2761) in Taiwan^[1]
- Paired index-secondary cases (n = 22) occurred more frequently with exposure just before or within 5 days of symptom onset vs later
- Pre-symptomatic infections

Med. 2020;180 1156. 2. Wei. M!

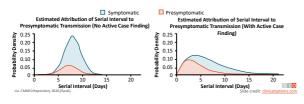
- Accounted for 6.4% of locally acquired infections in a study in Singapore (N = 157)^[2] Modelling study of transmission in China (n = 154) estimated that 44% of transmissions may have occurred just before symptoms appeared^[3]
- A recent systematic review and meta-analysis estimated that the proportion of total infections that are truly asymptomatic range from 6% to 41% (pooled estimate of 15%)^[4] Asymptomatic transmission rates ranged from 0% to 2.2% vs symptomatic transmission rates of 0.8% to 15.4%

 - 3 studies reported that the cycle threshold from RT-PCR assays did not differ between symptomatic and asymptomatic individuals

C C O Slide credit: clinicalo

Presymptomatic Transmission

- Transmission events in Shenzen, China were inferred to be asymptomatic or presymptomatic using the probability for symptom onset on a given day following exposure
- Estimated that 23% of transmissions prior to symptom onset before active case finding was implemented, increased to 46% with accelerated case isolation



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SARS-CoV-2 Transmission in Indoor Settings (Limited Air Circulation)

		Layout	of Secondary Cases	in Relation to Ind	ex Case in B
An outbreak investigation of Co among lay Buddhists worshipp temple in Zhejiang, China (N =	ing at a				Index Case
 Travel: ~ 50 mins each way 					
 Worship event: ~ 150 mins 					
(mostly outdoors)	Nonca	so 💌	Asymptomatic case	Mild case	Moderate
			isymptomatic case		wouldter
Area of Exposure	Cases	Total	Attack Rate (95% CI)	Relative Risk (95% CI)	P Value
Area of Exposure Bus 1	Cases 0	Total 60			P Value
			(95% CI)	(95% CI)	
Bus 1	0	60	(95% CI) 0 (0-6.0)	(95% CI) Ref	
Bus 1 Temple (excluding those arriving on bus 2)	0 7	60 232	(95% CI) 0 (0-6.0) 3.0 (1.3-6.2)	(95% CI) Ref Ref	
Bus 1 Temple (excluding those arriving on bus 2) Bus 2 (index case)	0 7 23	60 232 67	(95% CI) 0 (0-6.0) 3.0 (1.3-6.2)	(95% CI) Ref Ref 	

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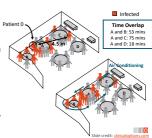
SARS-CoV-2 Transmission in Enclosed vs Outdoor Settings

- Study in Japan traced contacts of 110 people with COVID-19 in ten indoor clusters and assessed the environment in which transmission between contacts occurred $^{\left[1\right] }$ - 27 primary cases generated secondary cases (24.6%)
- Odds that a primary case transmitted SARS-CoV-2 in an enclosed environment 18.7 x higher compared with odds of estimated transmission rates in an open-air environment (95% CI: 6.0-57.9)[1]
- 6 of 7 superspreading events (to 3 or more people) occurred in enclosed environments (OR vs open-air environments: 32.6; 95% CI: 3.7-289.5)^[1]
- Consistent with cluster in Germany from indoor work meeting, cluster from a ski chalet France, cluster from choir practice in the US, and church- and hospital-associated clusters in South Korea^[2-5] C C O

ewed. 2. Hijnen. Emerging Infectious Dise . medRxiv;[Preprint]. Note: this study has not been h] 3. Danis. Clin Infert Dis. 2020;71:825.4. Hamne Slide c redit: clinical

SARS-CoV-2 Transmission: Recirculated Air and Poor Ventilation

- 3 families (A, B, and C) ate lunch at a restaurant on January 24, 2020 at 3 neighboring tables
 - 10 of those sitting at these tables (including the index case) were later found to have been infected with sARS-CoV-2 at the restaurant
 - None of the waiters or 68 patrons at the remaining 15 tables became infected
- Authors note that these results do not show that long-range aerosol transmission can occur in *any* indoor space, but that transmission may occur in crowded/poorly ventilated spaces



Summary of SARS-CoV-2 Transmission in Various Settings

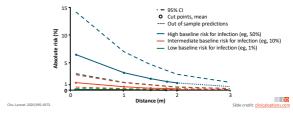
- Crowded enclosed spaces facilitate SARS-CoV-2 transmission
- Transmission rates in enclosed spaces appear to be correlated with duration of exposure
- Longer duration ightarrow greater risk of transmission
- Airborne transmission hypothesized
 - Biologically plausible → aerosol generated with greater than normal force or if air current moves aerosol > 1 meter and droplets remain intact
- Continued observational study and sentinel animal study required to better understand airborne transmission potential

							Ű	C	
2	credit:	clinica	alop	ti	on	s.	0	20	

Slid

Physical Distance and Transmission

 Systematic review and meta-analysis of data from 172 studies investigating the spread of SARS-CoV-2, SARS, and MERS (n = 10,736)



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Efficacy of Face Coverings in Prevention of SARS-CoV-2 Transmission

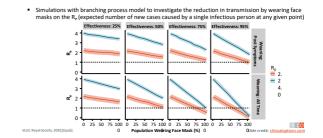
- Systematic review and meta-analysis of data from 172 studies investigating the spread of SARS-CoV-2, SARS, and MERS (n = 2647)^[1]
- Face mask use (surgical, N95, or cotton mask) resulted in large reduction in infection (OR: 0.15; 95% CI: 0.07-0.34)
- Association was stronger for N95 or respirators vs disposable or 12-16 layer cotton masks (*P*_{interaction} = 0.090)

1. Chu. Lancet. 2020;395:1973. 2. Leung. Nature Medicine. 2020;26:676

- Study of human coronaviruses in exhaled breath of children and adults with acute respiratory illnesses wearing surgical face masks vs no mask (N = 246)^[2]
 - Virus detected in respiratory droplets in 3 of 10 samples collected without face masks vs 0 of 11 samples with a mask (P = .07)
 - Virus detected in aerosols in 4 of 10 samples collected without face masks vs 0 of 11 samples with a mask (*P* = .02)

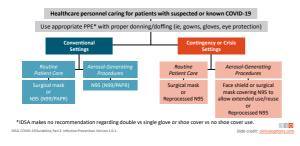
Slide credit: <u>clinical</u>options com

Predicted Efficacy of Face Masks on SARS-CoV-2 Transmission Dynamics



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Nonpharmacologic Preventative Interventions

Recommended Prevention Strategies ^[1,2]
Identify and quickly test suspect cases with subsequent isolation of infected individuals
Quarantine close contacts of infected individuals
Wash hands often with soap and water
Maintain social distance (~ 6 feet)
Wear cloth face cover in public ^[3,4]
Practice respiratory etiquette
Disinfect frequent-touch surfaces regularly
Avoid crowds, close-contact settings, and poorly ventilated spaces

 Inactivation of SARS-CoV, MERS-CoV, and other endemic human coronaviruses readily accomplished with 62% to 71% ethanol, 0.5% hydrogen peroxide, or 0.1% sodium hypochlorite (in 1 min)^[5]

> - 0.05% to 0.2% benzalkonium chloride, 0.02% chlorhexidine digluconate less effective

> > C C<mark>O</mark>

Slide credit: clinicalo

 https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html 2. WHO. Scientific Brief. Ju 3. Leung. Nat Med. 2020;26:676. 4. Chu. Lancet. 2020;395:1973. 5. Kampf. J Hosp Infect. 2020;104:246.

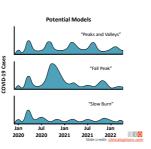
126

Projecting Postpandemic SARS-CoV-2 Transmission

- Recurrent outbreaks likely after initial, most severe pandemic period
 - Interval and height of coming waves will depend on multiple factors, including control measures
 - Prepare for ≥ 18-24 mos of significant COVID-19 activity with periodic hot spots across diverse geographies

nt. April 30, 202

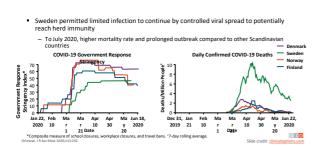
nce. 2020;368:860. COVID-19: The CIDRAP V



COVID-19 Elimination in New Zealand

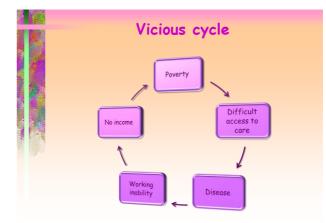










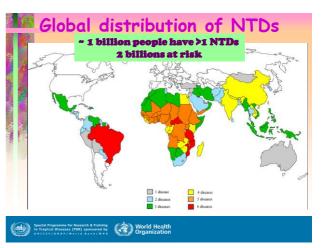


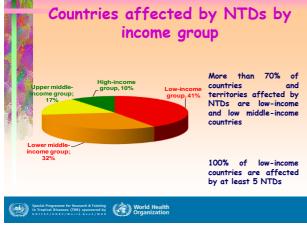


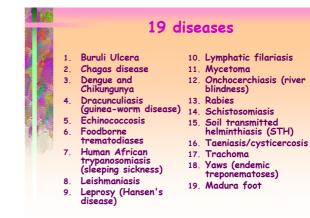
- Neglected by the public opinion because unknown
 Often neglected even by
- sanitary politics of affected countries

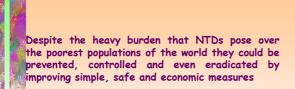










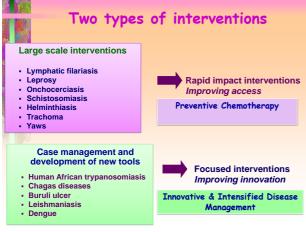


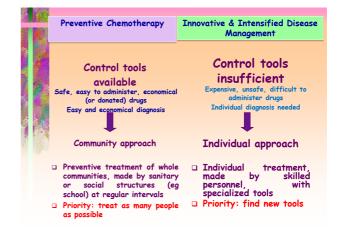
HOW TO FIGHT NTDs



- Chronic evolution
 Rarely deadly
- Less chronic evolution
- Often deadly

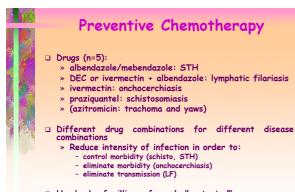
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Hundreds of millions of people "protected" every year
 Expense pro person: <1 US\$/yr





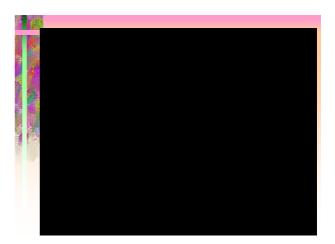




Onchocerchiasis

- Vector control + ivermectin distribution (once a year for 10-15 yrs)
 - 40 million people » 40
 - » blindness prevented in 600.000 people
 » 18 million children not at risk

 - » 25 million hectares land become farming again, able to feed 17 million people every year



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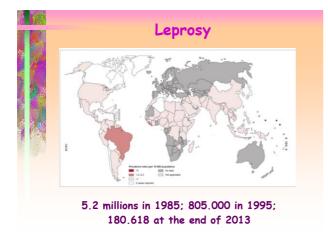
Leprosy

- Little contagious but transmissible on close contact

- Liftle contagious but transmissible on close contact
 Lift untreaated can cause progressive and permanent damage to the skin, nerves, limbs and eyes
 Leprosy is curable with multidrug therapy (MDT, association of dapsone, rifampicin, clofazimin), freely distributed worldwide by WHO since 1995
 What still must be fought is the stigma bound to such disease: patients may hide their symptoms and do not seek medical advice, fearing to be isolated





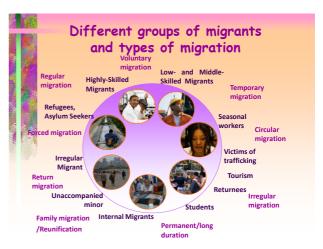






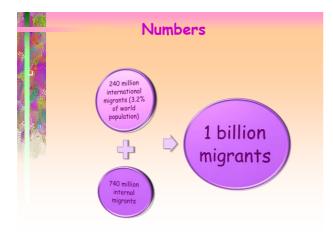
Migration

The action with which a person or a group of people leaves ۵ geographical area with the aim of settling definitevely temporarely in or another

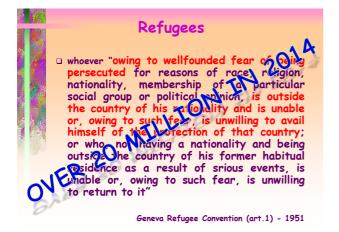


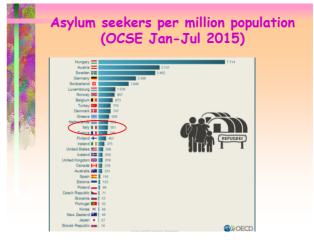
152

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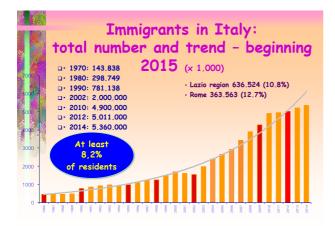


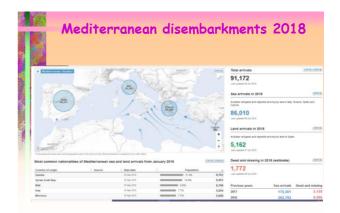


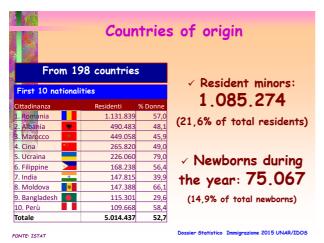












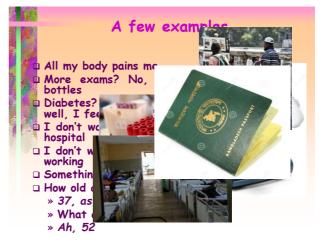


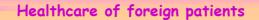
Healthcare of foreign patients

Interaction problems **Regulatory problems Clinical problems**

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Interaction problems Regulatory problems Clinical problems Art. 32 della Costituzione Italiana
 La Repubblica tutela la salute come fondamentale diritto dell'individuo ed interesse della collettività e garantisce cure gratuite agli indigenti



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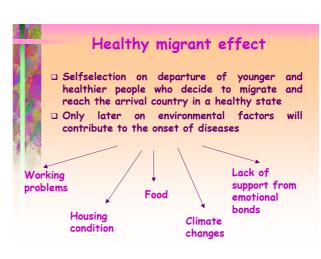




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Interaction problems Regulatory problems Clinical problems



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Environmental factors

Working problems

Main Solution

Mousing condition

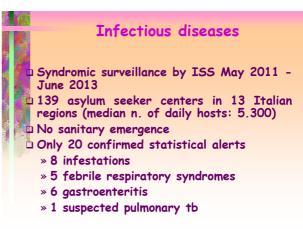
dormitories, immigration centers, huts,
temporary shelters (train wagons, bridges or
arcades, waiting rooms of metro or rail
stations, etc.), overcrowded rooms

Inadequate personal hygiene with clear risks
of infectious disease diffusion



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Rapporto Osservasalute 2014

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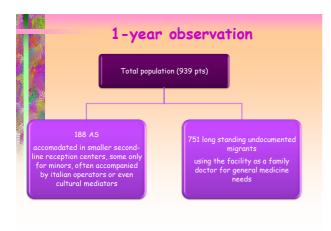


Umberto I Hospital answer Birth of the service

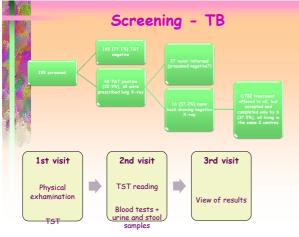
December 2002

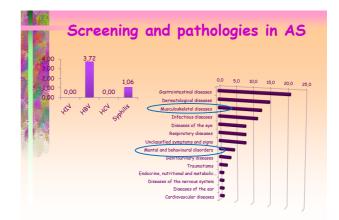
- » Pilot unit near the Emergency Dpt, with volunteer medical doctors and nurses
- May 2003
- » An Infectious Disease office is added, 3 days a week
- December 2005
 - » The unit is transferred to Infectious Disease Dpt
- December 2008
 - » Recognized as Day Service of Migration Medicine







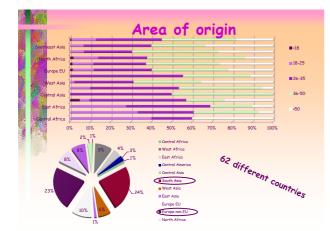


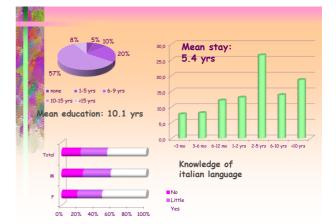


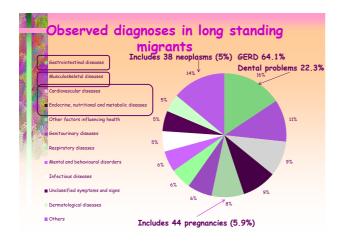


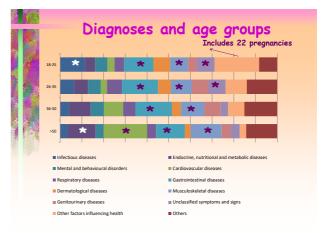


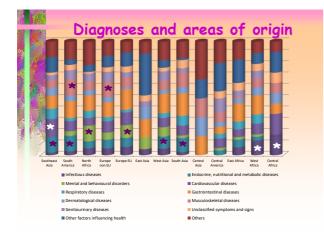
60% males Mean age: 38.6 years (F 40.5 - M 37.4)

























HE, , Bosnia, 65 yrs

