From Production Plants to the People: The Logistics of Distributing the COVID-19 Vaccine.

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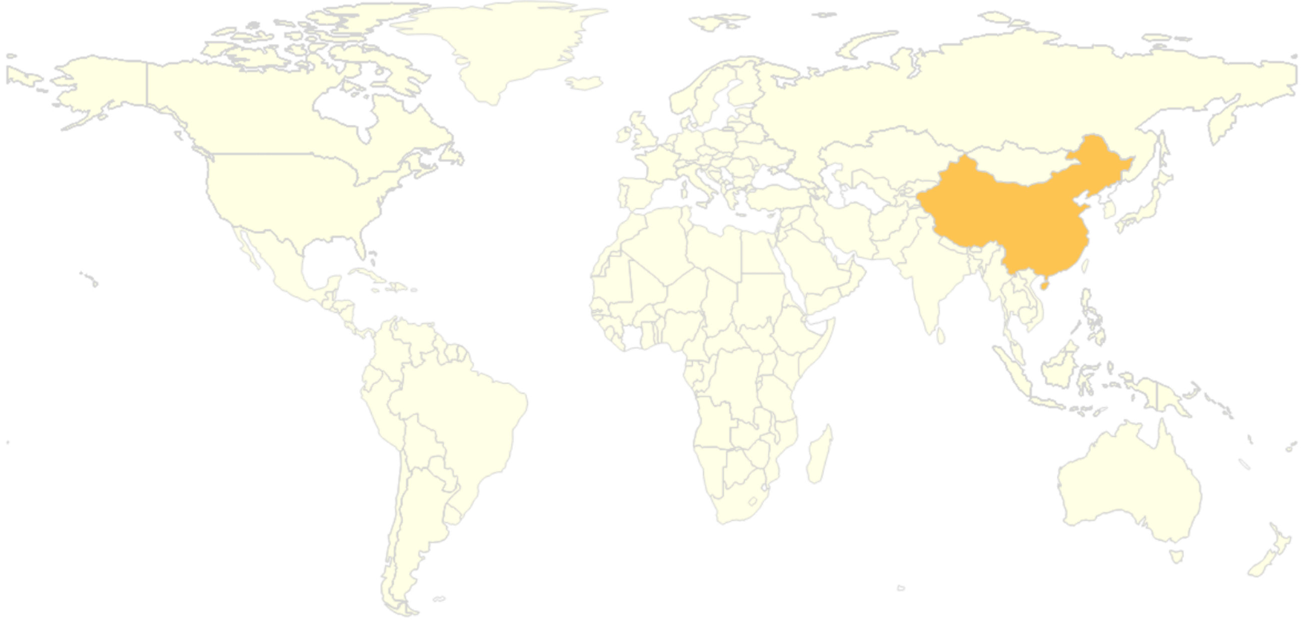
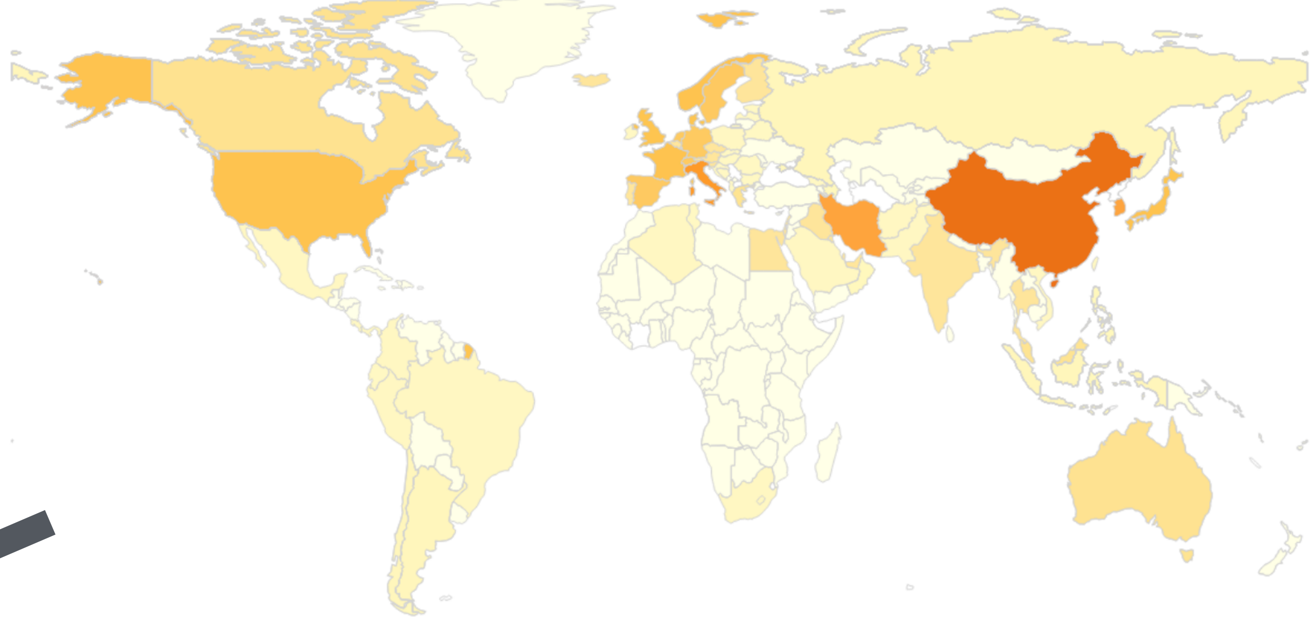
International Situation

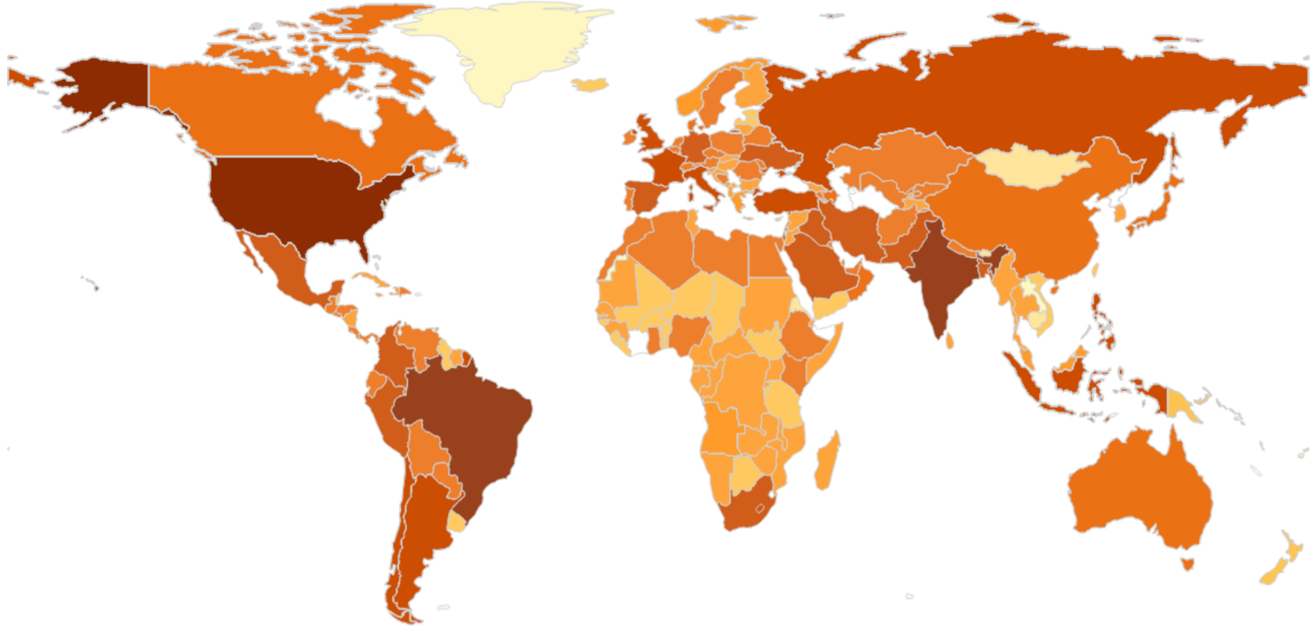
13/01/20: Clusters of cases in Wuhan, China



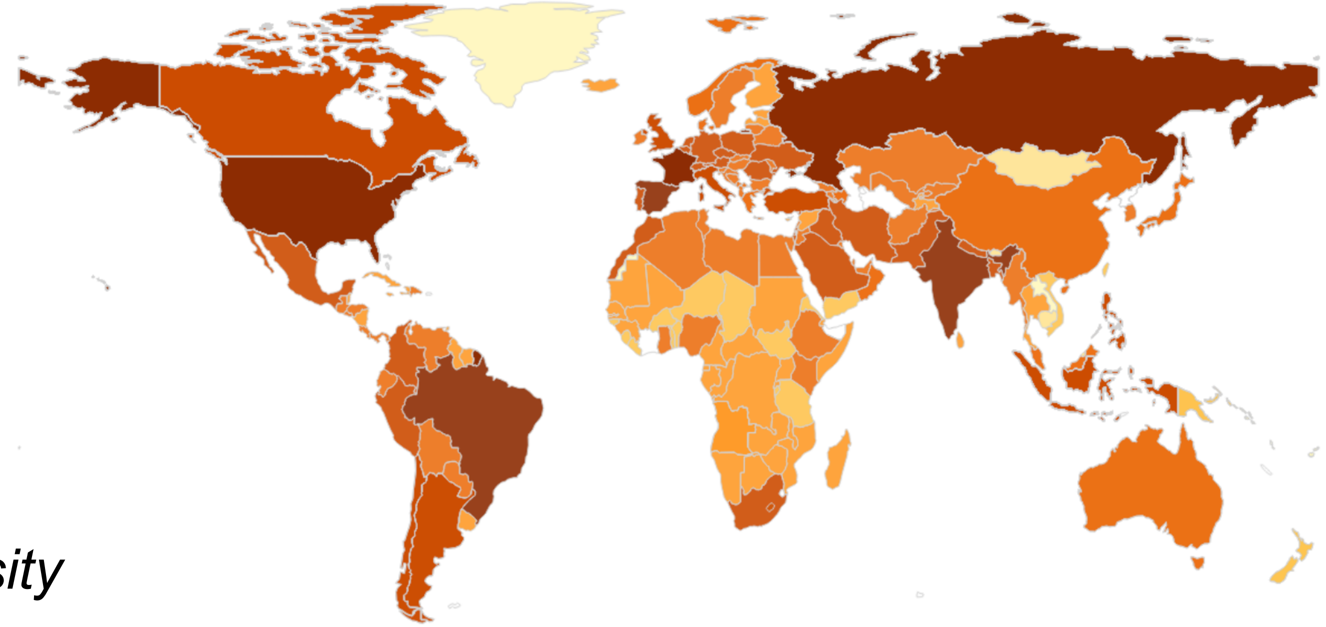
11/03/20: First 100k cases



28/09/20: First 1M deaths



01/12/20: 63M cases and 1.5M deaths

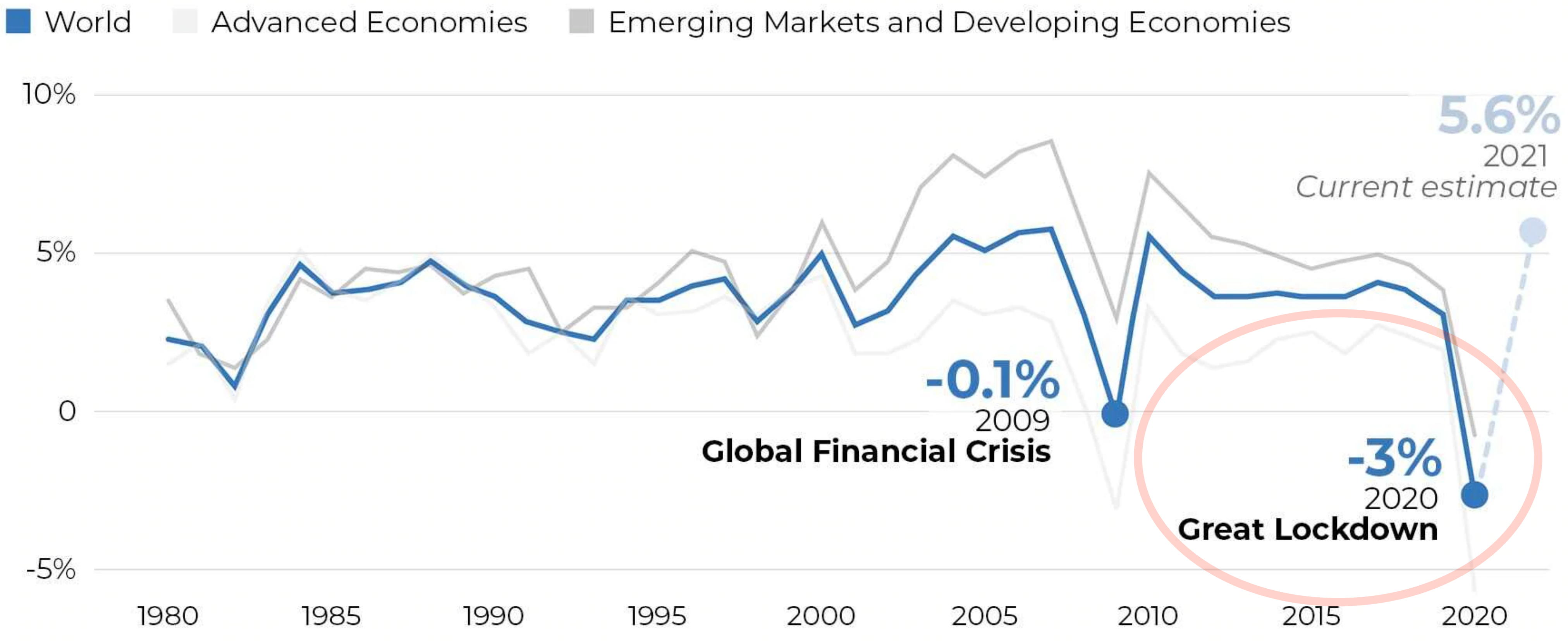


Source: John Hopkins University

Coronavirus

Global Economy Projected to Contract by 3%, Surpassing 2009 Global Financial Crisis

Last updated: April 14



Source: IMF World Economic Outlook

Coronavirus

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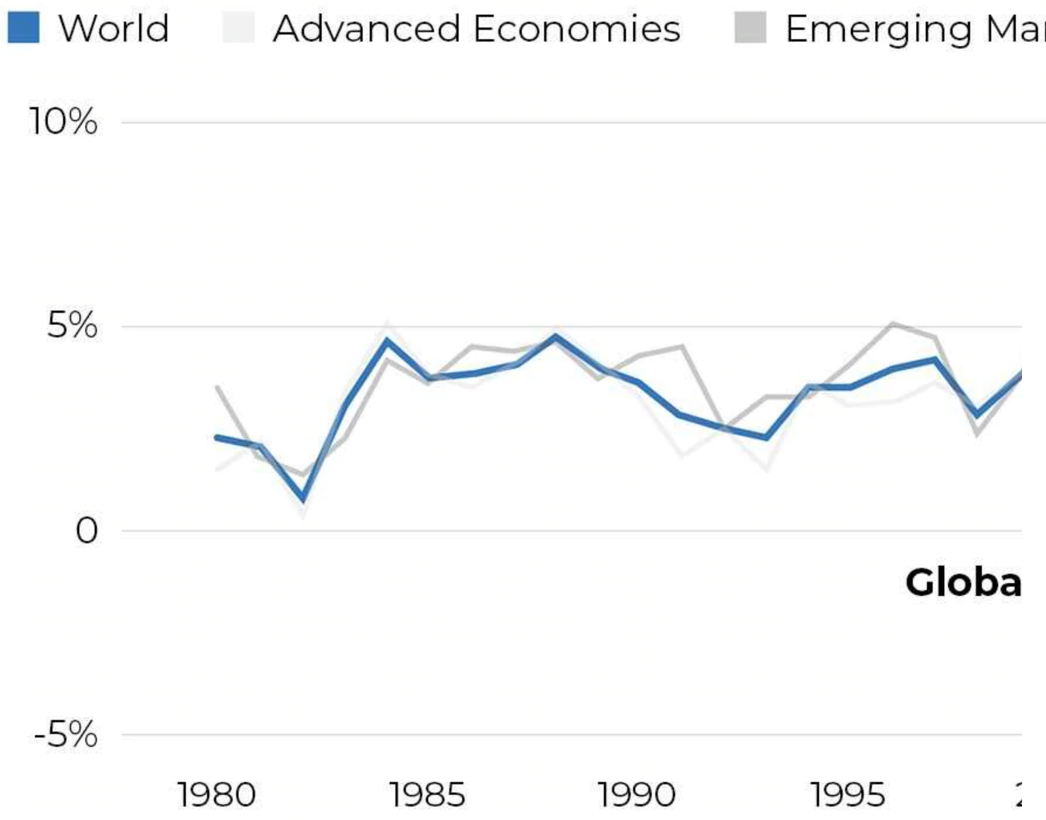
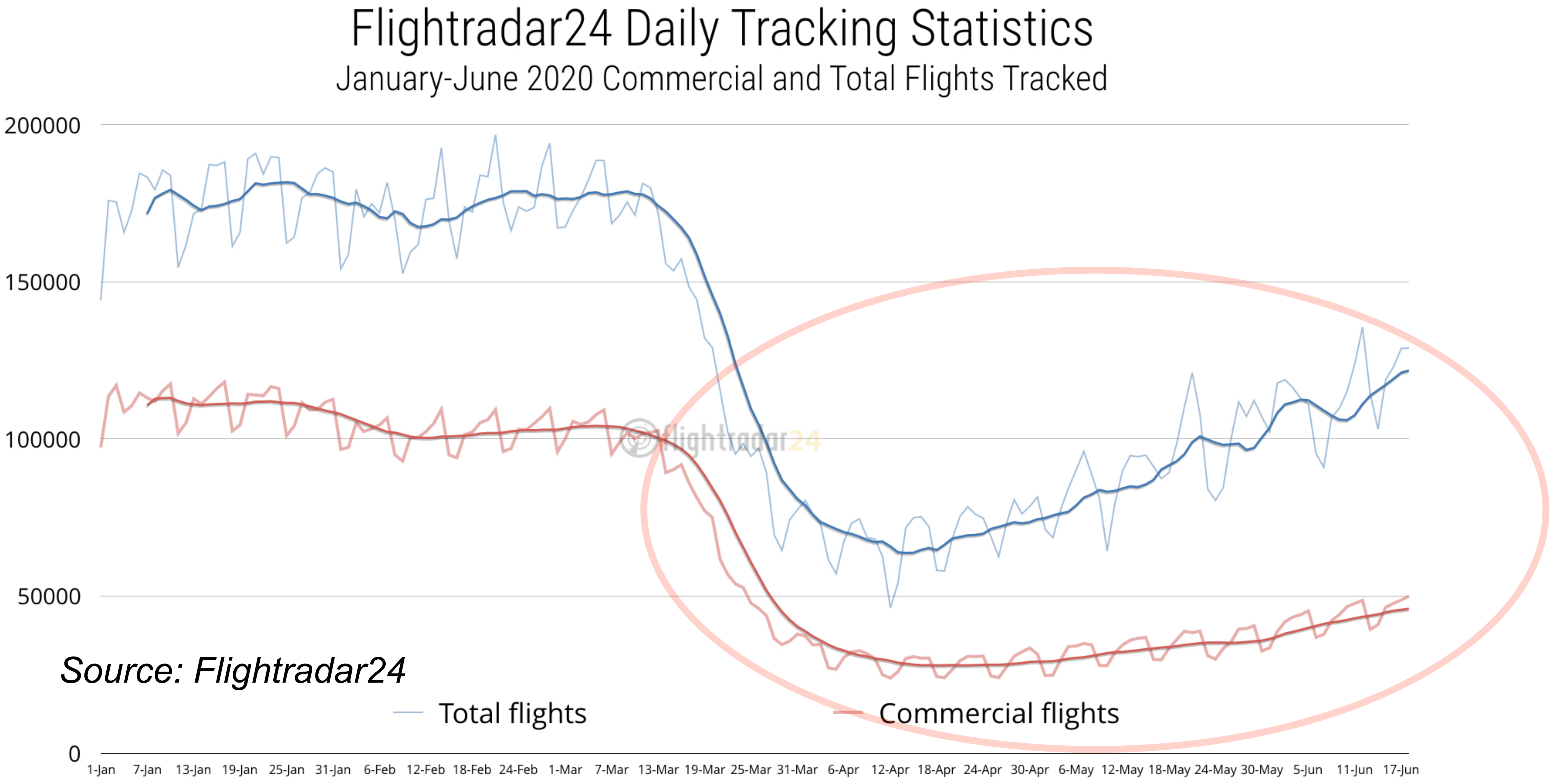
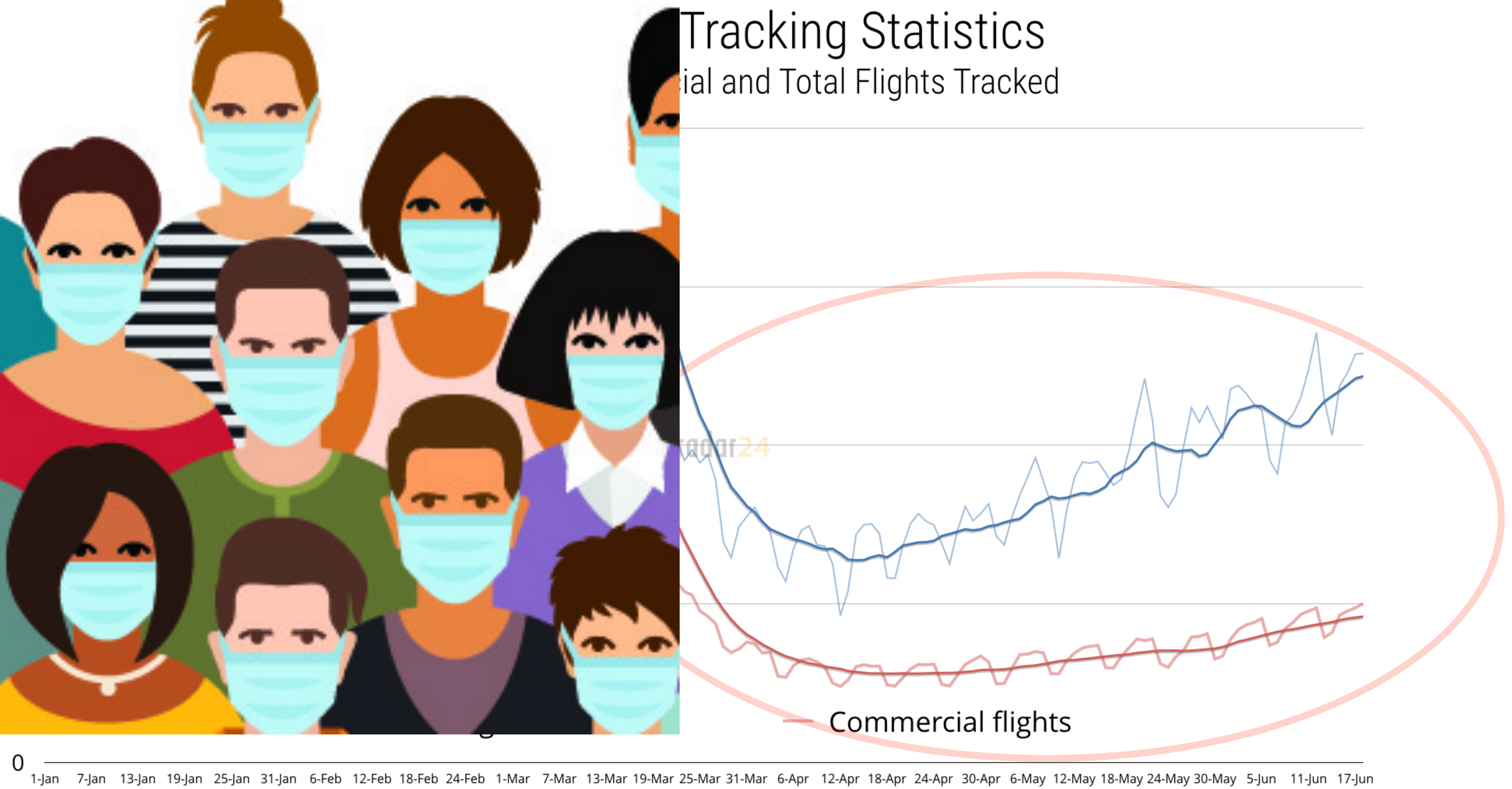


Source: IMF World Economic Outlook



Source: Flightradar24

Photo: https://engagious.com/why-people-dont-wear-masks



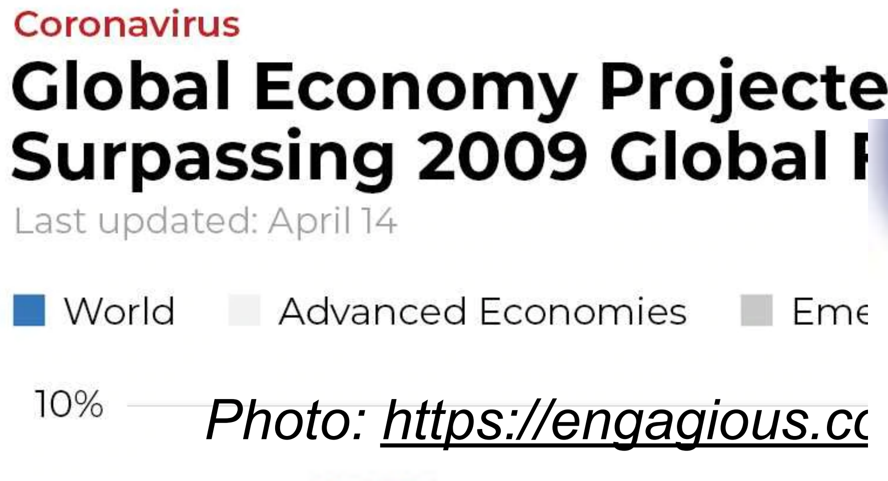
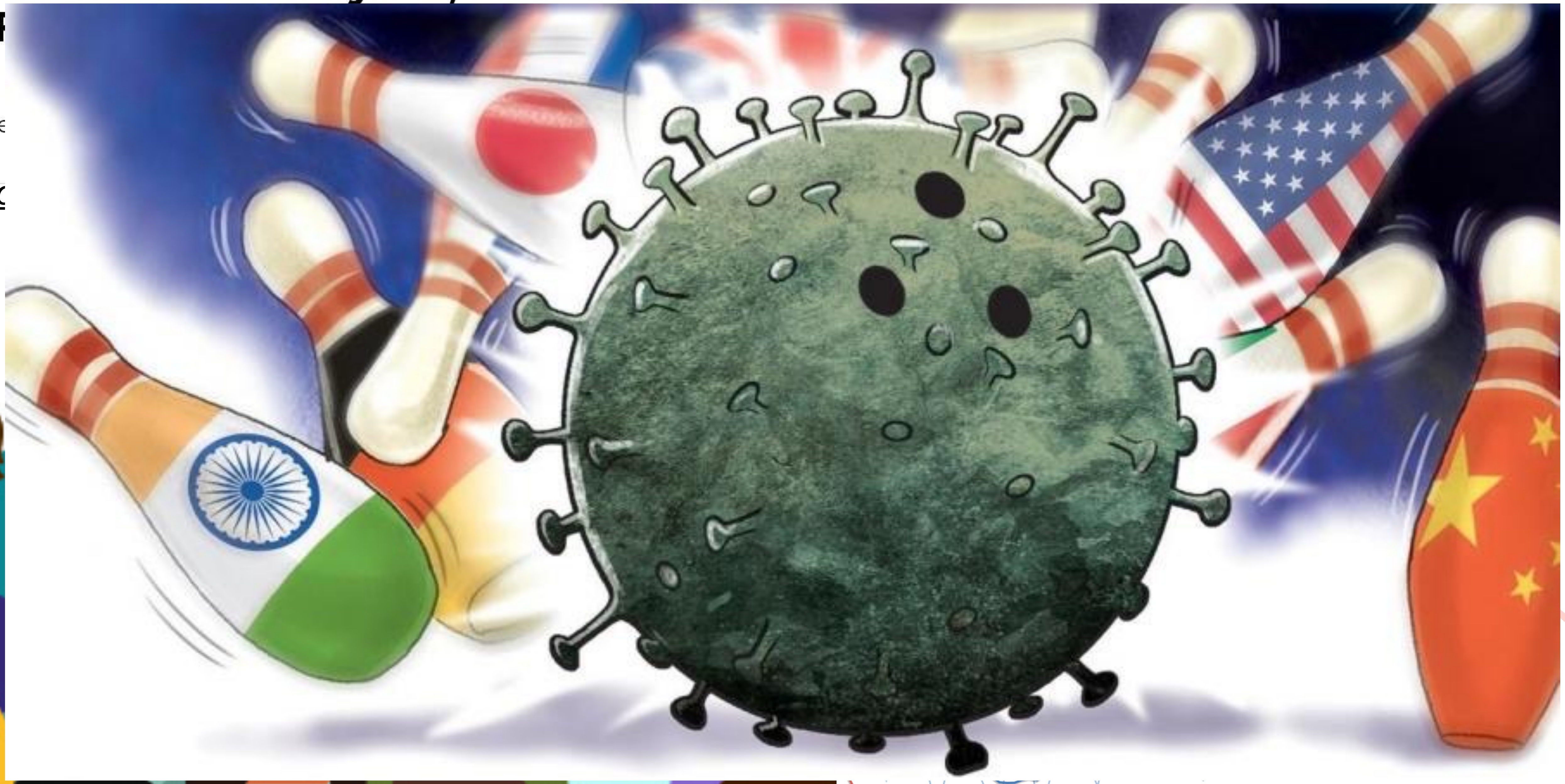
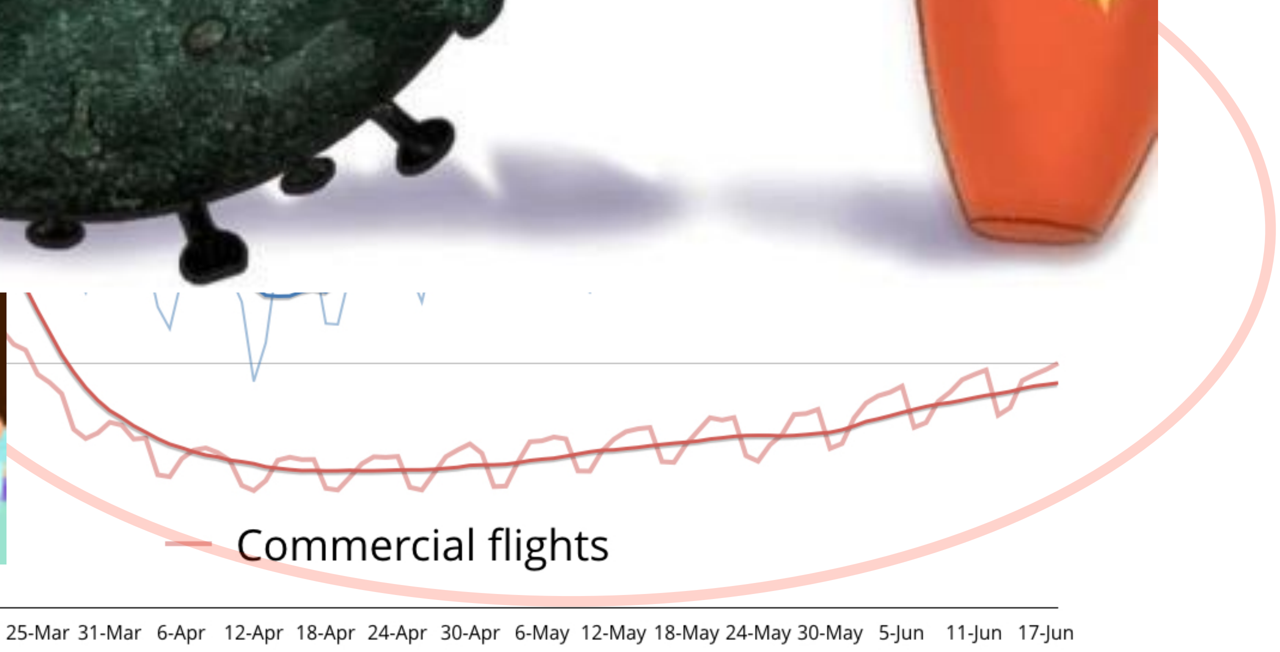


Photo: https://engagious.cc

Photo: https://newindianexpress.com (Express Illustrations)





Vaccines as the only long term solution

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Vaccines stimulate the immune system to produce antibodies and develop immunity

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CanSinoBIO
INOVIO POWERING DNA MEDICINES
SINOPHARM
sinovac
moderna messenger therapeutics
TaKaRa
EnViVa a Tetis Company
PharmaJet
BioNet
Greffex

OSAKA UNIVERSITY
DYNAVAX
CODAGENIX INC.
UNIVERSITY OF OXFORD
GeoVax
BravoVax
janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson
REITHERA
DZIF German Center for Infection Research
altimmune
VAXART

CNB CENTRO NACIONAL DE BIOTECNOLOGIA
University of Manitoba
cobra:bio Expertise Experience Excellence
Zydus Cadila
UNIVERSITY OF WATERLOO CONCORDIA CUM VERITATE
adaptVAC
EXPRES2ION BIOTECHNOLOGIES
imv™
WRAIR Walter Reed Army Institute of Research Soldier Health • World Health
NIID NATIONAL INSTITUTE OF INFECTIOUS DISEASES

NIBIOHN
Clover Biopharmaceuticals
UNIVERSITY OF PITTSBURGH
VAXIL VAXIL BIO THERAPEUTICS
BE Biological E. Limited Celebrating Life Every Day
flow pharma
AJVaccines
GENEREX
EpiVax
SANOFI

NOVAVAX
Heat Biologics
Baylor College of Medicine
iBio
St Petersburg University
innovax ND-IBD
VIDO
MIGAL Galilee Research Institute LTD.
UNIVERSITY OF ALBERTA QUAECUMQUE VERA

TONIX PHARMACEUTICALS
BIOCAD Biotechnology Company
SAPIENTIA ET VIRTUS
iavi
Western
AstraZeneca
東京大学 THE UNIVERSITY OF TOKYO
ARCTURUS therapeutics
BIONTECH
Pfizer

Imperial College London
CUREVAC
Saiba
medicago
imophoron
Doherty Institute
ImmunoPrecise
Tulane University
UNIVERSITÉ LAVAL
oncogen

The long road to vaccination

- Several COVID-19 vaccines have been produced, however vaccination speed does not depend on when a vaccine has been produced but **how fast vaccines can be distributed**

- Millions of lives are saved yearly by vaccines, however half as many deaths could have been averted

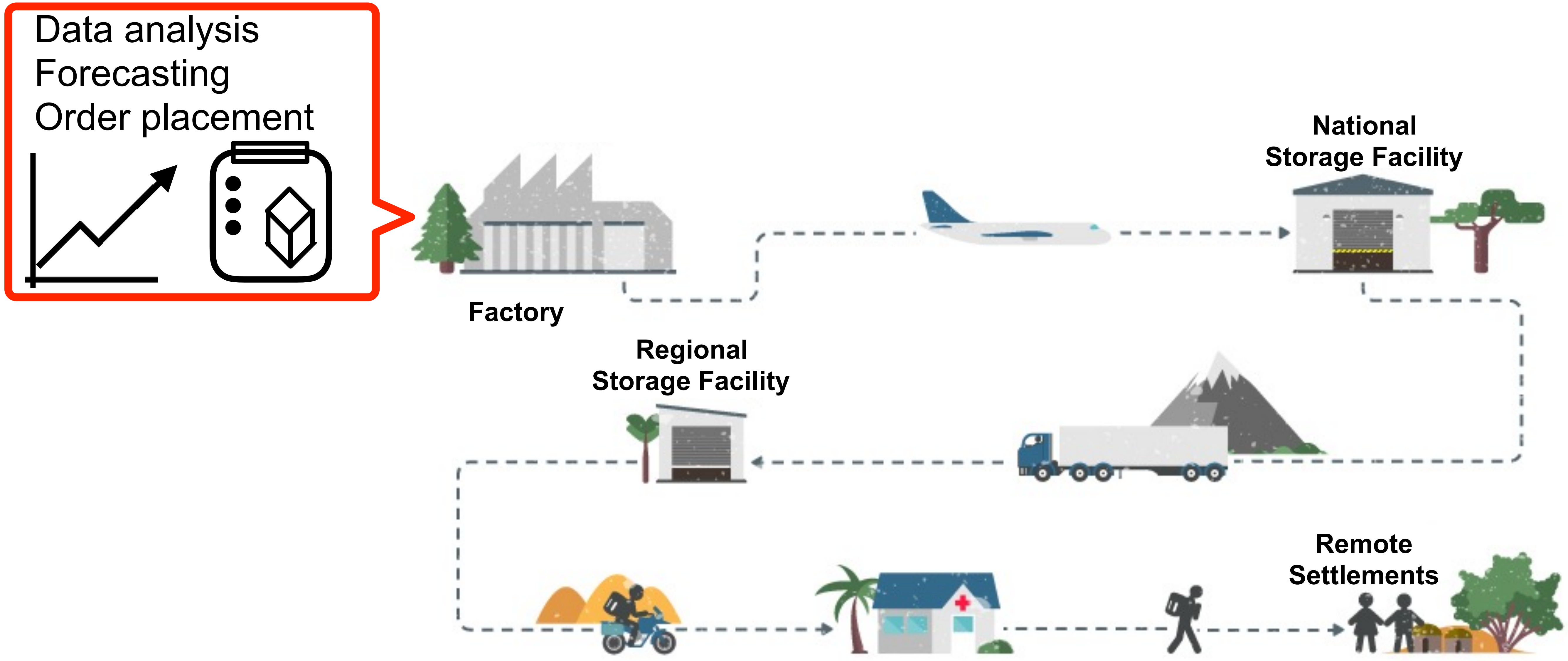
- Existing legacy medical supply chains will be used for distribution and they must be expanded

- Large scale distribution of the vaccine might be e bigger challenge than production

The long road to vaccination

Source: MSF

The long road to vaccination



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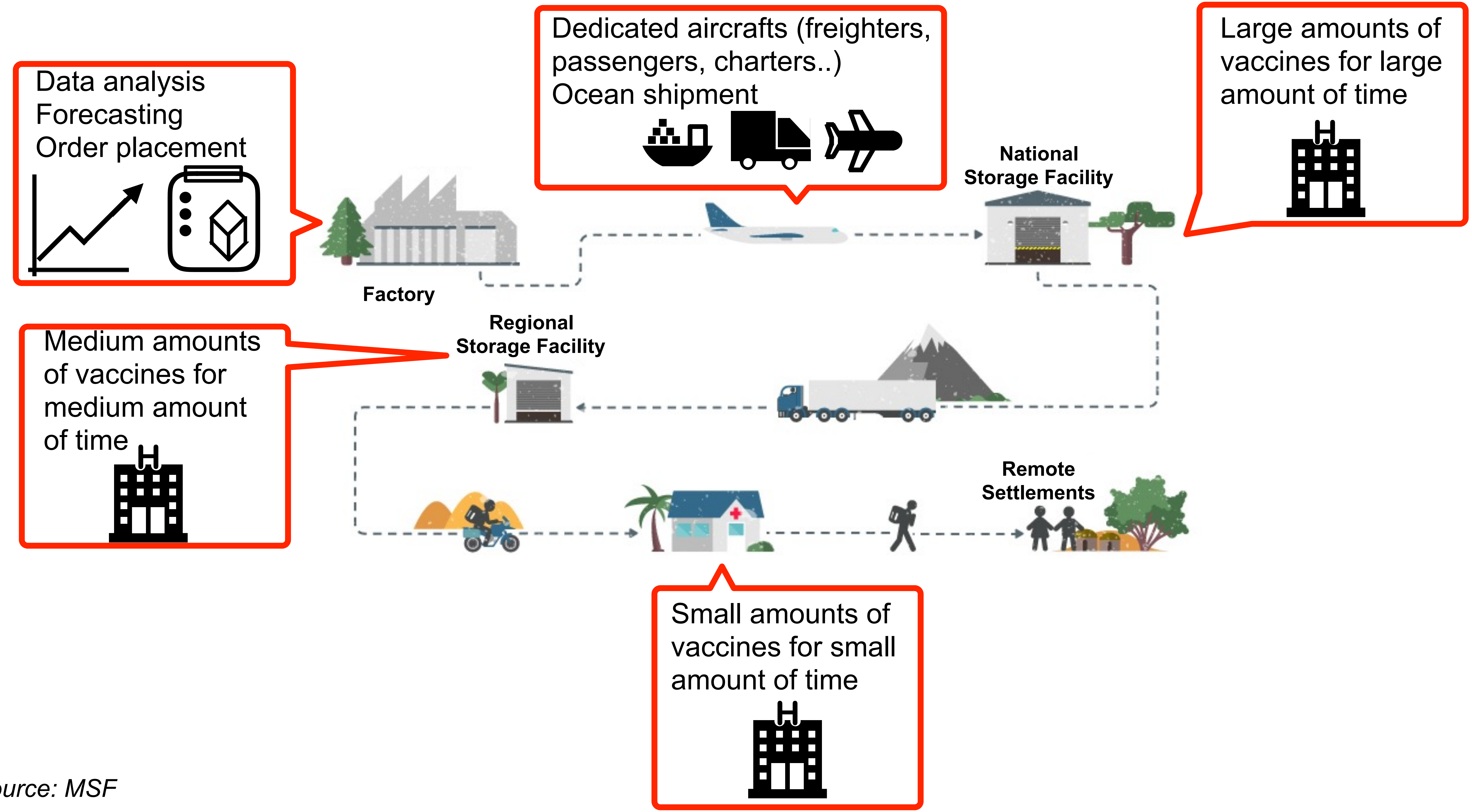
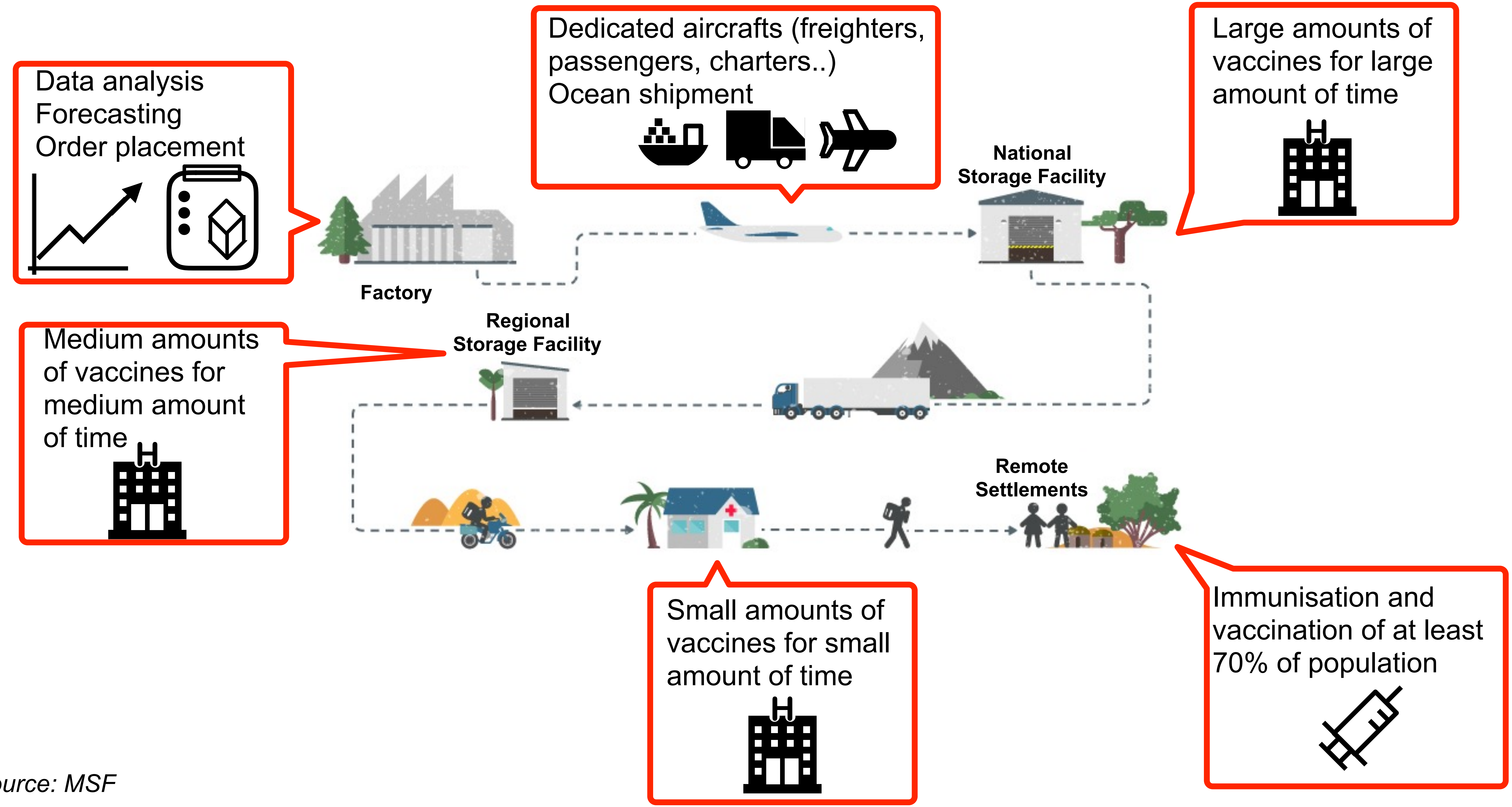


Source: MSF

The long road to vaccination



Source: MSF

Major Challenge I: The Cold Chain

Vaccines are temperature sensitive and they must be kept in a temperature-controlled environment in order to remain safe and effective

Special containers are necessary to safely ship batches of vaccines

Some vaccines must be stored at very low temperatures (some up to -60 or -20 degrees Celcius) during long-haul shipments

Most storage and distribution centres don't have the facilities to keep vaccines in such low temperatures

Storage infrastructure must be developed and expanded in parallel to vaccine production

Major Challenge I: The Cold Chain

Ensuring high quality temperature-controlled packaging of Vaccines during international transportation

Increasing shipping needs of the healthcare and aviation industries must be met

COVID-19 vaccine transportation containers must maintain product temperatures in the prescribed range

Reliable refrigeration systems must be installed to guarantee this temperature stability

They should be large enough to maximise the amount of space that they fill

Photo: Envirotainer AB

Major Challenge I: The Cold Chain

Short term vaccine storage through cold boxes

Cold boxes are insulated containers stocked with water/ice packs to keep vaccines in the required temperature range

The usual cool life spans between few hours up to 2 days depending on various factors (2-8 degrees Celcius - AstraZeneca)

These can be used to carry vaccine supplies from storage units to small local healthcare facilities or from local health facilities to vaccination centres

What about containment at the very low temperatures?

Photo: B Medical Systems

Major Challenge I: The Cold Chain

Pfizers's solution for the COVID-19 vaccines cold boxes

Novel cool box containers have been designed to keep vaccines at ultra low temperatures for a substantial amount of time

Pfizer's newly designed cool box can keep 1000-5000 doses of COVID-19 vaccines at -100 degree Celsius for up to 10 days

Pfizer boxes are re-usable, packed with dry ice and can be tracked by GPS

Trained personnel to handle these boxes

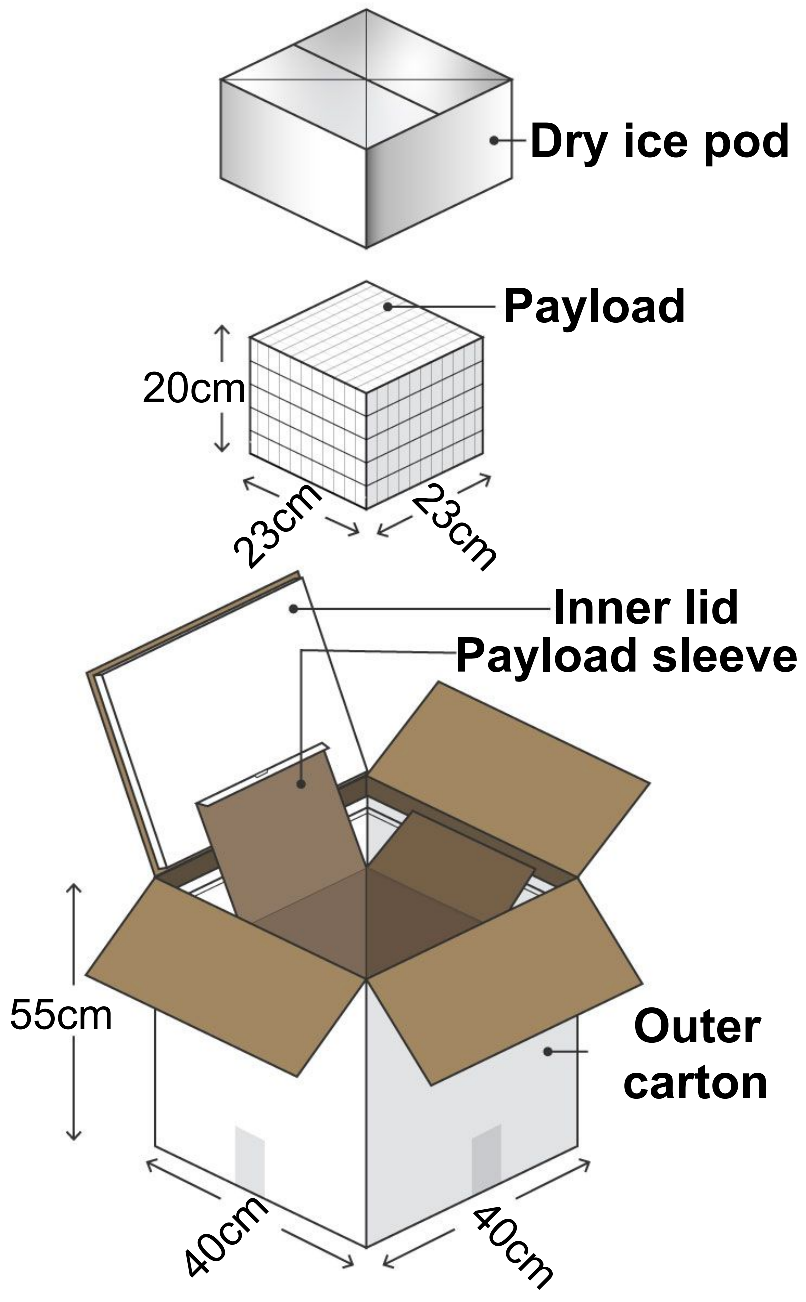
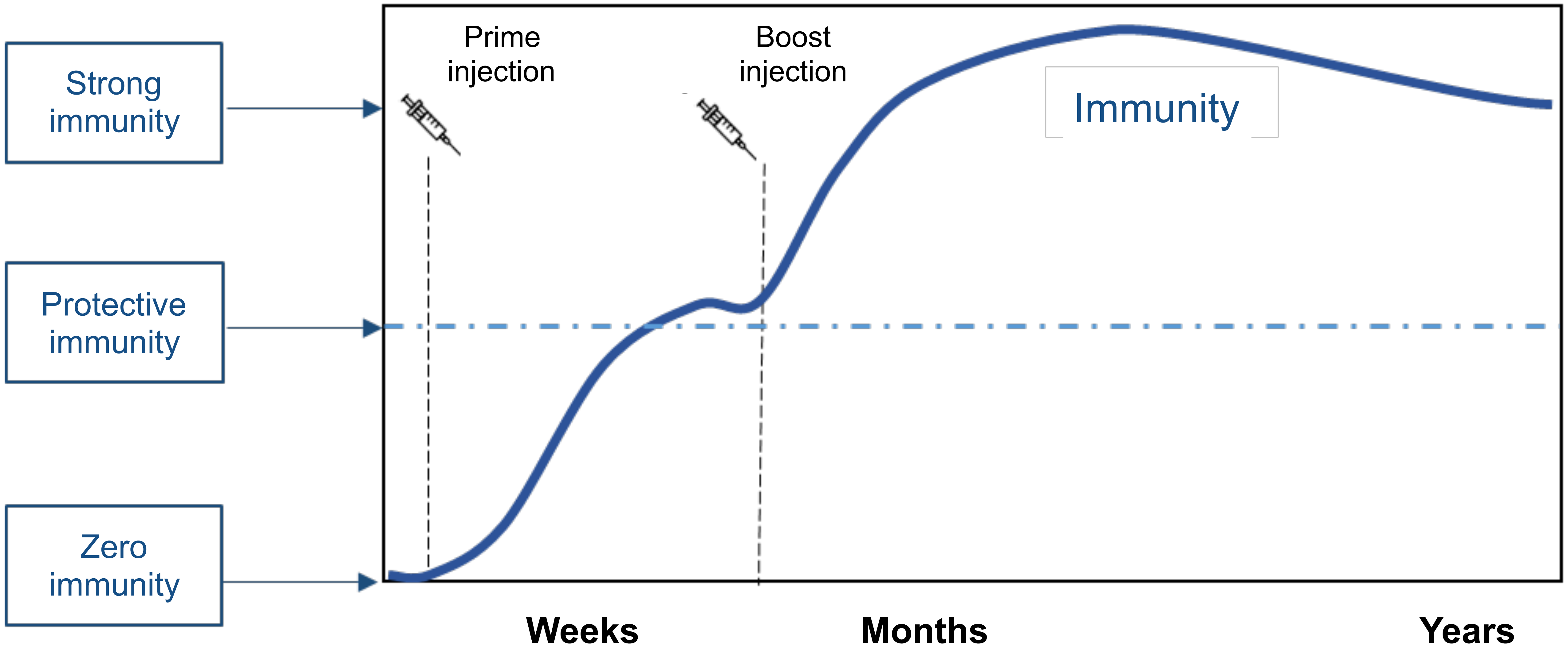


Photo: Pfizer Pharmaceuticals

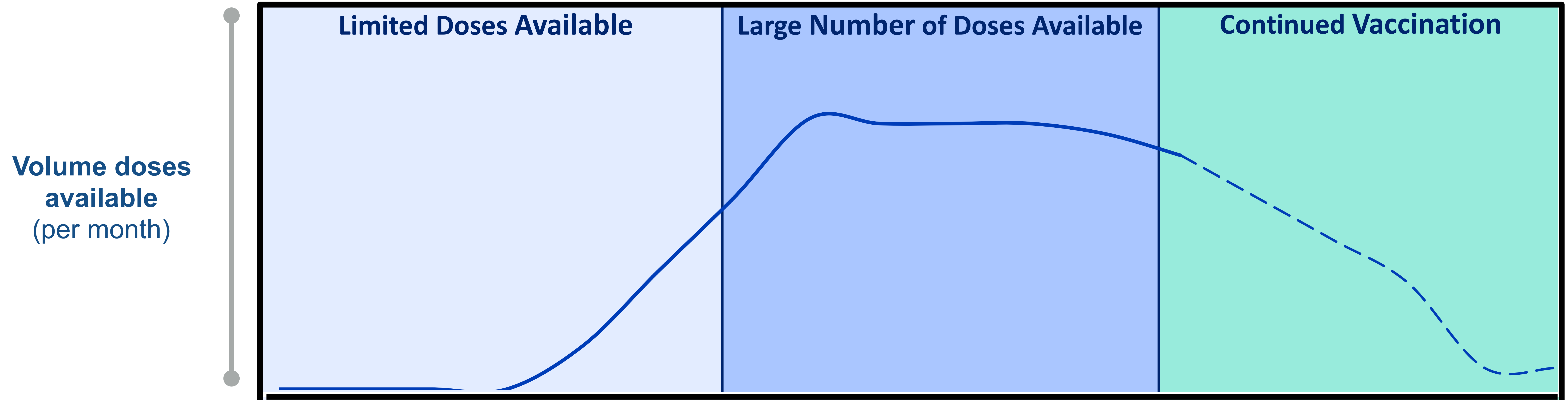
Major Challenge II: More than one dose might be needed

Two doses separated by 21-28 days will be needed for immunity for most COVID-19 vaccines currently under development



BNT162 COVID-19 mRNA Vaccine Program

Major Challenge III: Phased Administration



	Limited Doses Available	Large Number of Doses Available	Continued Vaccination
Key factors	1. Constrained supply 2. Cold chain & handling may require specialised equipment and high throughput	1. Likely sufficient supply 2. Additional vaccine products	1. Sufficient supply
Likely administration strategies	1. Highly targeted administration	1. Broad administration network required 2. Focus on increasing access to critical population	1. Harness vaccine provider network to reach remote populations

ACIP COVID-19 Vaccines Work Group

Other Challenges:

Short time-frame for reaching a large number of people

New resources need to be allocated ad-hoc

Cargo capacity is down during the pandemic

Potential bottlenecks along key supply-chain transferring nodes

Large work-force needs to be trained and made available

It will cost…A LOT!!

How to find the best way to deliver vaccines?

Vaccine delivery is a scale problem

A transportation network design problem can be modelled through various mathematical programs

The transportation network of the COVID-19 vaccine will contain a set of discrete decisions and continuous phenomena

How to find the best way to deliver vaccines?

Vaccine delivery is a scale problem

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The transportation network of the COVID-19 vaccine will contain a set of discrete decisions and continuous phenomena

ILP

$$\min c^T x$$

A cost minimisation objective function

$$Ax \leq b$$

A set of linear constraints

$$l \leq x \leq u$$

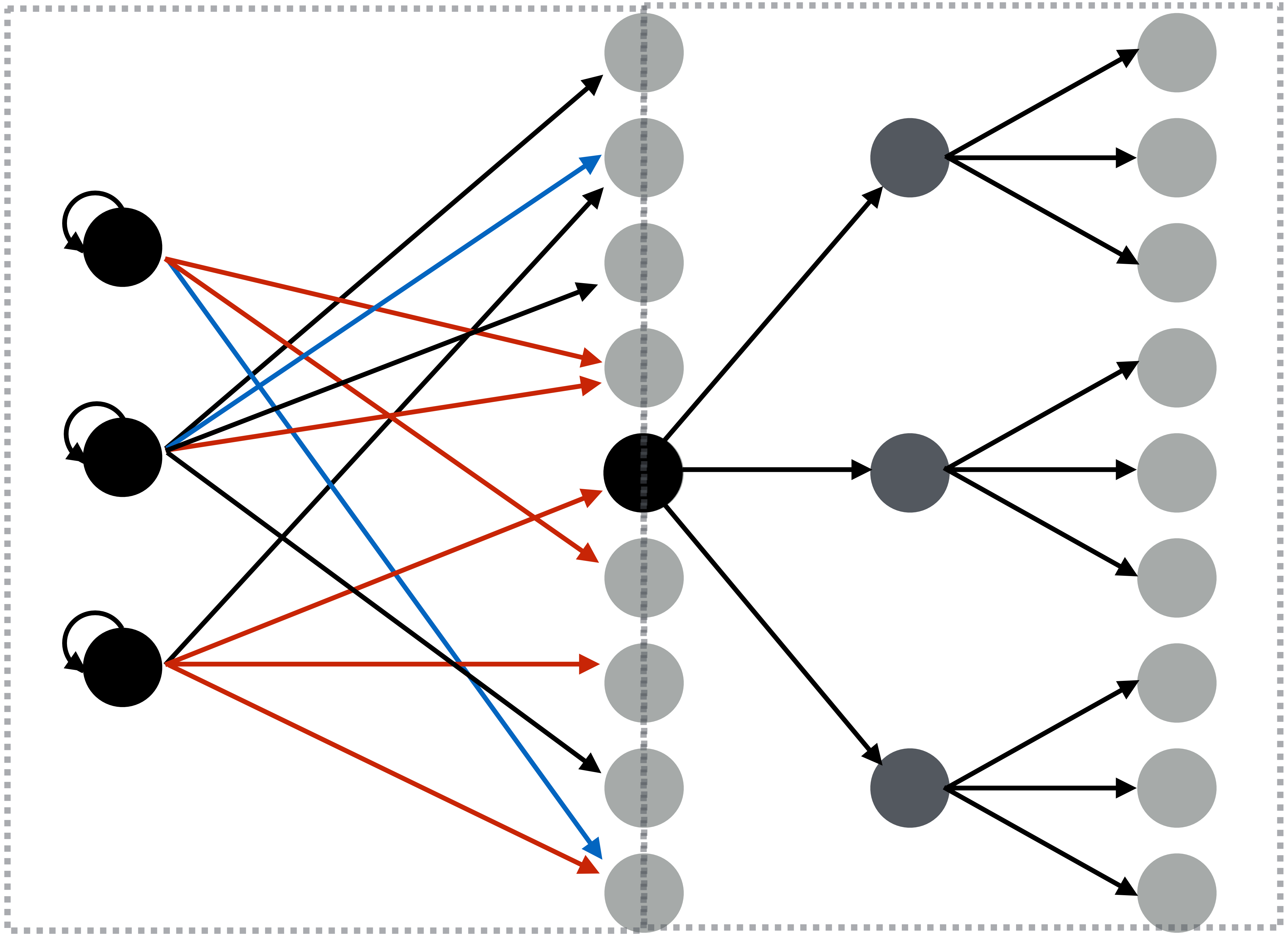
A set of variable bounds

$$x \in Z^n$$

ILP formulation for solving the distribution problem

<u>ILP formulation on two domains:</u> International and National distribution

International Domain

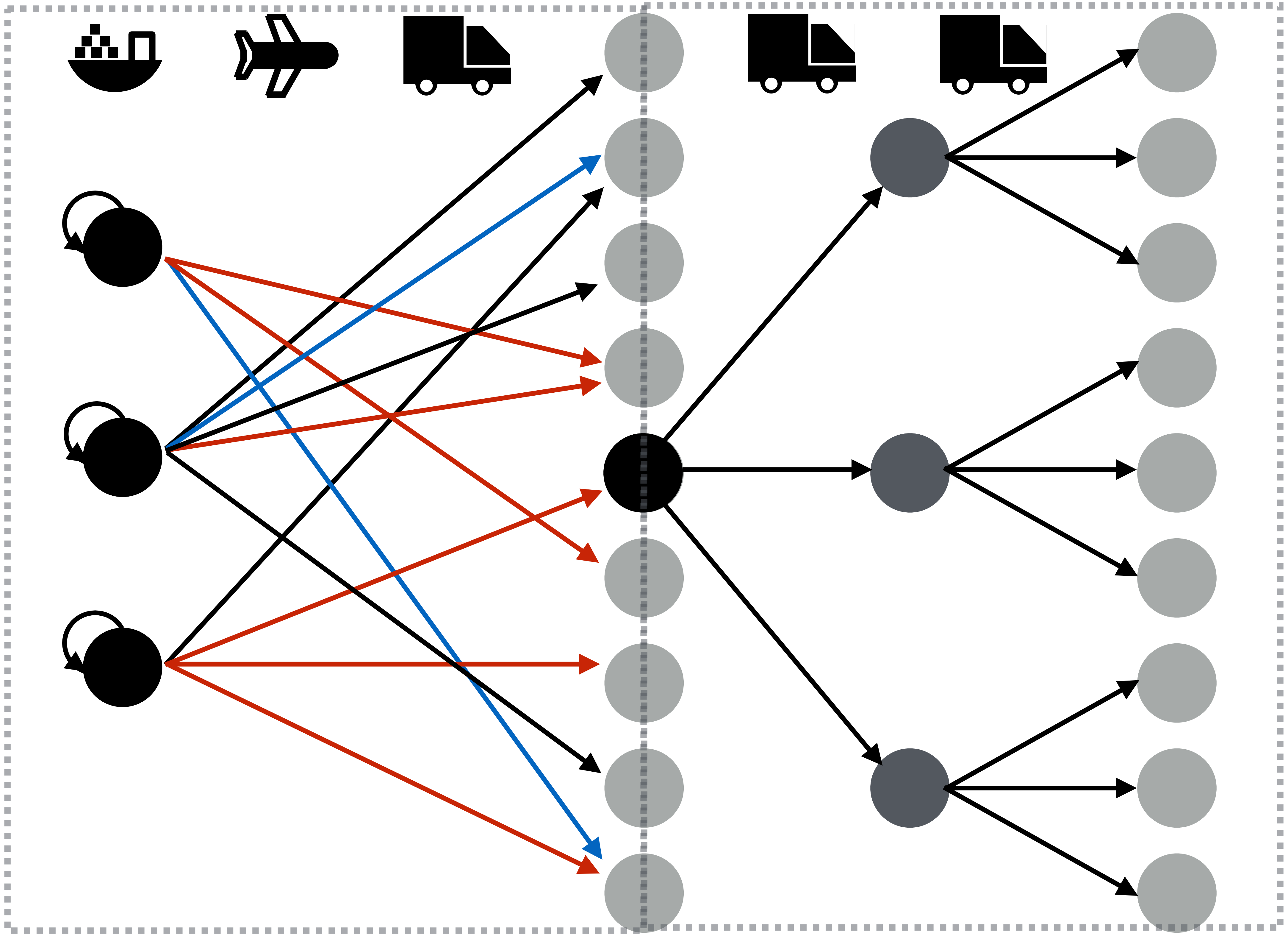


National Domain

ILP formulation for solving the distribution problem

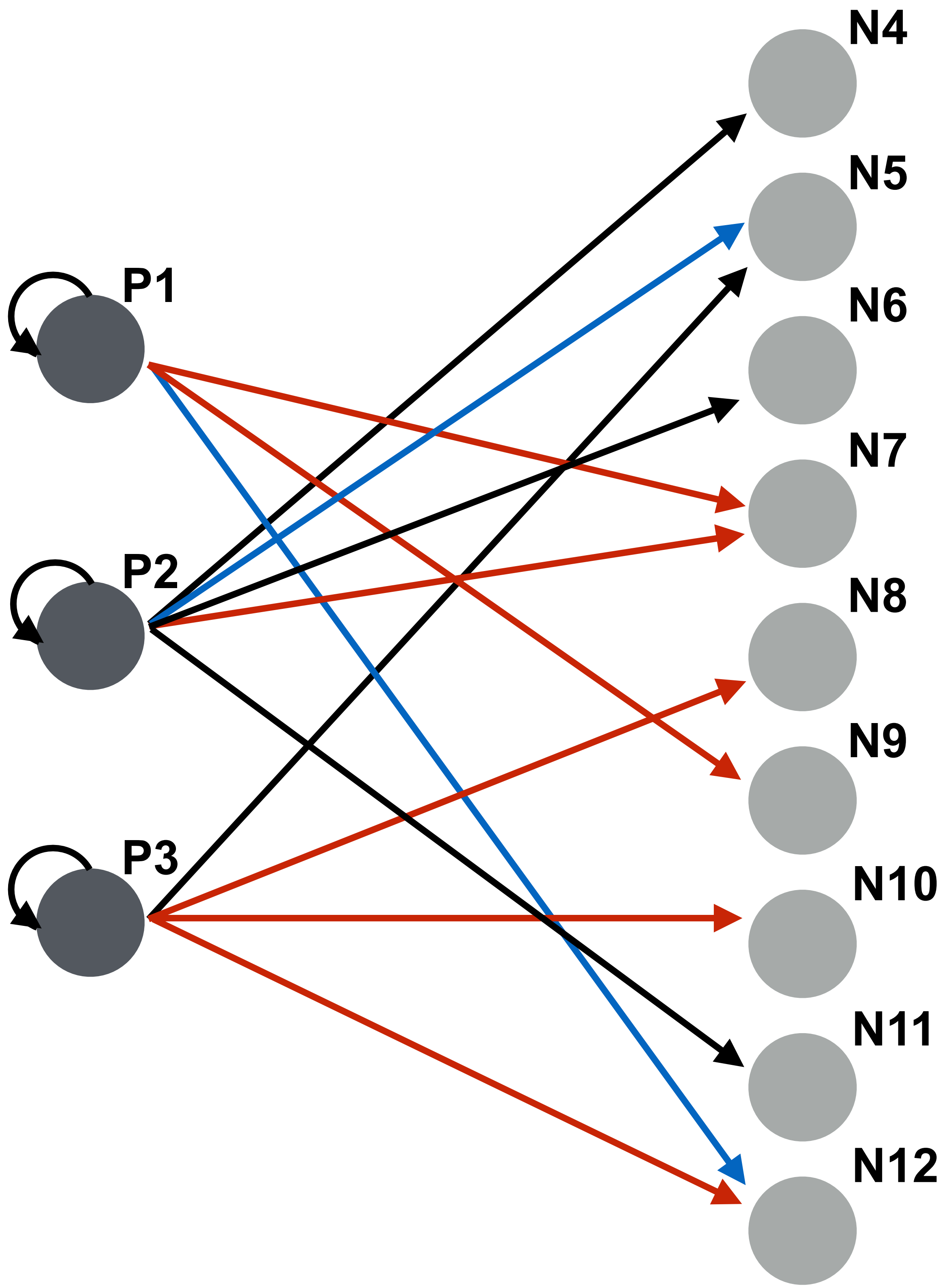
ILP formulation on two domains: International and National distribution

International Domain



National Domain

International Distribution



Legacy infrastructure can be exploited and new transportation routes can be established

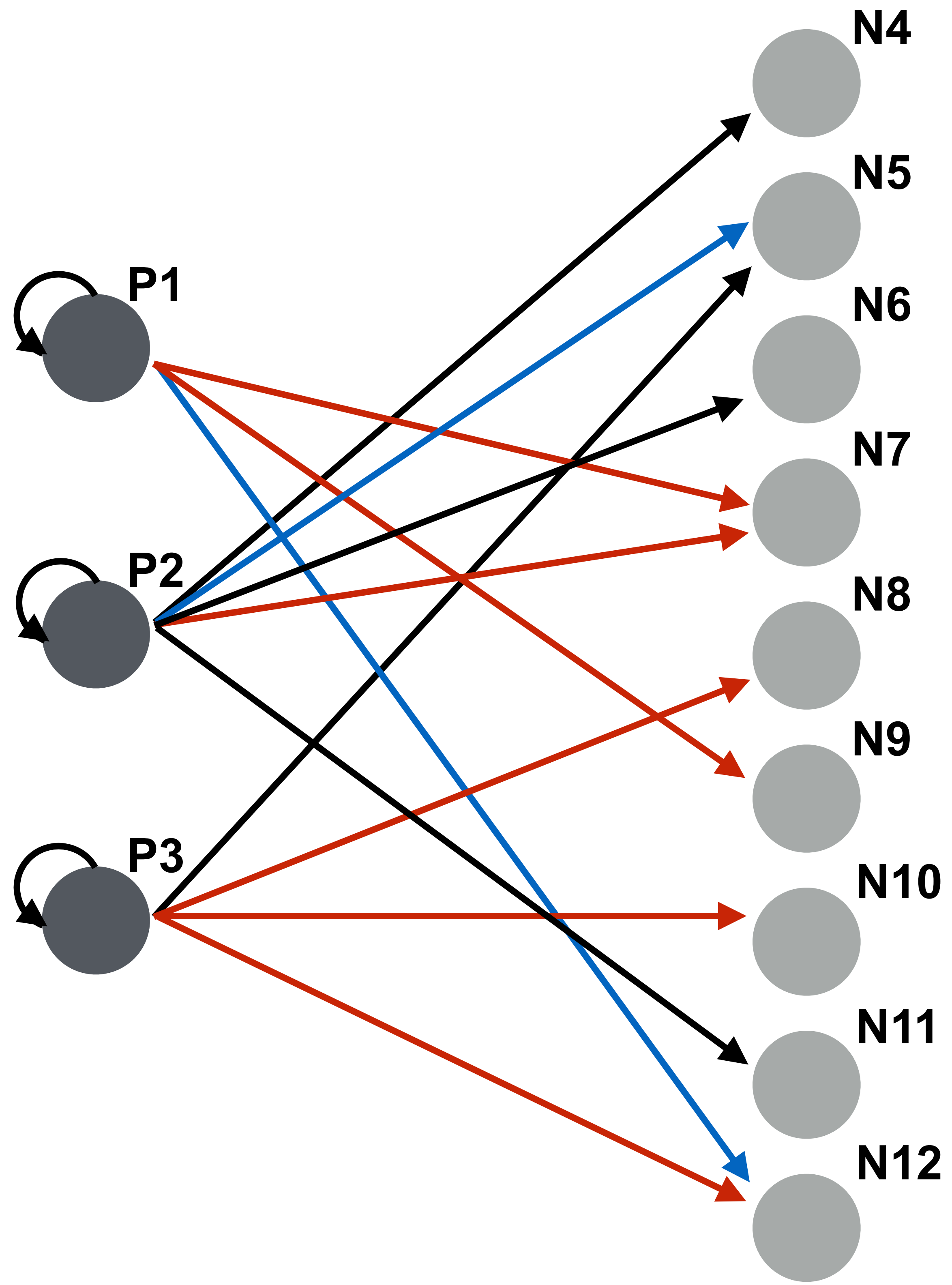
The infrastructure can be represented as a bipartite graph

International routes can be from land, air or sea

Planning models can be designed to maximise distribution and minimise costs within a specific time-frame

International Distribution

The graph representing the transportation routes: $G = (N, V)$



Index set:

N : set of nodes (countries) in the graph

V : set of edges (routes) in the graph

(u, v) : route from $u \in P$ to $v \in N$ in V

A, S, L : set of air, sea and land vehicles that can be used

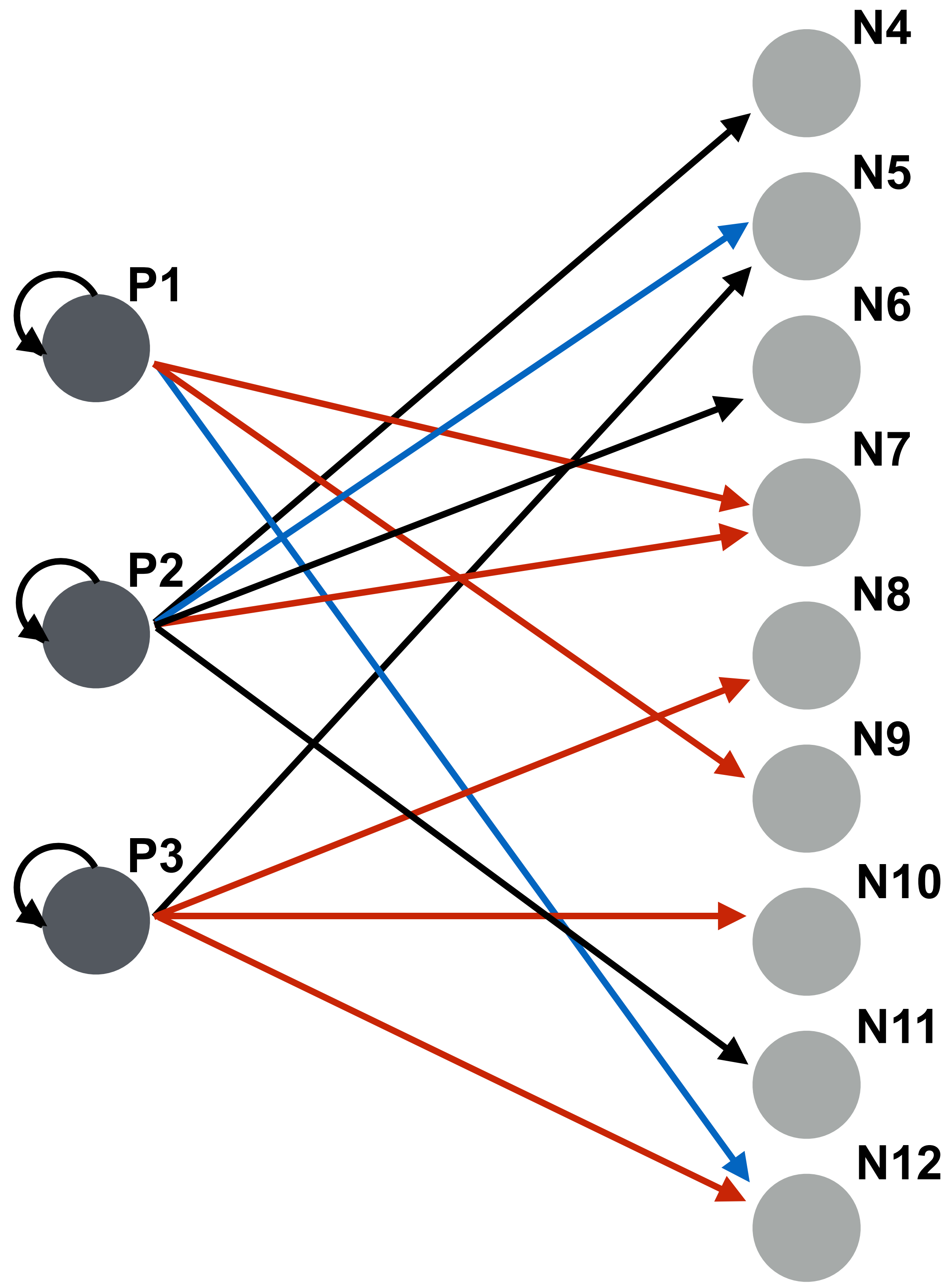
i : vehicle index

$\delta^-(u)$: set of outgoing routes from u

$\delta^+(v)$: set of incoming routes to v

International Distribution

The graph representing the transportation routes: $G=(N,V)$



Parameters set - 1:

D_v : demand in v

T : a distribution time-frame

λ_v : priority parameter for fulfilling demands for each v

$c^i_{(u,v)}$: cost for vehicle i to travel once in (u,v)

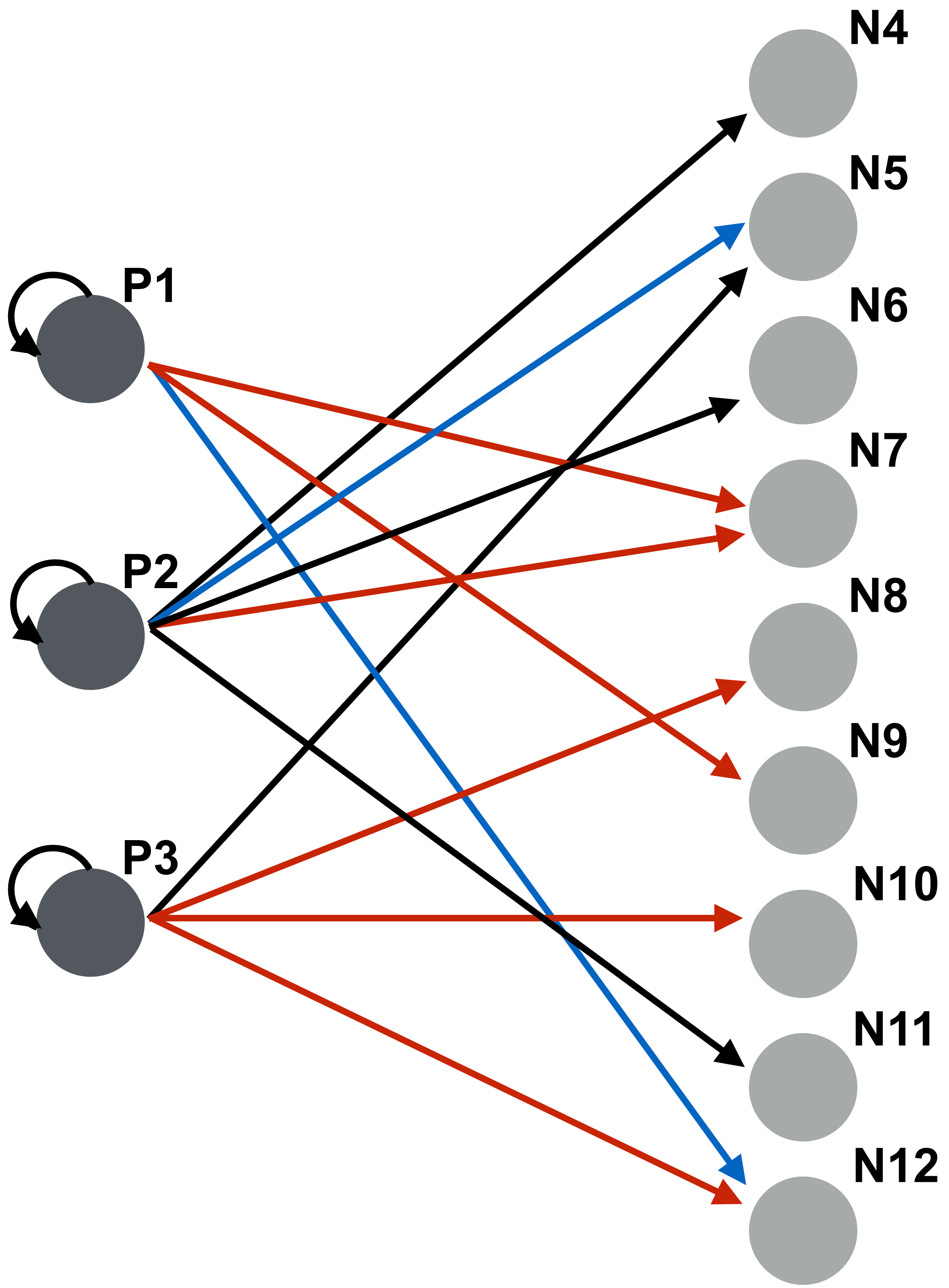
p_u : total vaccine amount produced in $u \in P$

ω^i : amount of vaccines that can be transported through vehicle i

$\tau^i_{(u,v)}$: is the time needed for i to travel (u,v) back and forth

International Distribution

The graph representing the transportation routes: $G=(N,V)$



Parameters set - 2:

n_A, n_S, n_L : total number of available air, sea and land vehicles respectively

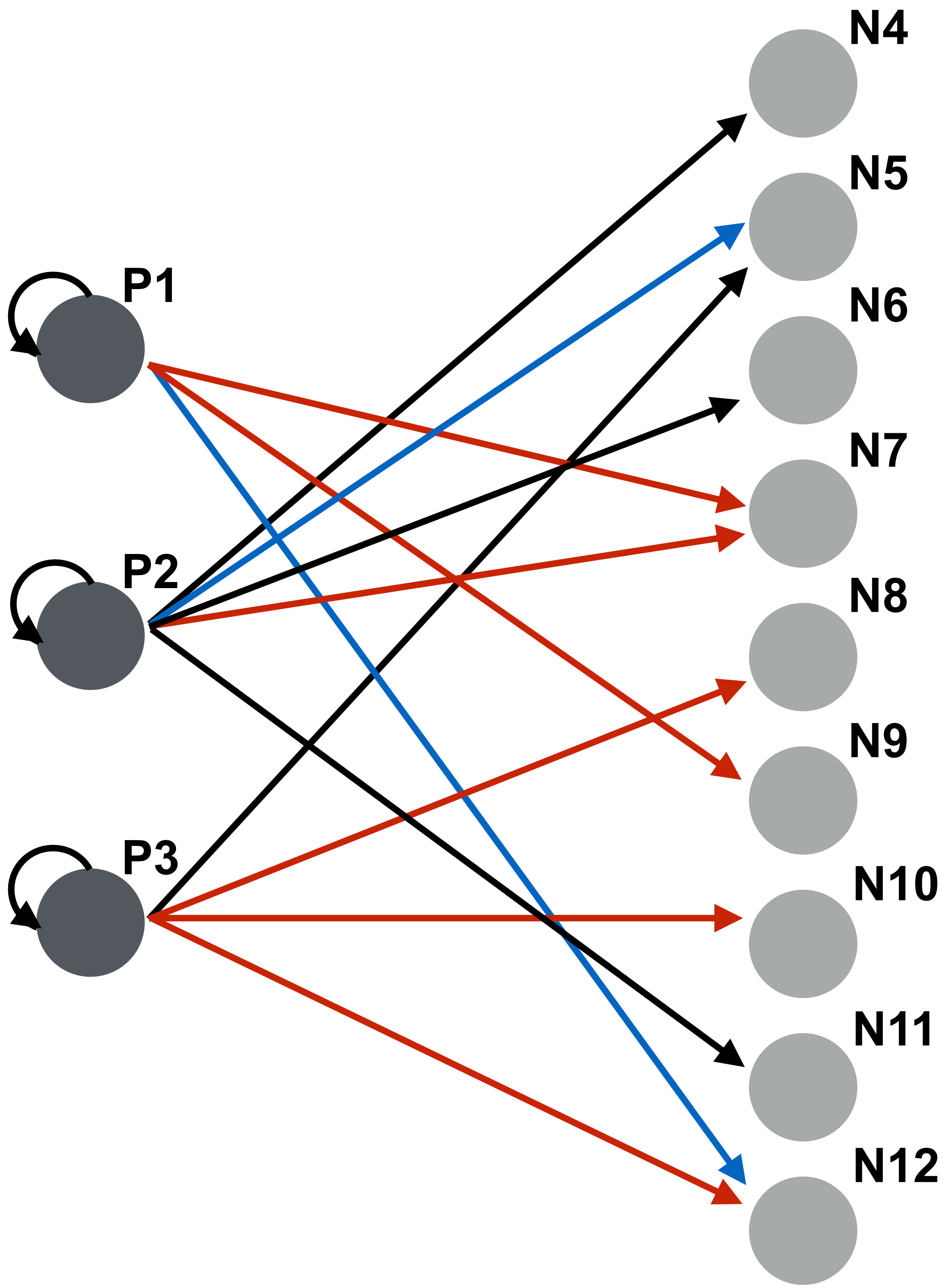
$v_{(u,v)}$: Capacity of route (u,v)

$\theta_v^A, \theta_v^S, \theta_v^L$: Capacity of node v to process air, sea and land vehicles

B_v : budget limitations in v

International Distribution

The graph representing the transportation routes: $G=(N,V)$



Variables set:

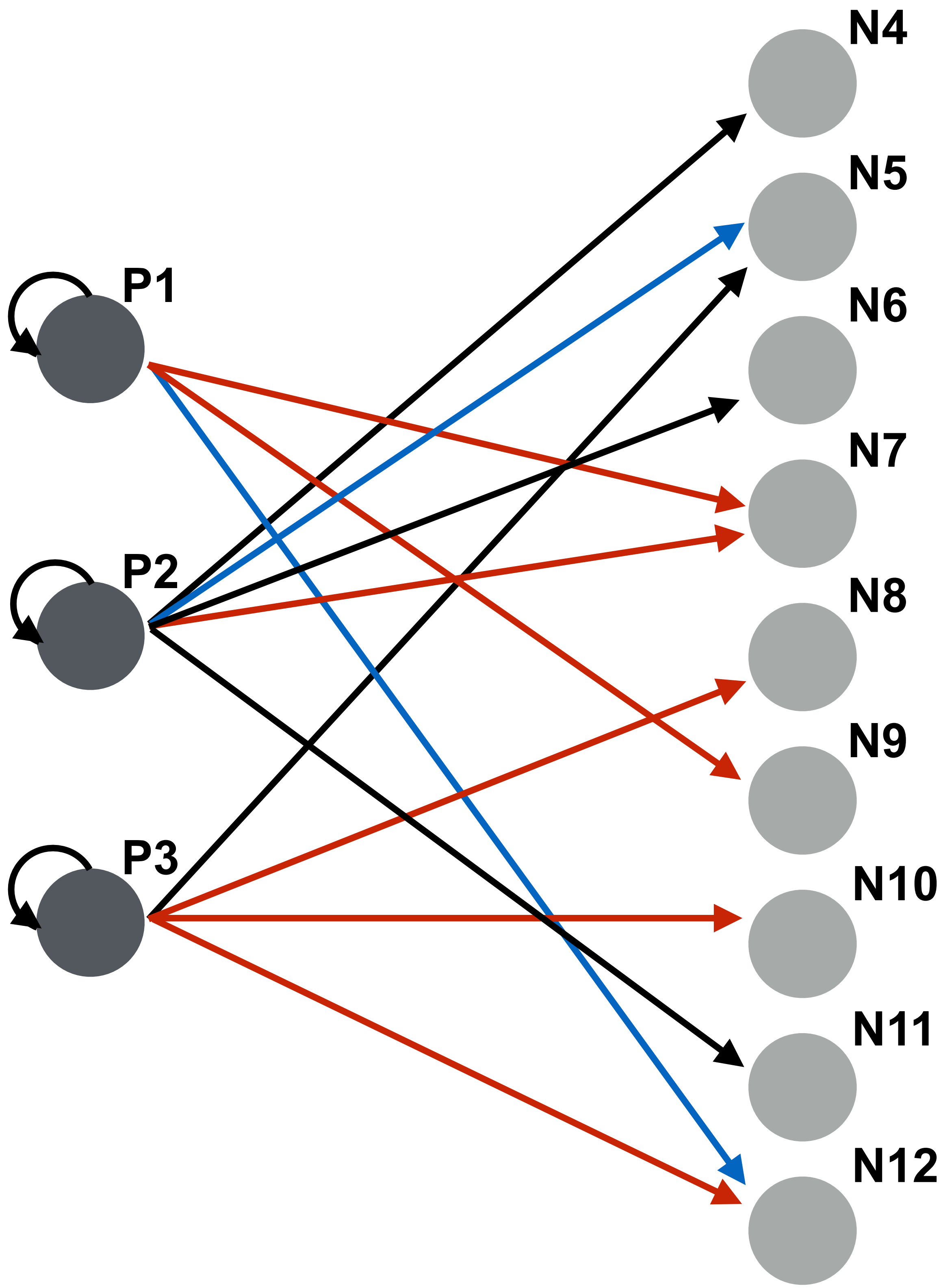
$x_{(u,v)}$: total vaccine amount transported from u to v

X_v : total vaccine amount imported in v

$b^i_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle i is assigned to route (u,v)

$\mu^i_{(u,v)}$: number of times that i travels in (u,v)

International Distribution



Goal: Optimal assignment of distribution vehicles across each route in order to meet as much of the demands as possible while minimising costs

Obj. Fun.: $$\min \left[\sum_{v \in N} \lambda_v \left| D_v - X_v \right| + \beta \sum_{i \in (S \cup A \cup L)} \sum_{(u,v) \in V} c^i_{(u,v)} \mu^i_{(u,v)} \right]$$

v : node index

i : vehicle index

(u,v) : route from $u \in P$ to $v \in N$ in V

D_v : demand in v

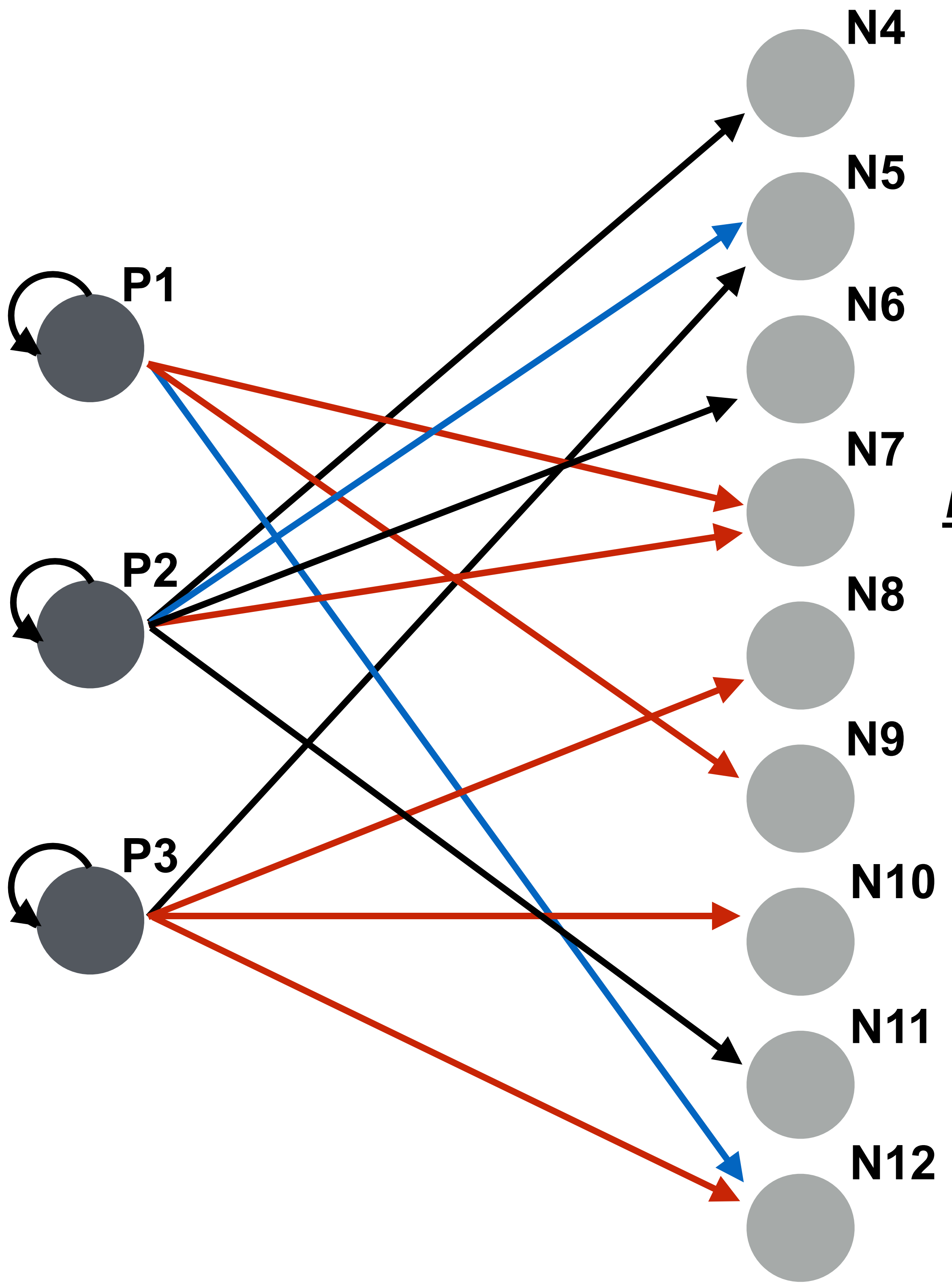
X_v : total supply in v

$c^i_{(u,v)}$: cost for vehicle i to travel once in (u,v)

$\mu^i_{(u,v)}$: number of times that i travels in (u,v)

λ_v : priority parameter for fulfilling demands for each v

International Distribution

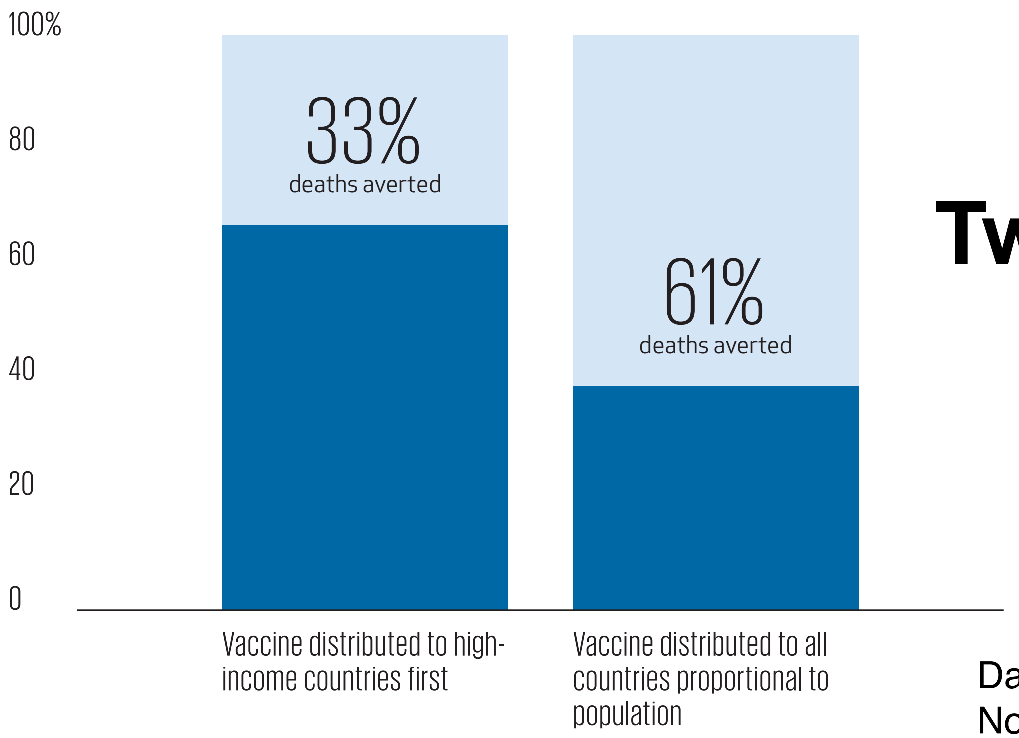


Goal: Optimal assignment of distribution vehicles across for each route to meet demands as much as possible while minimising costs

Obj. Fun.: $$\min\left[\sum_{v\in N}\lambda_v\left|D_v - X_v\right| + \beta \sum_{i\in(S\cup A\cup L)}\ \sum_{(u,v)\in V} c^{i}_{(u,v)}\mu^{i}_{(u,v)}\right]$$

It is expected for producers to fulfil their domestic demands first

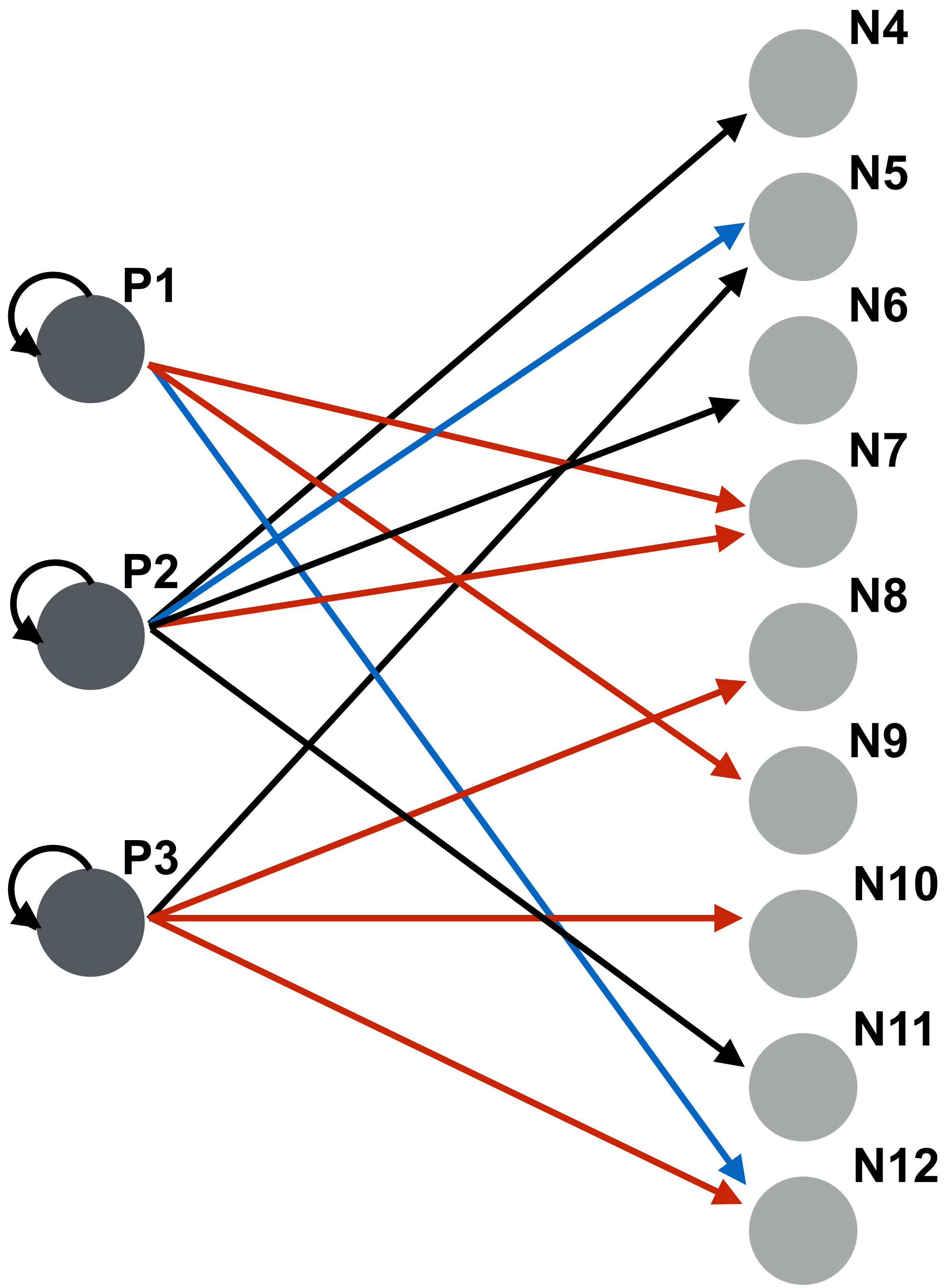
MODELLED PERCENTAGE OF DEATHS



Twice less deaths are expected to happen if priorities are set as equal

Data from MOBS LAB, Northeastern University.

International Distribution



Constraint 1: The total supply amount exported from each producing node cannot exceed the amount they can produce

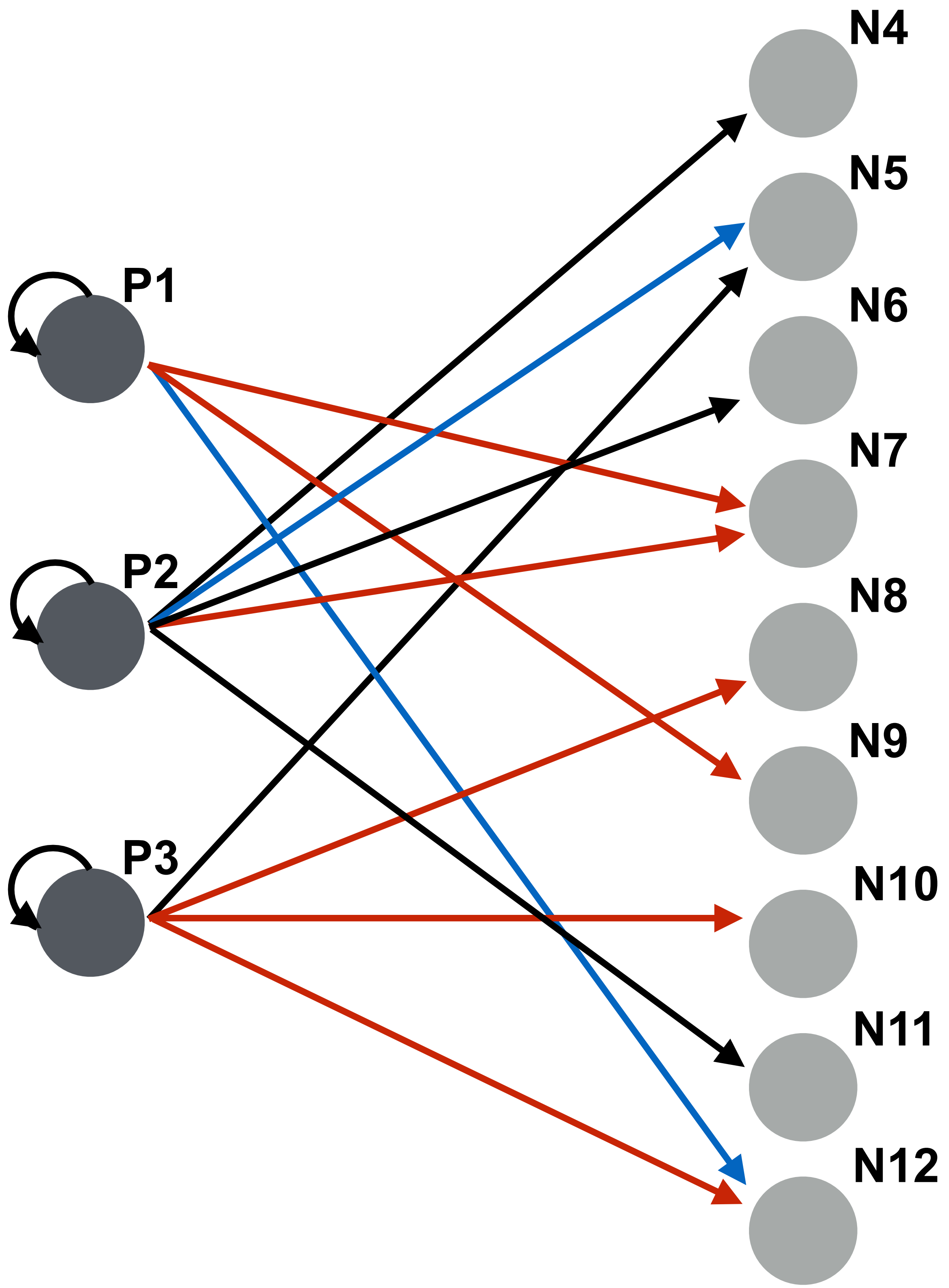
$$\sum_{(u,v)\in\delta^-(u)} x_{(u,v)} \le p_u \qquad \forall u \in P$$

p_u : total vaccine amount produced in u

$x_{(u,v)}$: total vaccine amount transported from u to v

$\delta^-(u)$: set of outgoing routes from u

International Distribution



Constraint 2: The total supply amount imported on each node is the same as the sum supply provided through each route

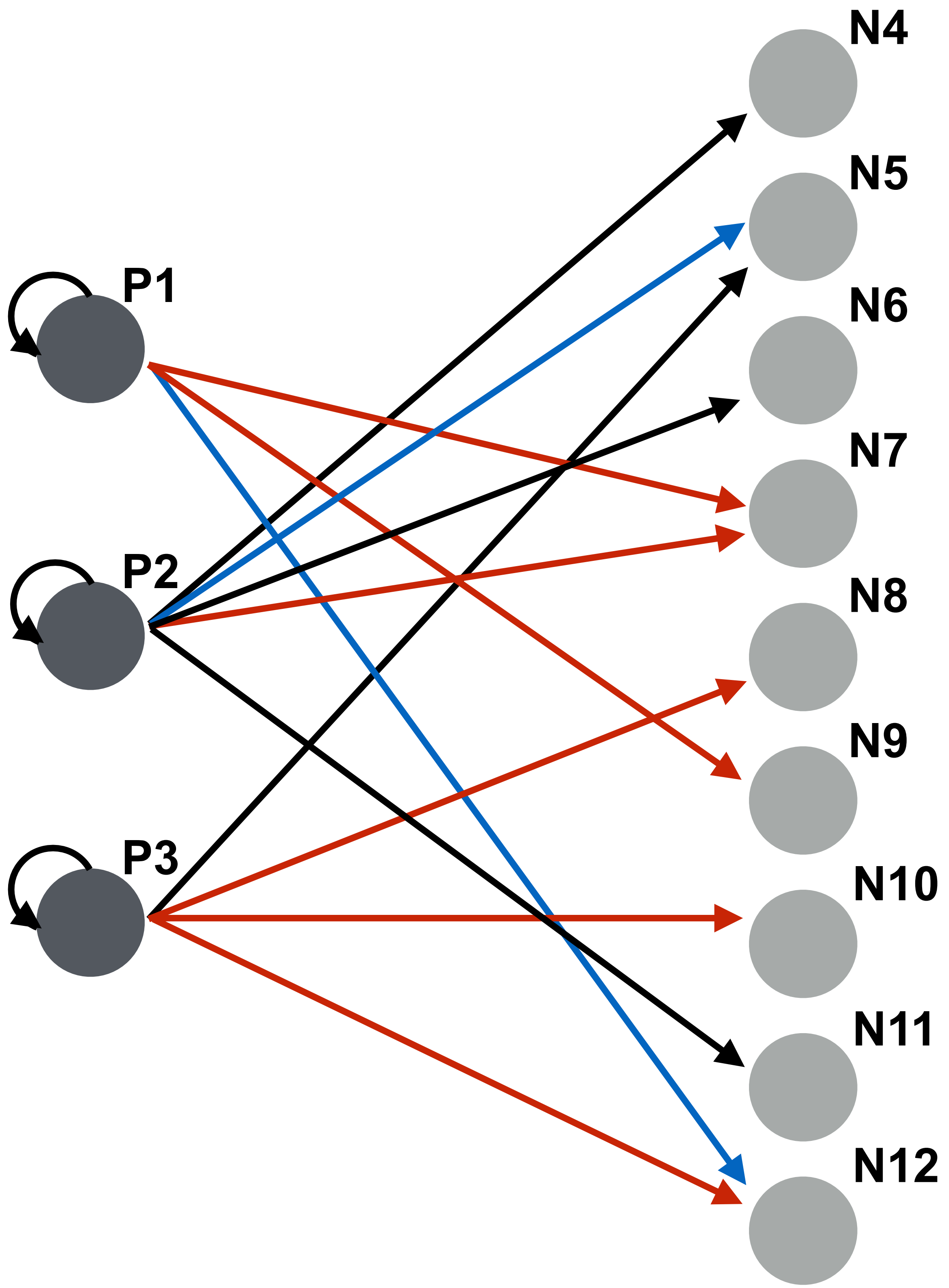
$$X_v = \sum_{(u,v)\in\delta^+(v)} x_{(u,v)} \qquad \forall v \in N$$

X_v : total vaccine amount imported in v

$x_{(u,v)}$: total vaccine amount transported from u to v

$\delta^+(v)$: set of incoming routes to v

International Distribution



Constraint 3: The total supply amount imported through each route depends on how often a vehicles travels on that route

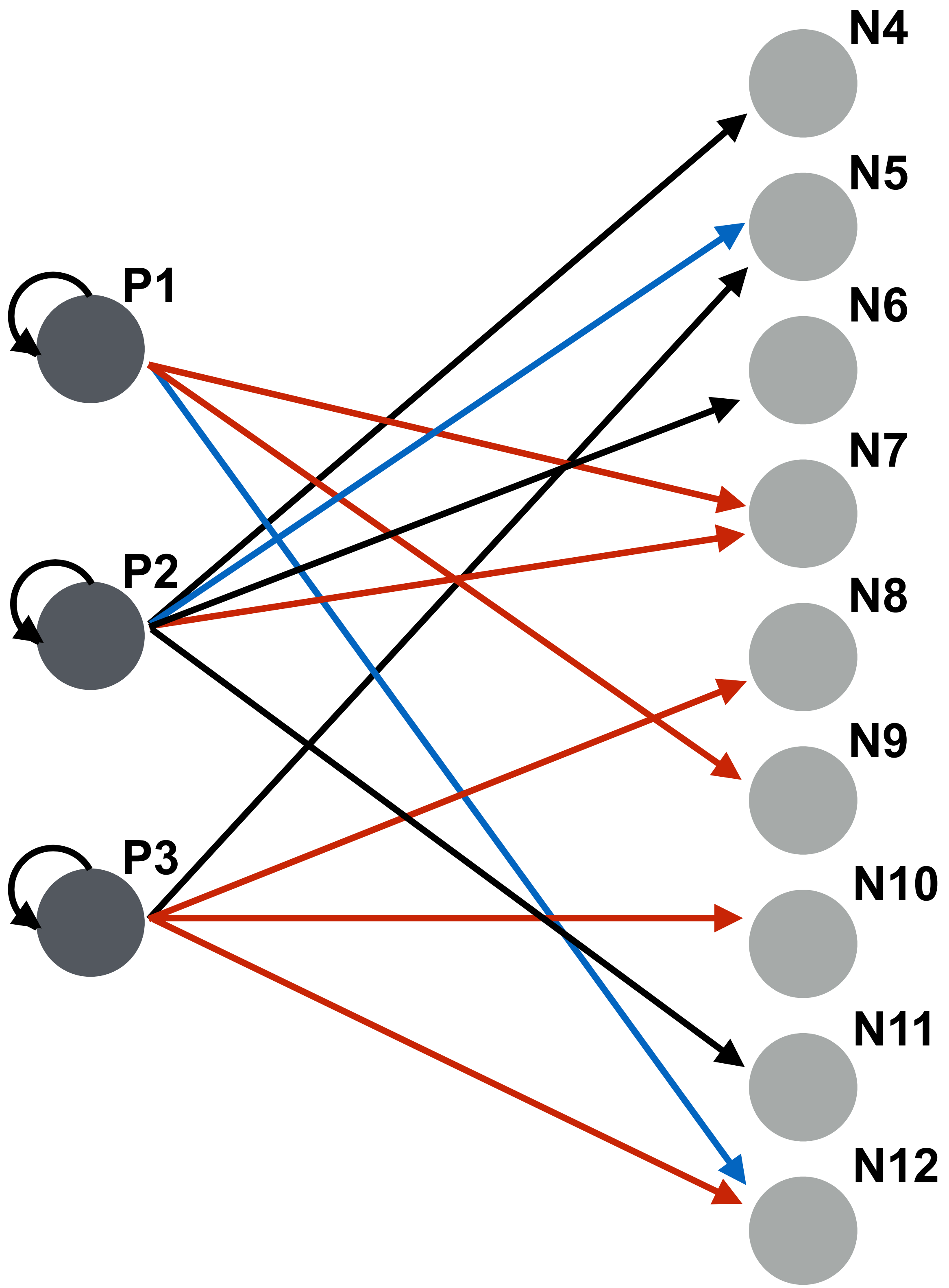
$$x_{(u,v)} = \sum_{i \in (S \cup A \cup L)} \sum_{(u,v) \in \delta^+(v)} \mu^i_{(u,v)} \omega^i \qquad \forall v \in N$$

$\mu^i_{(u,v)}$: number of times that i travels in (u,v)

ω^i : amount of vaccines that can be transported through vehicle i

Here we assume that a vehicle is transporting vaccines at full capacity

International Distribution



Constraint 4: One vehicle can potentially only be assigned to one path

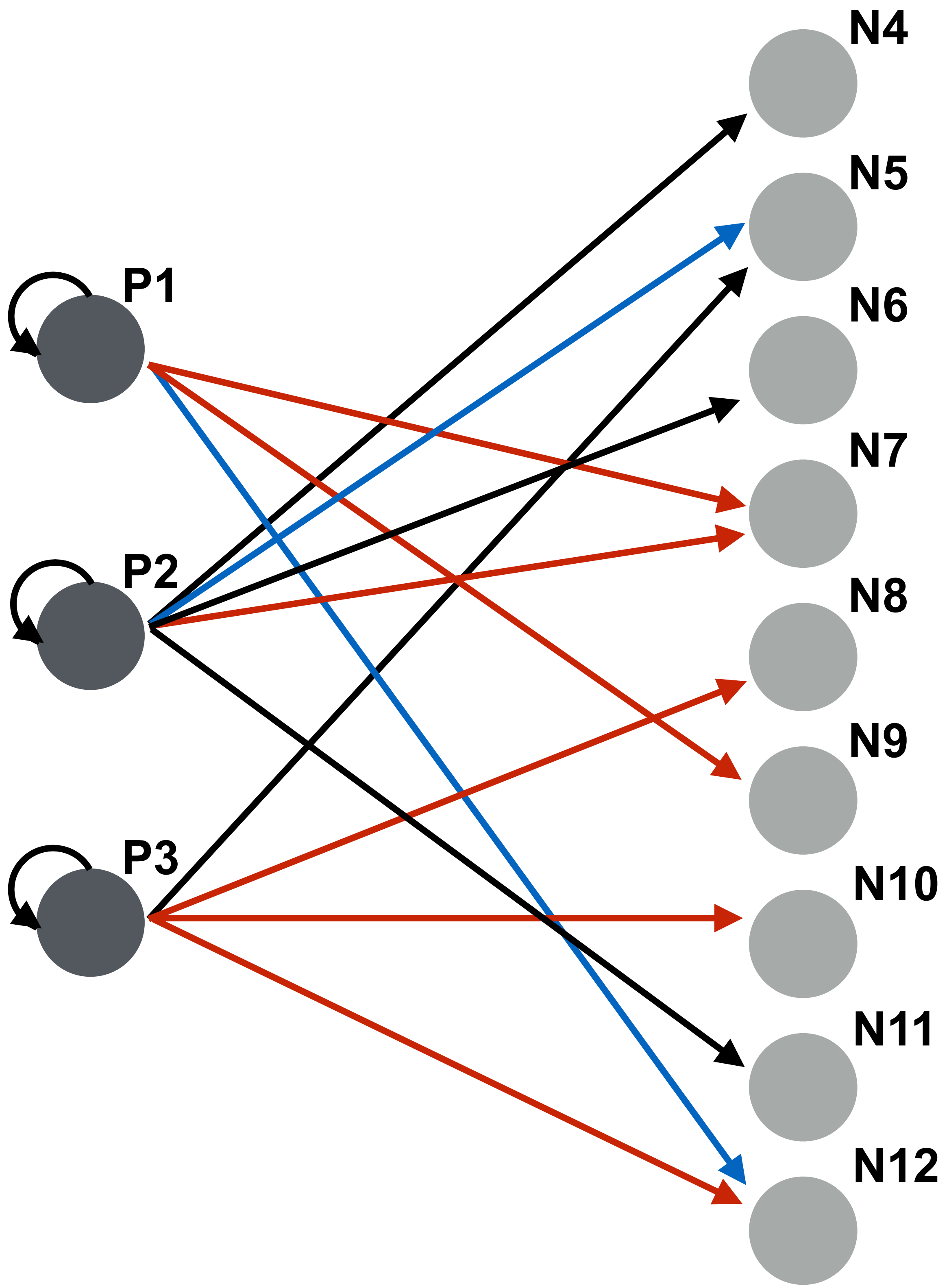
$$\sum_{(u,v)\in V(A)} b^{i}_{(u,v)} \leq 1 \qquad \forall i \in A$$

$$\sum_{(u,v)\in V(S)} b^{i}_{(u,v)} \leq 1 \qquad \forall i \in S$$

$$\sum_{(u,v)\in V(L)} b^{i}_{(u,v)} \leq 1 \qquad \forall i \in L$$

$b^{i}_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle i is assigned to route (u,v)

International Distribution



Constraint 5: Number of vehicles to be used cannot exceed the total amount available

$$\sum_{(u,v)\in V(A)} \sum_{i\in A} b^i_{(u,v)} \le n_A \qquad \forall i \in A$$

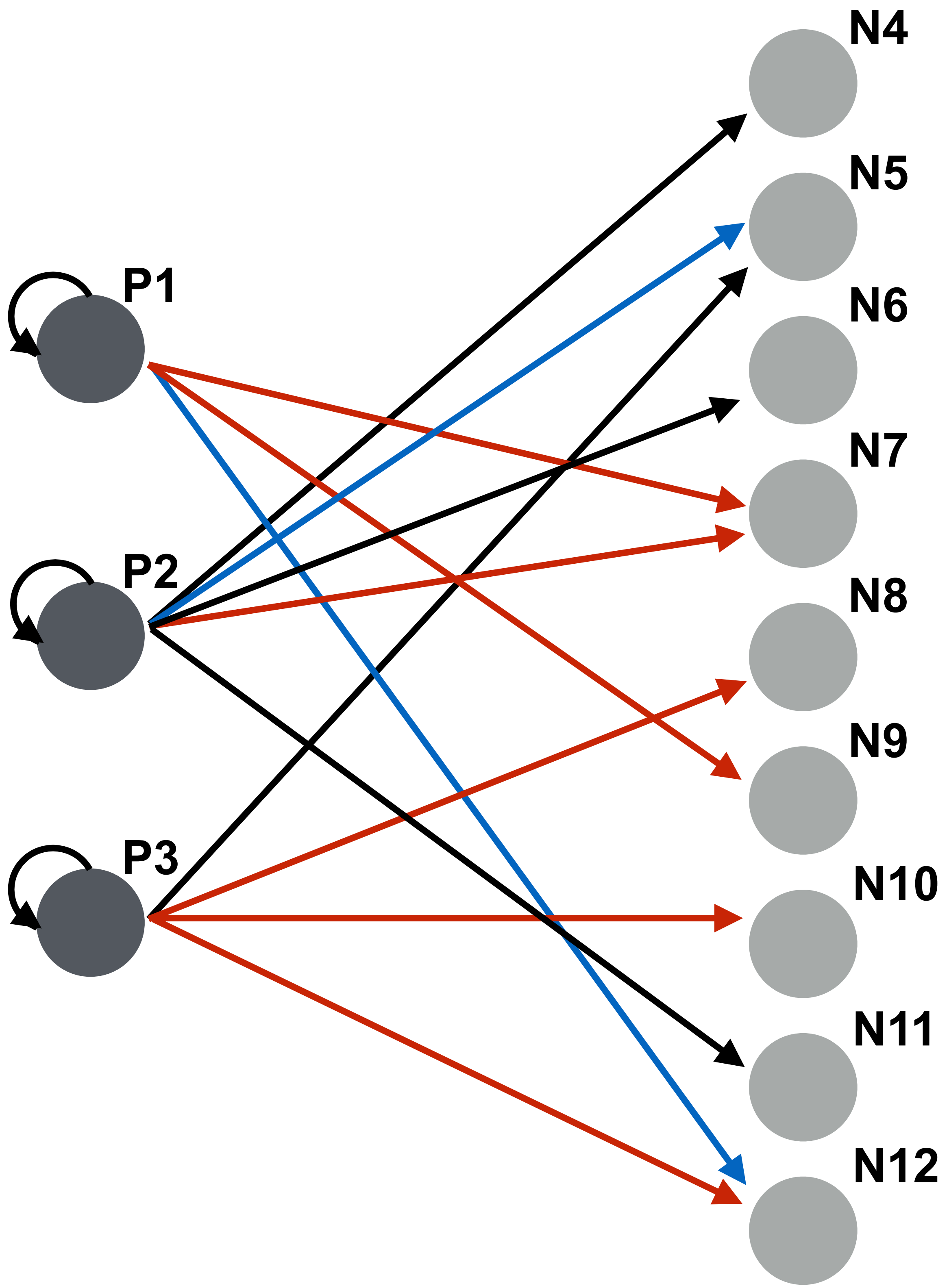
$$\sum_{(u,v)\in V(S)} \sum_{i\in S} b^i_{(u,v)} \le n_S \qquad \forall i \in S$$

$$\sum_{(u,v)\in V(L)} \sum_{i\in L} b^i_{(u,v)} \le n_L \qquad \forall i \in L$$

$b^i_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle i is assigned to route (u,v)

n_A, n_S, n_L : total number of available air, sea and land vehicles respectively

International Distribution



Constraint 7: If a vehicle is not assigned to a route, then it will make this route for 0 times

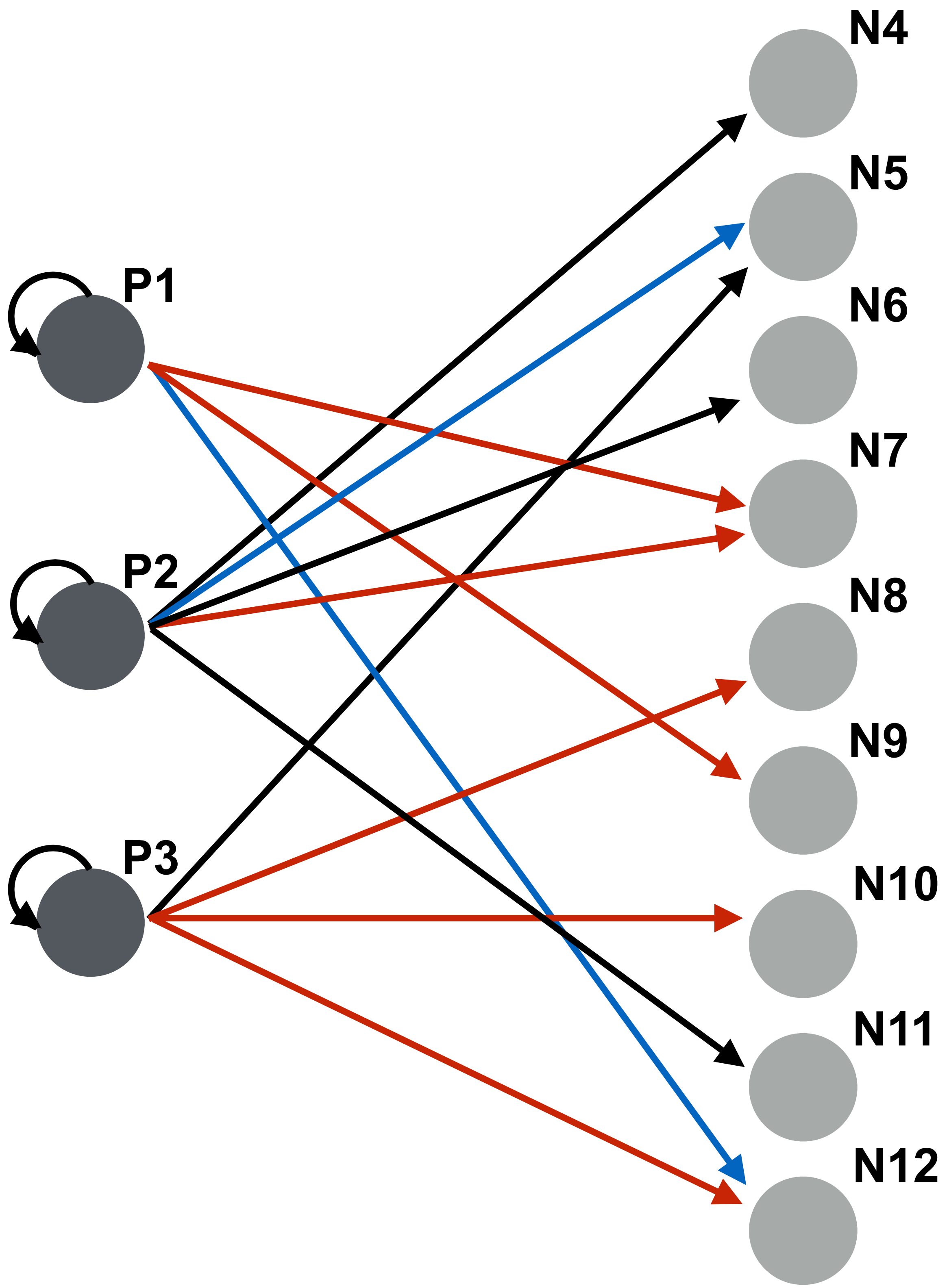
$$0 \le \mu^i_{(u,v)} \le b^i_{(u,v)} M_1$$

$\mu^i_{(u,v)}$: number of times that i travels in (u,v)

$b^i_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle is assigned to route

M_2 : A sufficiently large number

International Distribution



Constraint 8: The number of times of vehicles going through a route cannot exceed the capacities of that route

$$\sum_{i \in A} \mu^i_{(u,v)} \leq v_{(u,v)} \qquad \forall (u,v) \in V(A)$$

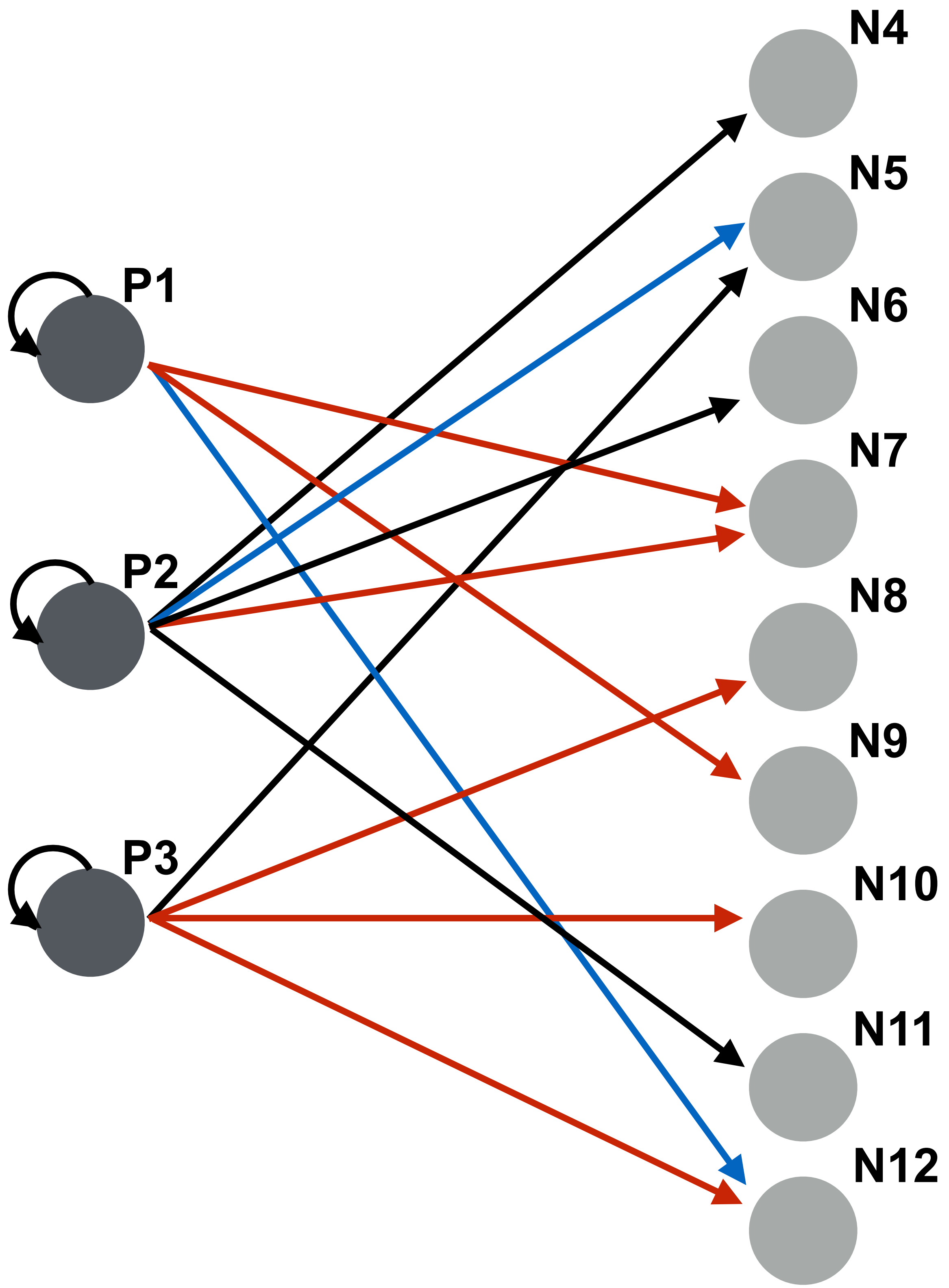
$$\sum_{i \in S} \mu^i_{(u,v)} \leq v_{(u,v)} \qquad \forall (u,v) \in V(S)$$

$$\sum_{i \in L} \mu^i_{(u,v)} \leq v_{(u,v)} \qquad \forall (u,v) \in V(L)$$

$v_{(u,v)}$: Capacity of route (u,v)

$\mu^i_{(u,v)}$: number of times that i travels in (u,v)

International Distribution



Constraint 9: The amount of incoming vehicles should not exceed the ability of a node to process them

$$\sum_{i \in A} \sum_{(u,v) \in V(A)} \mu^{i}_{(u,v)} \leq \theta^{A}_{v} \qquad \forall v \in N$$

$$\sum_{i \in S} \sum_{(u,v) \in V(S)} \mu^{i}_{(u,v)} \leq \theta^{S}_{v} \qquad \forall v \in N$$

$$\sum_{i \in L} \sum_{(u,v) \in V(L)} \mu^{i}_{(u,v)} \leq \theta^{L}_{v} \qquad \forall v \in N$$

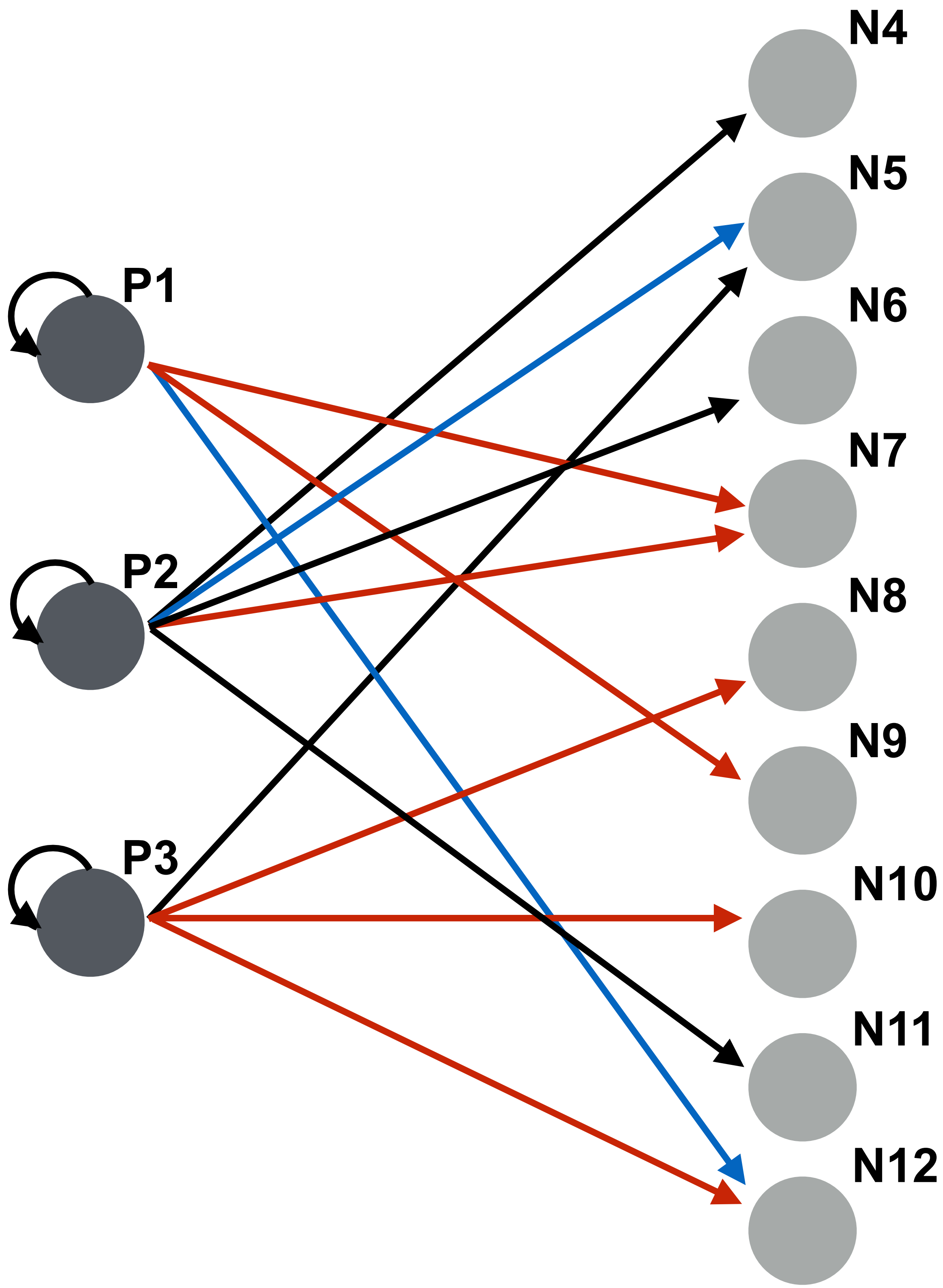
θ^{A}_{v} : Capacity of node v to process air vehicles within T

θ^{S}_{v} : Capacity of node v to process sea vehicles within T

θ^{L}_{v} : Capacity of node v to process land vehicles within T

$\mu^{i}_{(u,v)}$: number of times that i travels in (u,v)

International Distribution



Constraint 10: All the vehicles should route their assigned paths within the time-limit T

$$\mu^i_{(u,v)} \le T / \tau^i_{(u,v)} \qquad \forall i \in (A \cup S \cup L) \quad \forall (u,v) \in V$$

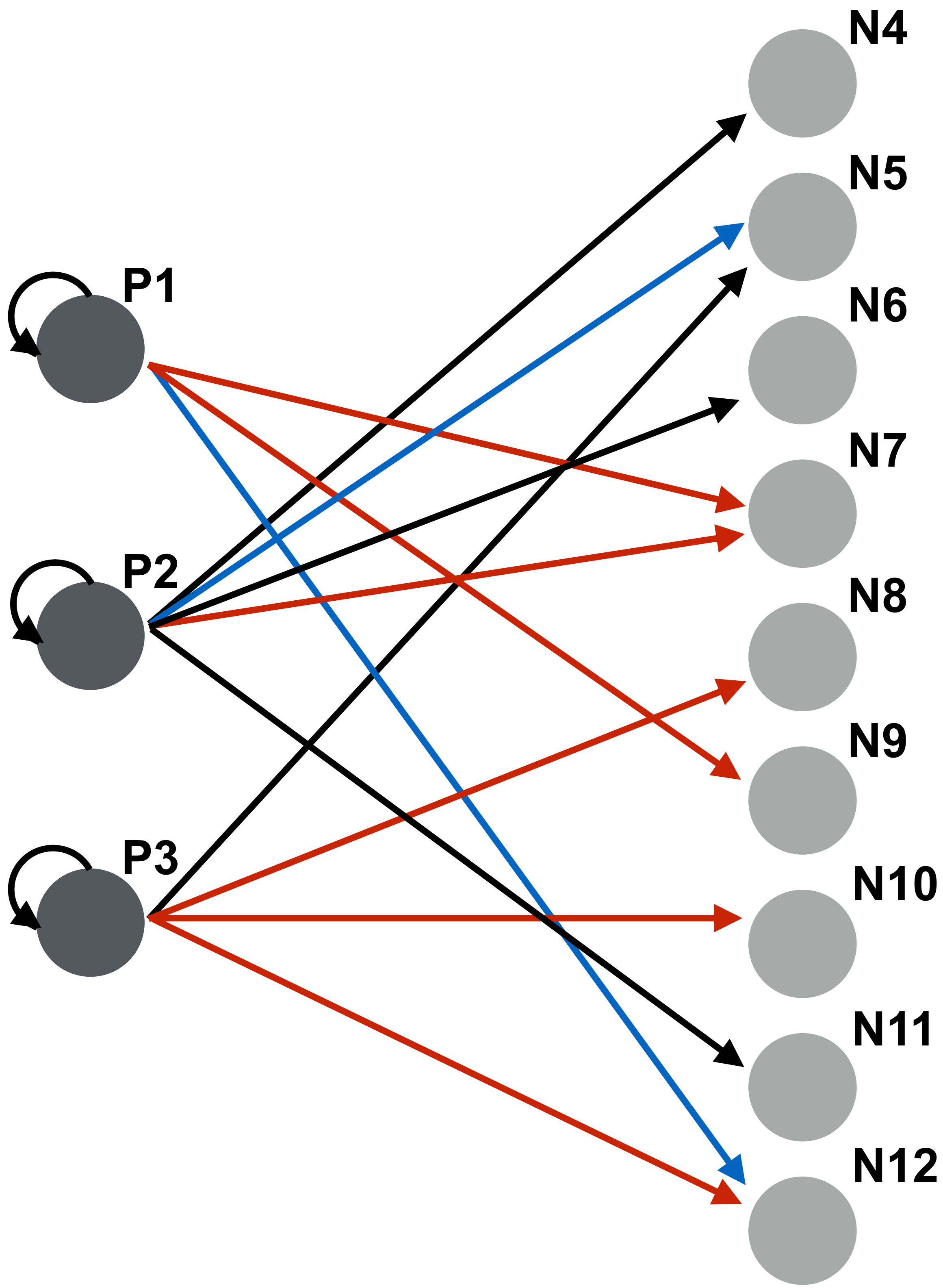
$\mu^i_{(u,v)}$: number of times that i travels in (u,v)

$\tau^i_{(u,v)}$: is the time needed for i to travel (u,v) back and forth

T : a distribution time-frame

International Distribution

Constraint 11: Budgetary constraints



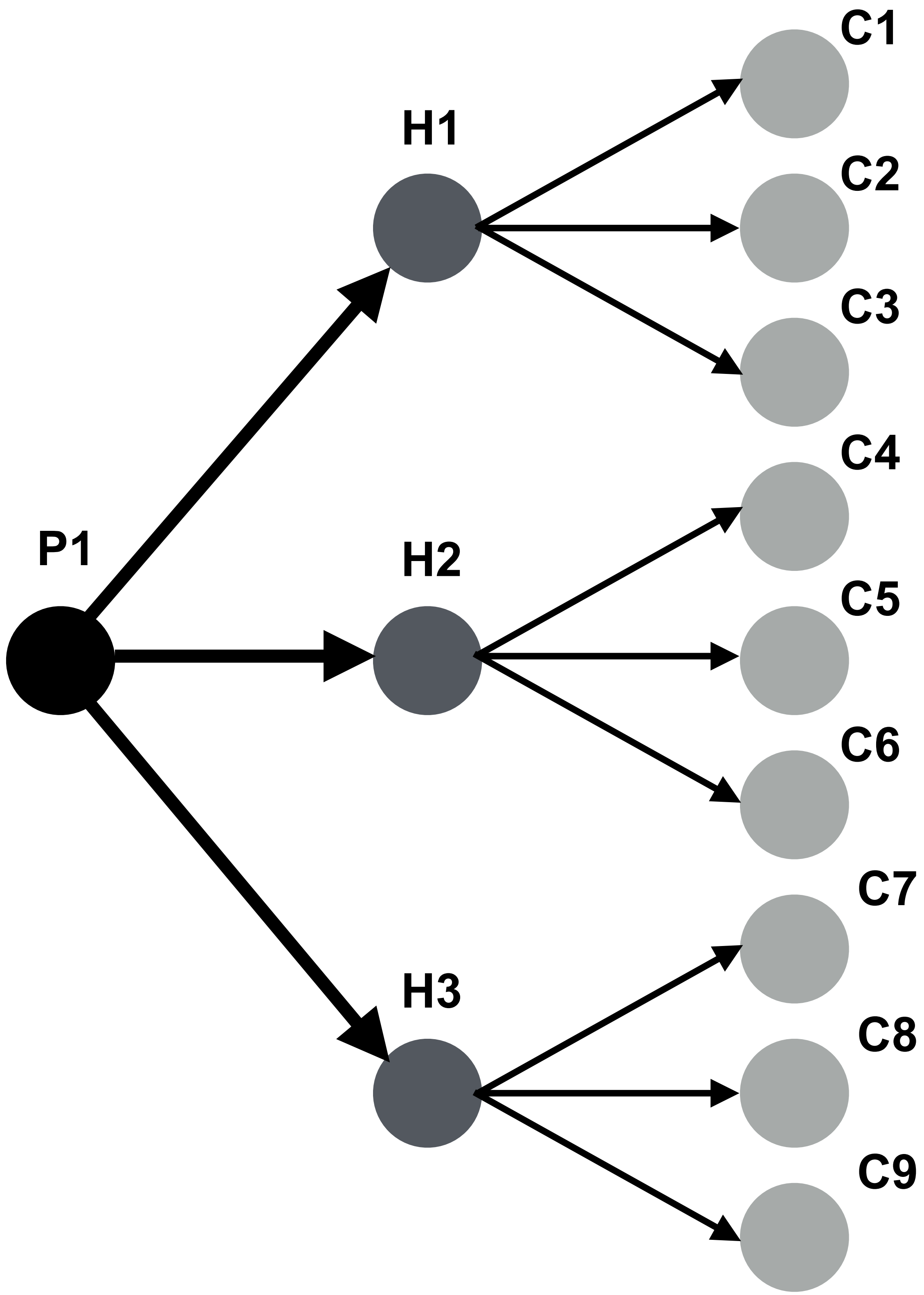
$$\sum_{i} \sum_{(u,v)\in\delta^{+}(v)} c^{i}_{(u,v)} \mu^{i}_{(u,v)} \leq B_{v} \qquad \forall i \in (A \cup S \cup L) \qquad \forall v \in N$$

$c^{i}_{(u,v)}$: cost for vehicle i to travel route (u,v) (vaccine cost can also be included here)

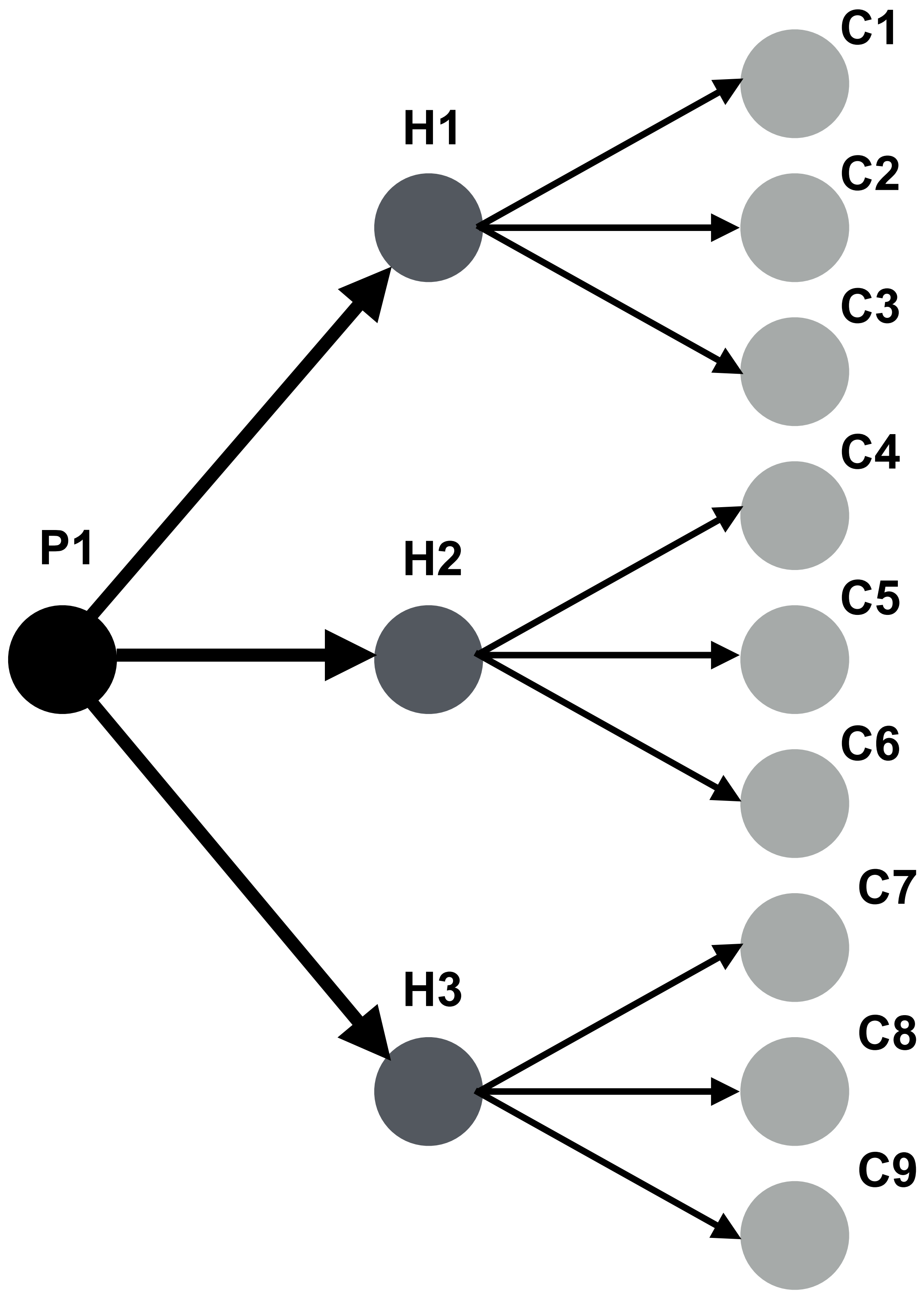
$\delta^{+}(v)$: set of incoming routes to v

B_{v} : budget limitations in v

National Distribution



National Distribution



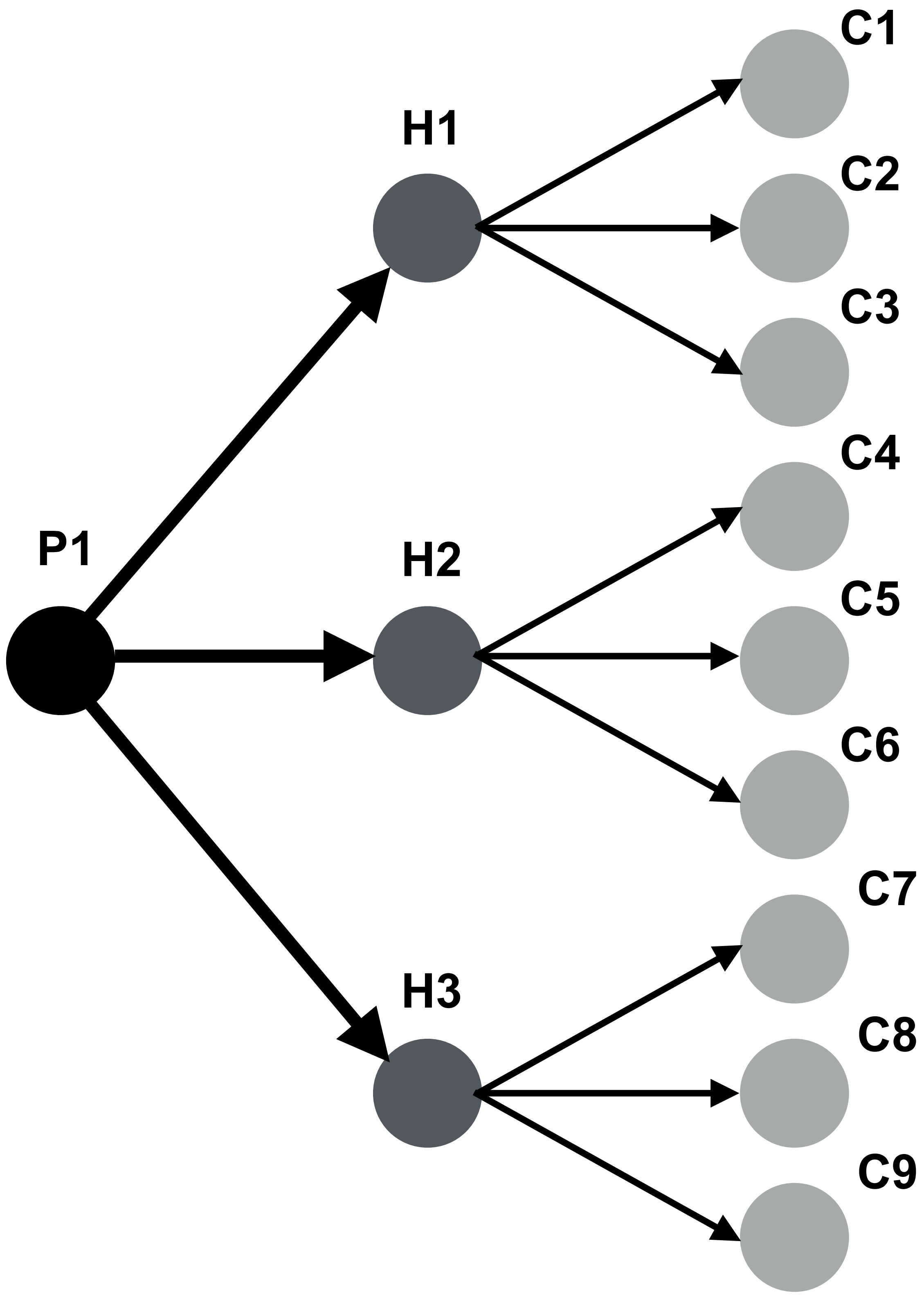
Legacy infrastructure can be exploited and new ad-hoc infrastructure can be established

The infrastructure consists of three layers: National storage centre, Regional hubs and Local clinics

All demands must be fulfilled and planning models can be designed to minimise costs

National Distribution

The graph representing the transportation routes: $G = (N, V)$



Index set:

$N = P \cup H \cup C$: Set of nodes (national storage centre, regional hubs and local clinics) in the graph

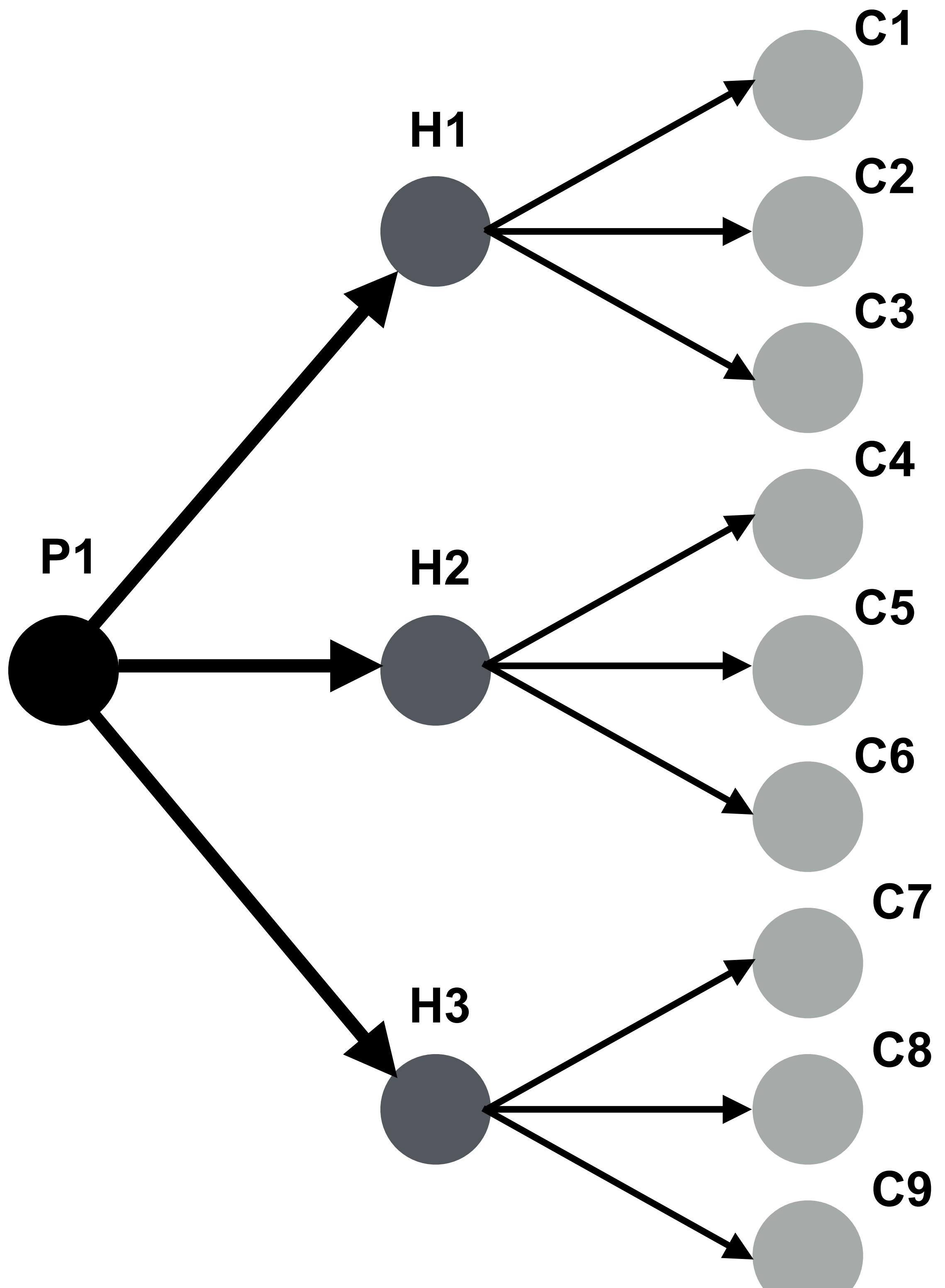
V: set of edges (routes) in the graph

(u, v): route from $u \in P \cup H$ to $v \in H \cup C$ in V

$t \in T$: transportation vehicle type index

National Distribution

The graph representing the transportation routes: $G=(N,V)$



Parameters set:

$$f_{(u,v)}=\begin{cases}1 & \forall v\in H\\ 6 & \forall v\in C\end{cases}$$: Replenishment frequency for each node $v\in H\cup C$ in the network

$c^t_{(u,v)}$: transportation cost of vehicle type t in (u,v)

ω_t : amount of vaccines that can be transported through vehicle of type t

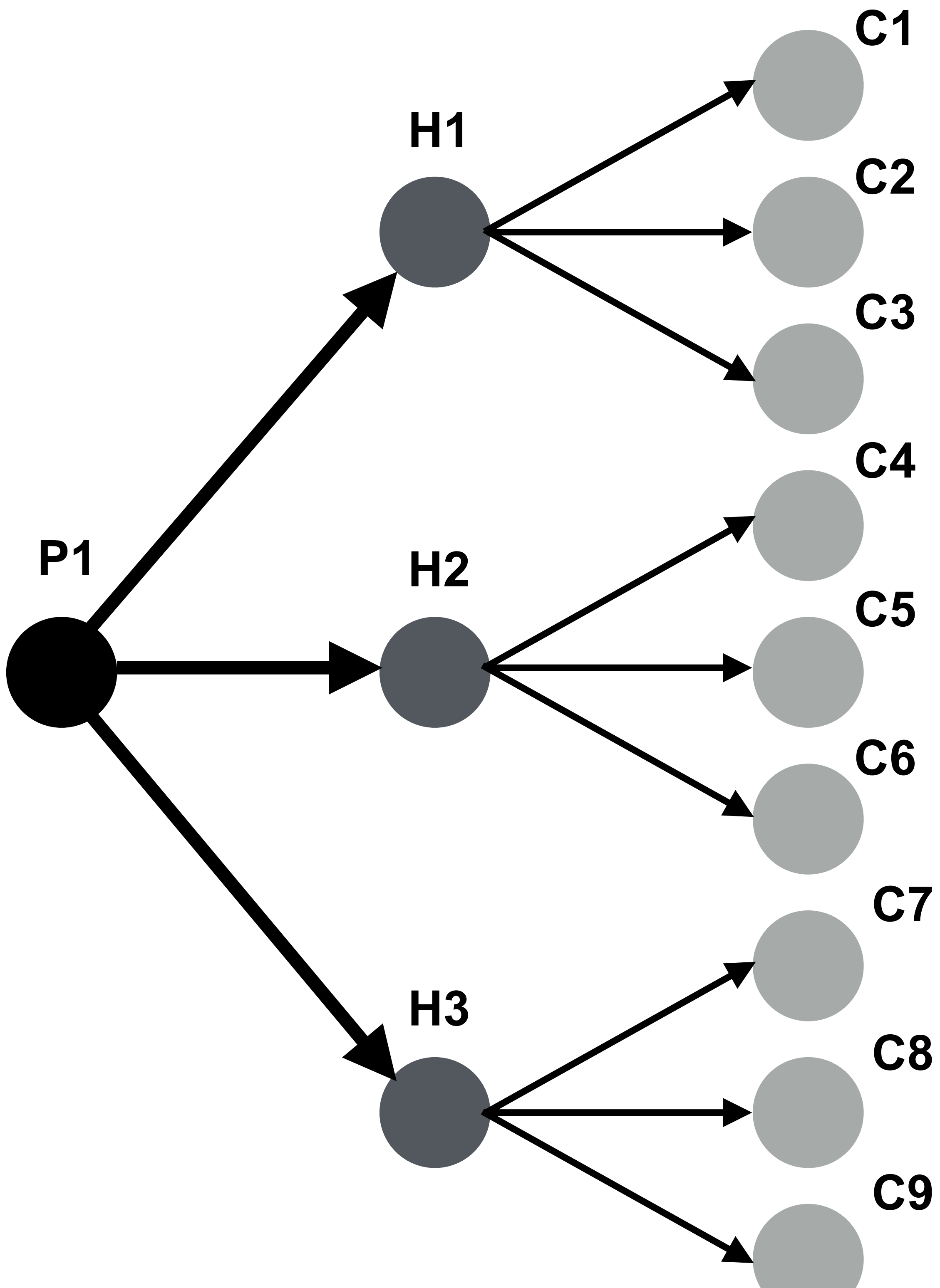
n_t : amount of available vehicles of type t

d_v : weekly vaccine demand in $v\in C$

$\tau^t_{(u,v)}$: time (in hours) needed for vehicle of type t to transport the vaccines in (u,v)

National Distribution

The graph representing the transportation routes: $G = (N, V)$



Variables set:

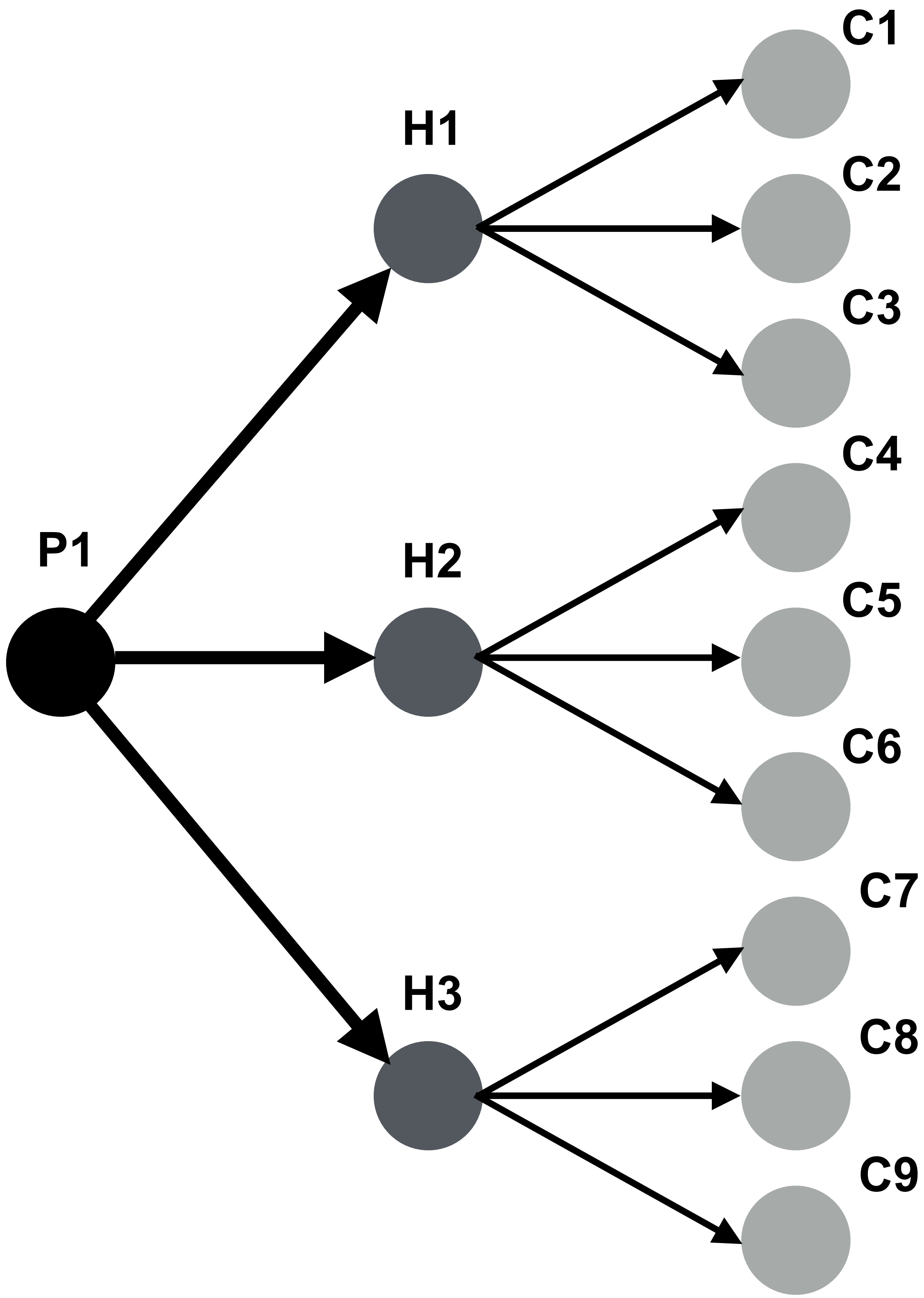
$b^t_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle of type t is assigned to route (u,v)

$x^t_{(u,v)}$: weekly vaccine amount transported from u to v by a vehicle of type t

$\mu^t_{(u,v)}$: number of vehicles of type t assigned in (u,v)

Transportation vehicles can only distribute vaccines once a week (for Hubs) or once a day (for Clinics)

National Distribution



Goal: Optimal assignment of distribution vehicles across for each route in order to minimise transportation costs

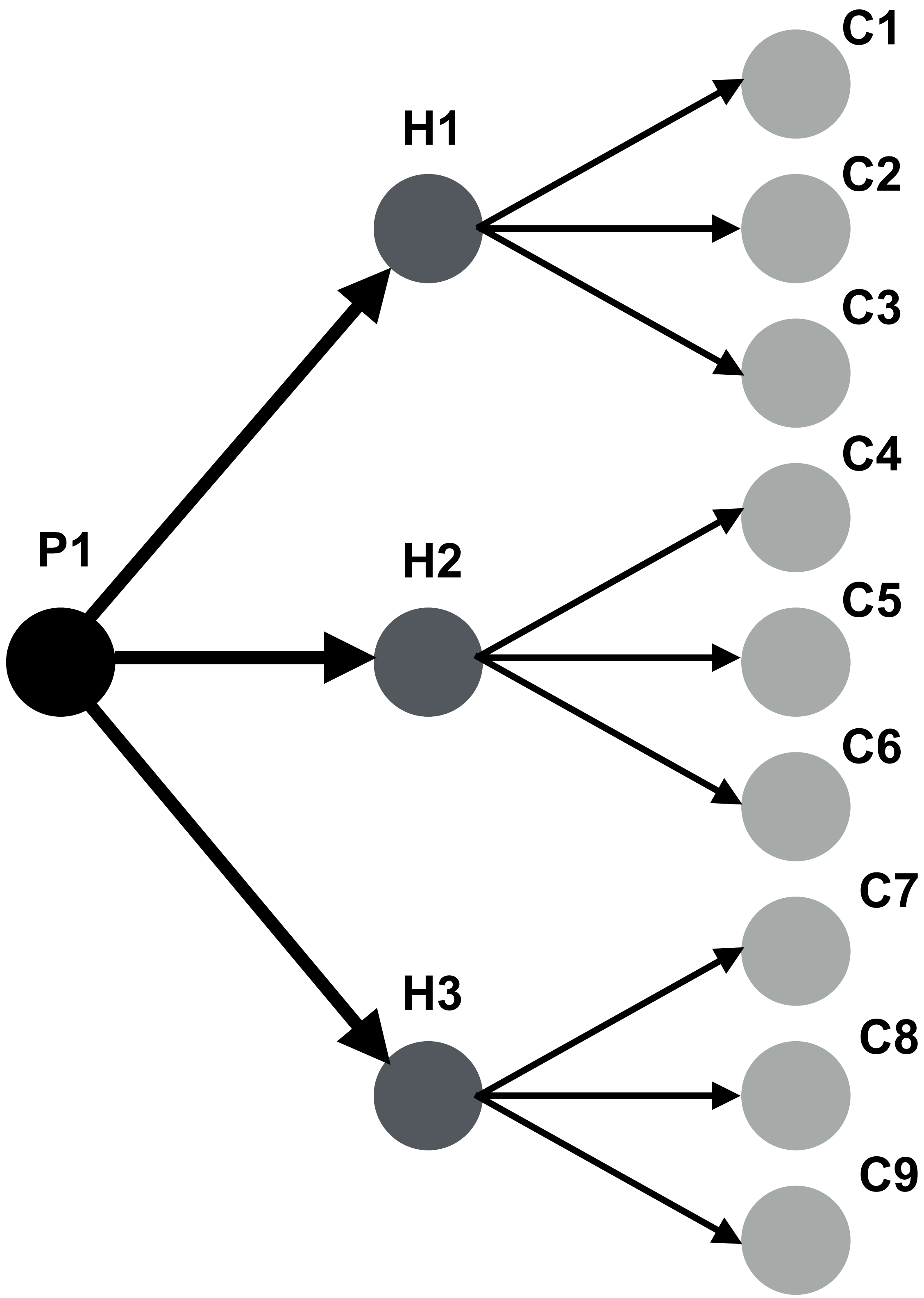
Obj. Fun.: $$\min\left(\sum_{(u,v)\in V}\sum_{t\in T}\mu^t_{(u,v)}f_{(u,v)}c^t_{(u,v)}\right)$$

$\mu^t_{(u,v)}$: number of vehicles of type t assigned in (u,v)

$$f_{(u,v)}=\begin{cases}1 & \forall v\in H\\ 6 & \forall v\in C\end{cases}$$: Replenishment frequency for each node $v\in H\cup C$ in the network

$c^t_{(u,v)}$: transportation cost of vehicle type t in (u,v)

National Distribution



Constraint 1: The weekly amount of vaccines stored in the hubs should equal the amount of vaccines delivered in the clinics and clinic demands should be met

$$\sum_{t \in T} \sum_{u \in P} x^t_{(u,v)} - \sum_{t \in T} \sum_{z \in C} x^t_{(v,z)} = 0 \qquad \forall v \in H$$

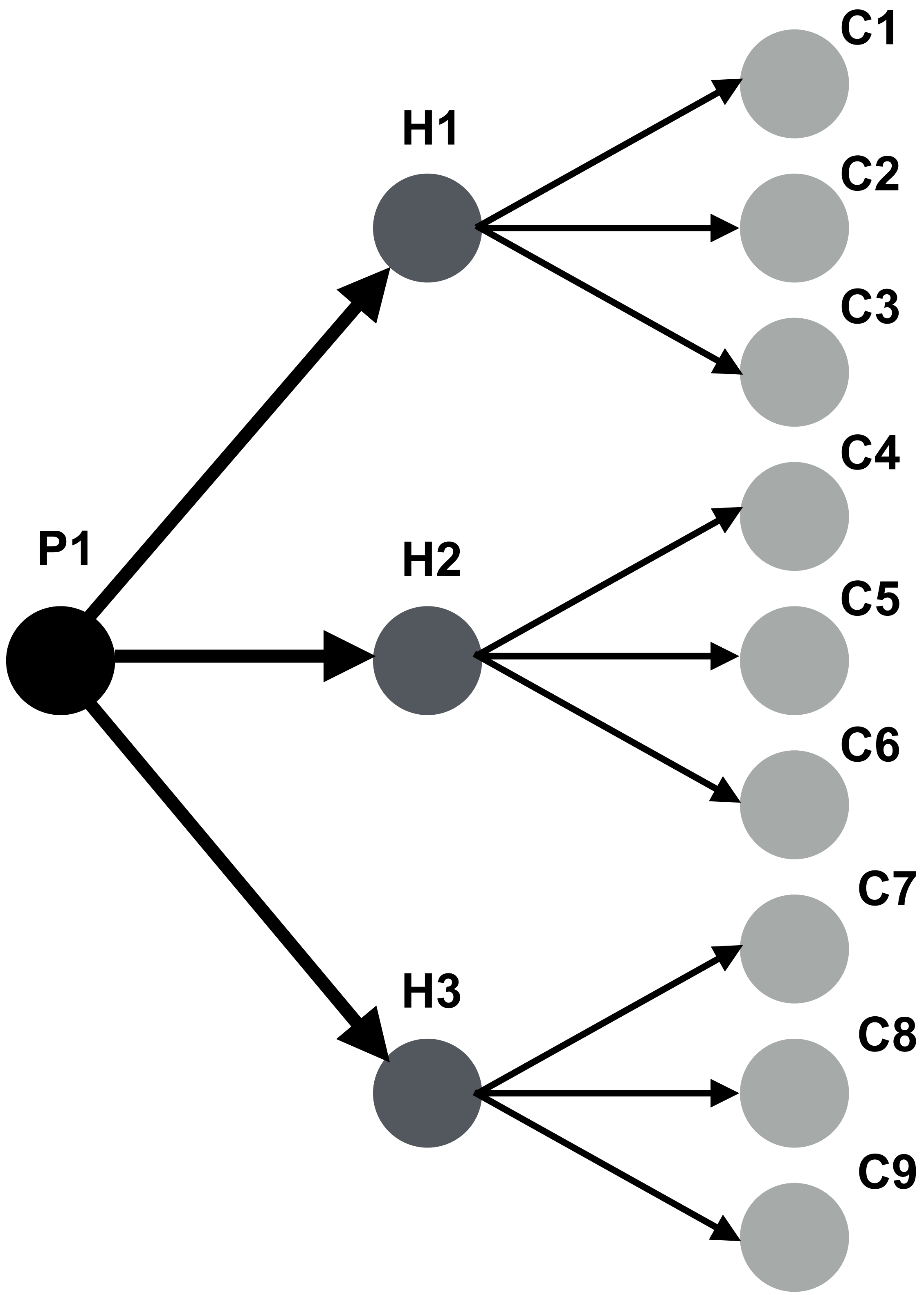
$$\sum_{t \in T} x^t_{(v,z)} = d_z \qquad \forall v \in H \qquad \forall z \in C$$

$x^t_{(u,v)}$: weekly vaccine amount transported from $u \in P$ to $v \in H$ through transportation type t

$x^t_{(v,z)}$: weekly vaccine amount transported from $v \in H$ to $z \in C$ through transportation type t

d_z : weekly vaccine demand in $z \in C$

National Distribution



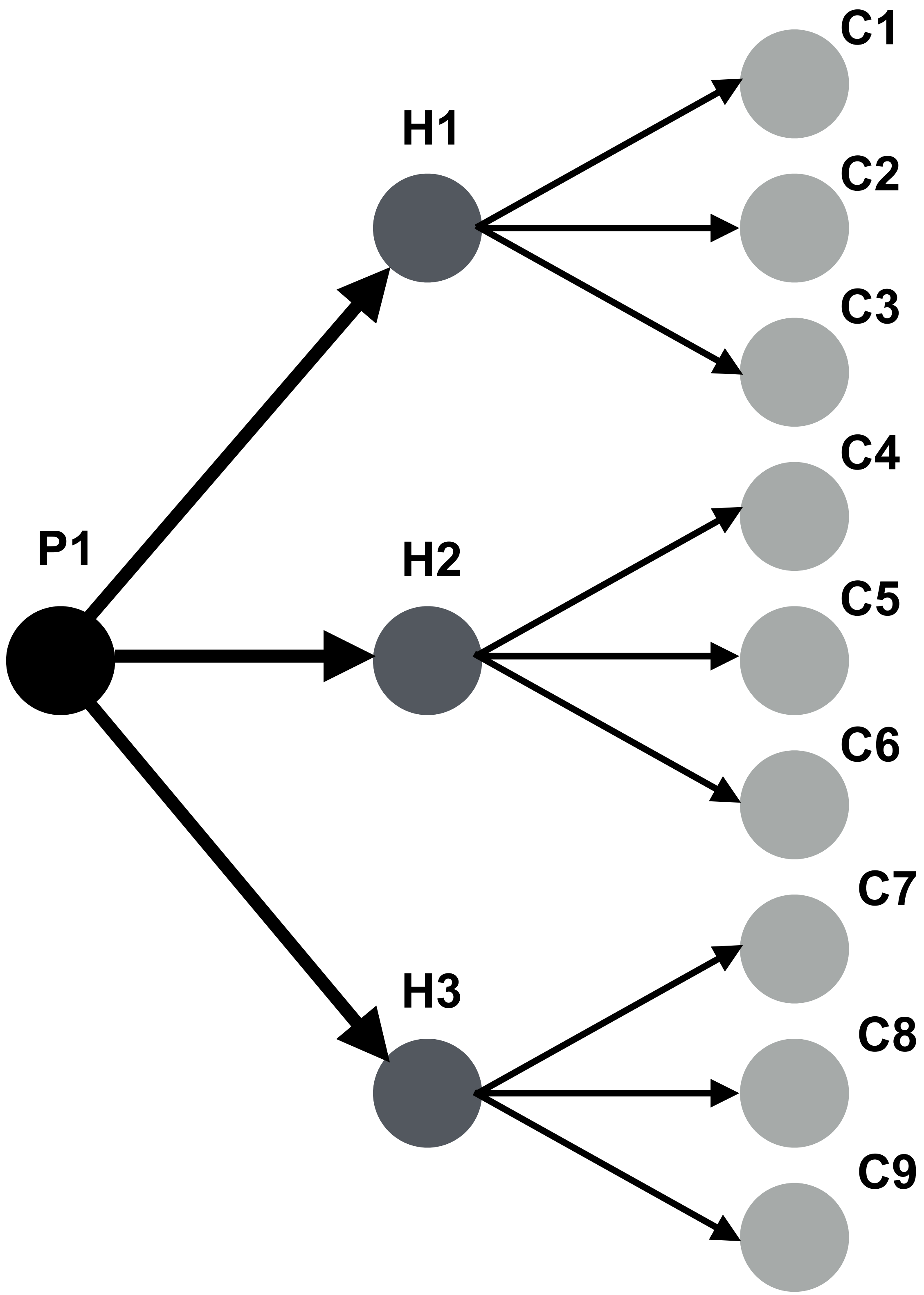
Constraint 2: Only one type of transportation vehicle can be assigned to one specific route

$$\sum_{t \in T} b^t_{(u,v)} = 1 \qquad \forall (u,v) \in V$$

$b^t_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle of type t is assigned to route (u,v)

(u,v): route from $u \in P \cup H$ to $v \in H \cup C$ in V

National Distribution



Constraint 4: If a vehicle type is not assigned to a route, then no vehicle of this type will assigned

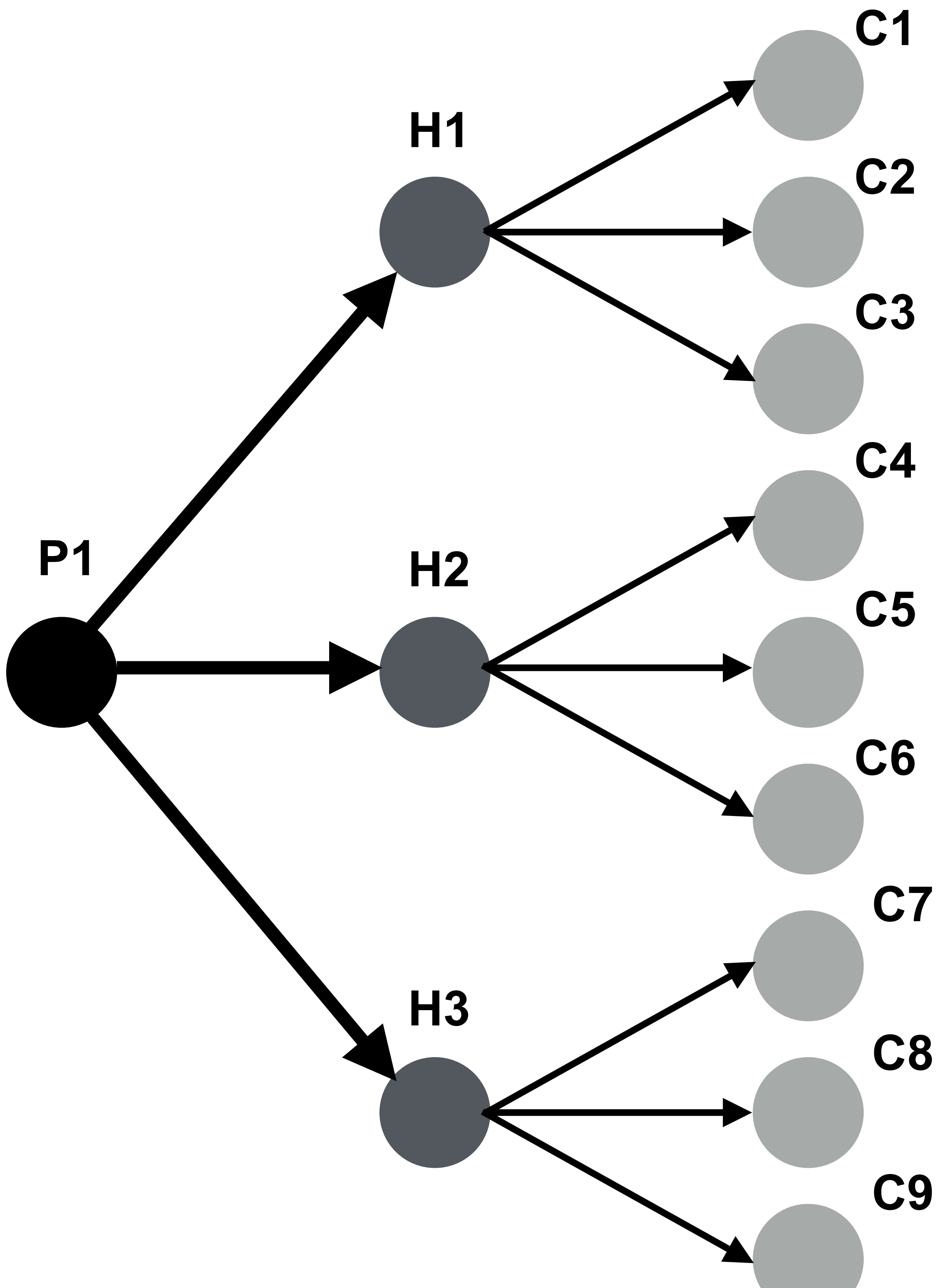
$$0 \le \mu^t_{(u,v)} \le b^t_{(u,v)} M_2 \qquad \forall (u,v) \in V \quad \forall t \in T$$

$\mu^t_{(u,v)}$: number of vehicles of type t assigned in (u,v)

$b^t_{(u,v)} \in \{0,1\}$: binary variable indicating whether a vehicle of type t is assigned to route (u,v)

M_2 : a sufficiently large number

National Distribution



Constraint 5: The number of assigned vehicle of a specific type over each route should be enough to meet demands on the destination of that route

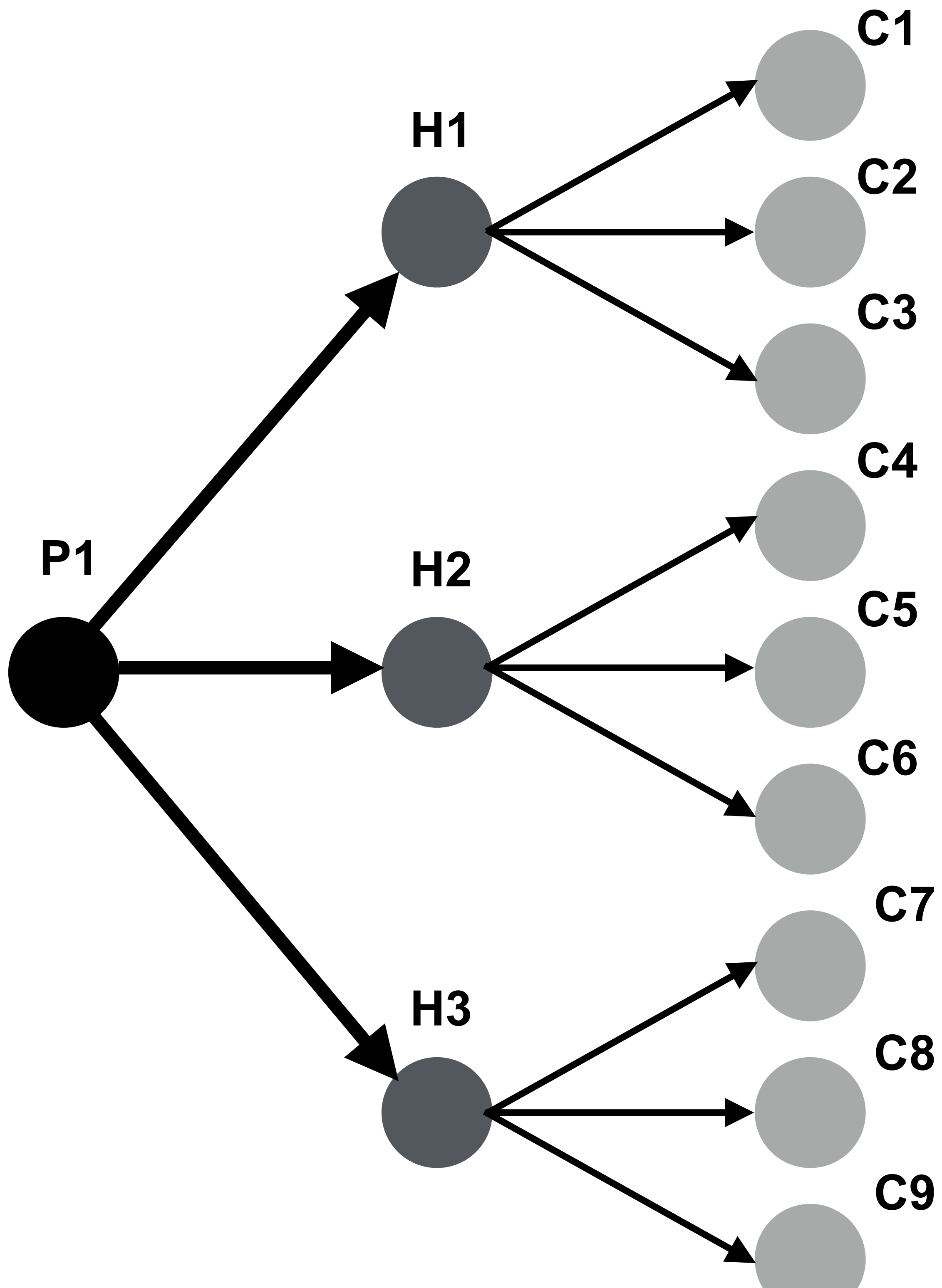
$$\mu_{(u,v)}^{t} \geq x_{(u,v)}^{t} / \omega_t \qquad \forall (u,v) \in V \quad \forall t \in T$$

$\mu_{(u,v)}^{t}$: number of vehicles of type t assigned in (u,v)

$x_{(u,v)}^{t}$: weekly vaccine amount transported from u to v by a vehicle of type t

ω_t : amount of vaccines that can be transported through vehicle of type t

National Distribution



Constraint 6: The total number of assigned vehicles of a specific type should not exceed the availabilities of that vehicle type

$$\sum_{(u,v)\in V} \mu_{(u,v)}^{t} \le n_t \qquad \forall t \in T$$

$\mu_{(u,v)}^{t}$: number of vehicles of type t assigned in (u,v)

n_t : amount of available vehicles of type t

Numerical Examples - Transportation Network

- Four were countries considered (A, B, C and D) with increasing number of hubs assigned (30, 50, 100 and 200 respectively)
- For each **Hub**, a random number of **Clinics** (between 5 and 10) is assigned
- Weekly demands for each clinic were assigned randomly (between 200 and 1000)
- Route distances (**Center→Hubs** and **Hubs→Clinics**) were assigned randomly (100-1000 km; and 5-150 km respectively)

Numerical Examples - Vehicles

- Four vehicle types were considered for transportation: **Trucks**, **4x4**, **Cars** and **Scooters** (with maximal capacity of 10000, 500, 200 and 20 respectively)

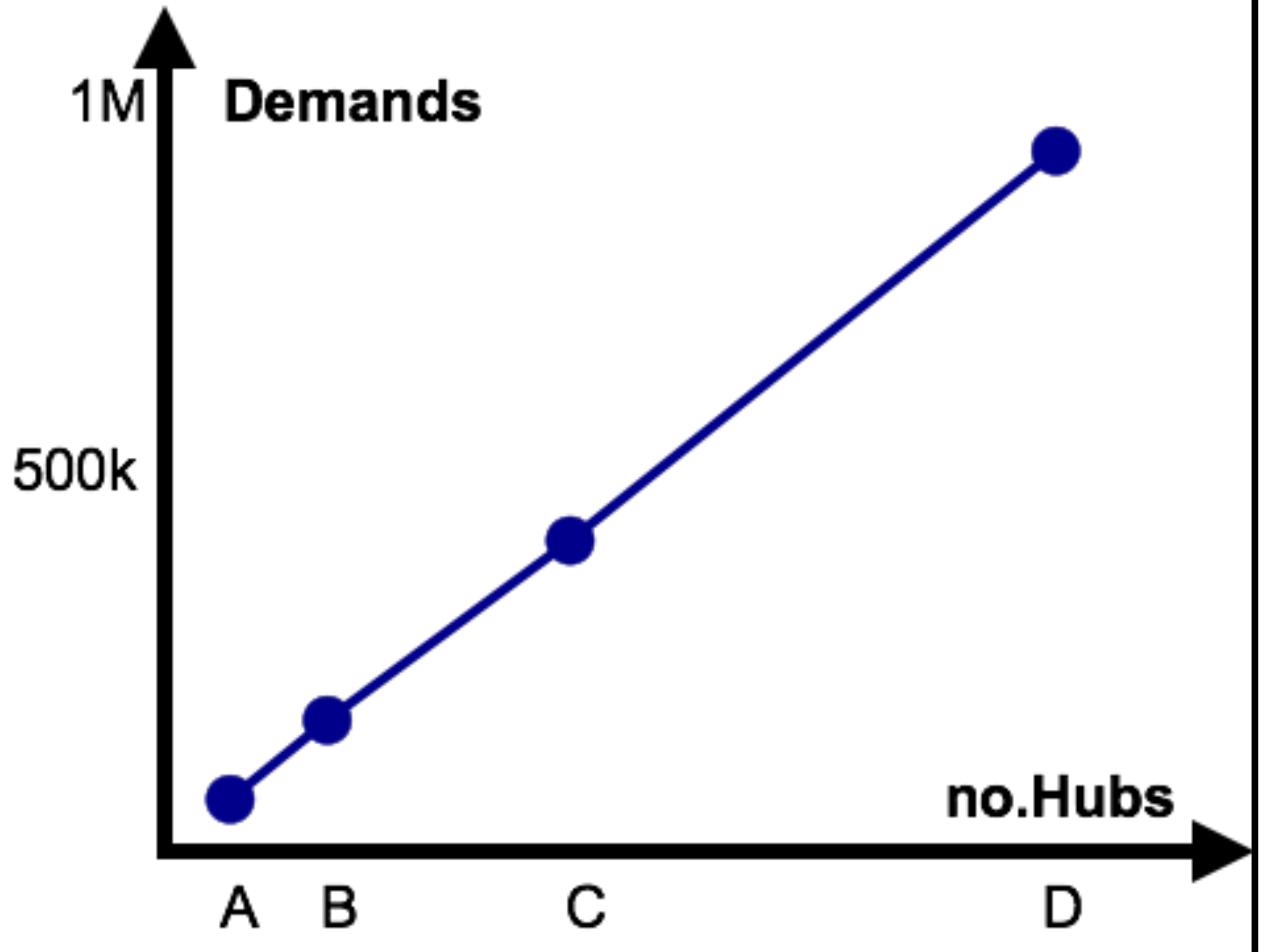
- Number of available vehicles was increased for each country from A to D
  - **Trucks:** 100, 150, 200, 250 (for A, B, C and D respectively)
  - **4x4:** 500, 750, 1000, 1250 (for A, B, C and D respectively)
  - **Cars:** 1000, 1500, 2000, 2500 (for A, B, C and D respectively)
  - **Scooters:** 200, 300, 400, 500 (for A, B, C and D respectively)

- Oil consumptions for each vehicle type were randomly assigned for each route in the network (**Trucks:** 35-50 L/100km; **4x4:** 7-11 L/100km; **Cars:** 4-6 L/100km; **Scooters:** 3-4 L/100km)

- Fixed oil price was considered: 1.034 Euro/L

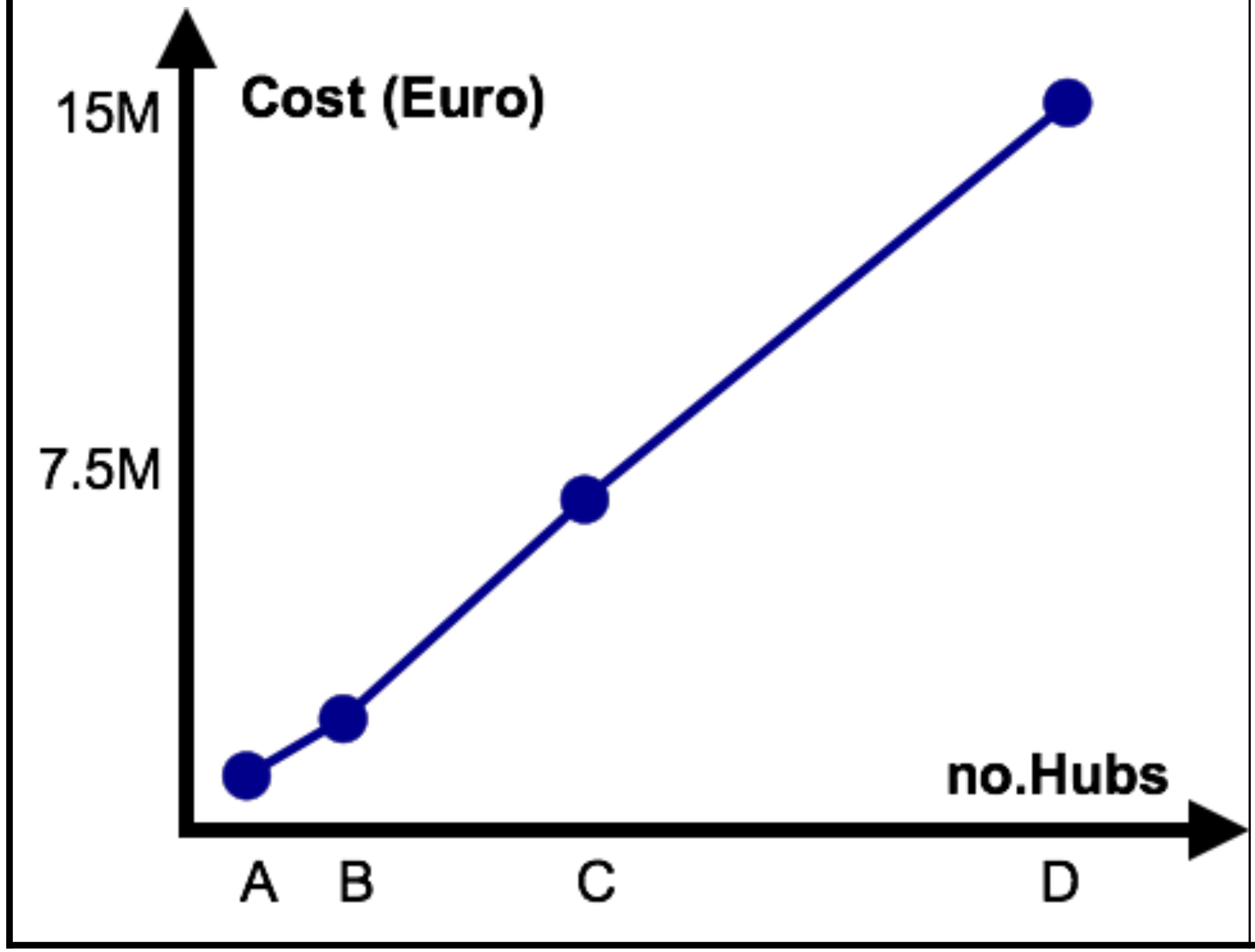
Network Size & Demands

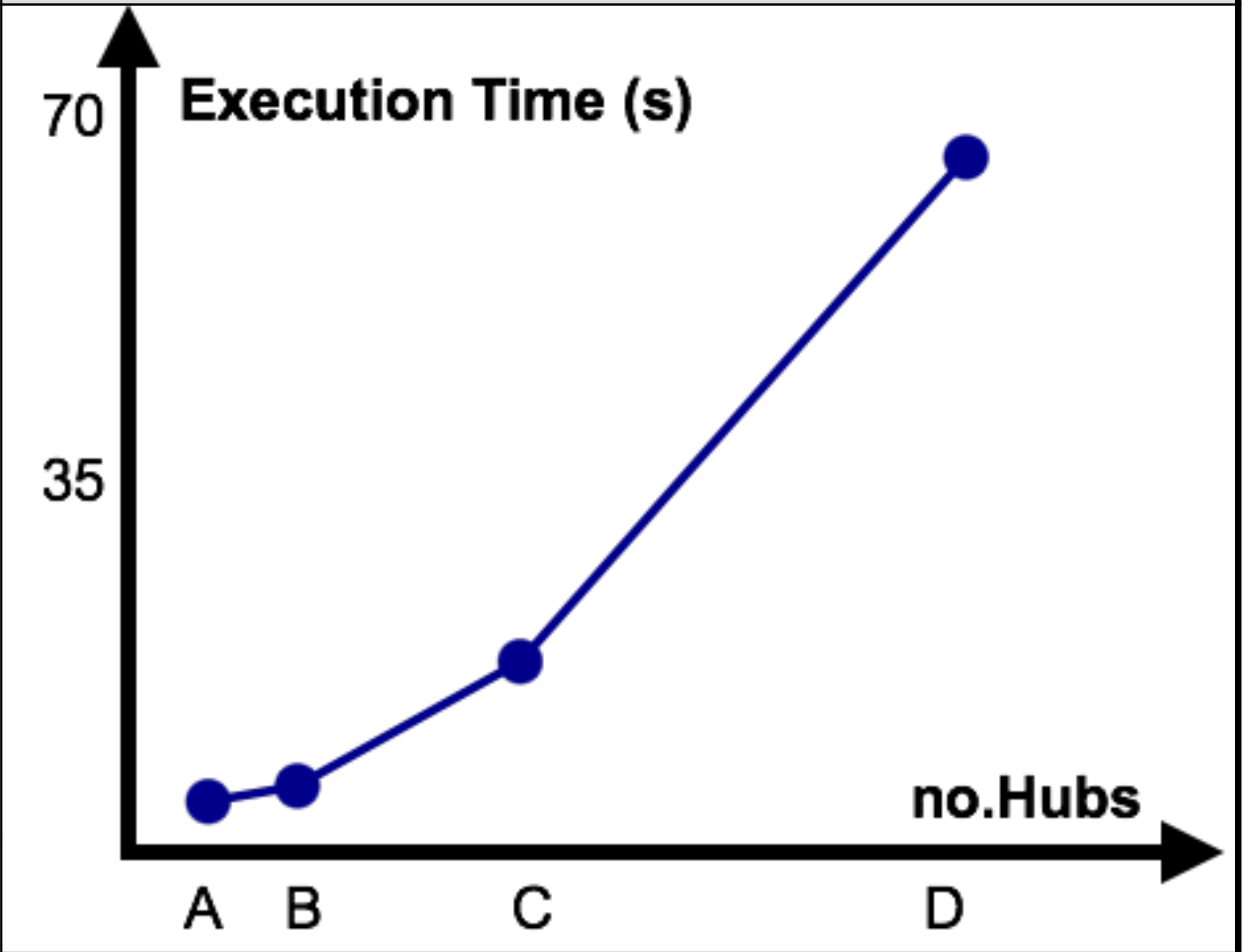
Number of routes	Vaccine Demands
A=236; **B**=409; **C**=837; **D**=1735	**A**=119k; **B**=218k; **C**=442k; **D**=928k



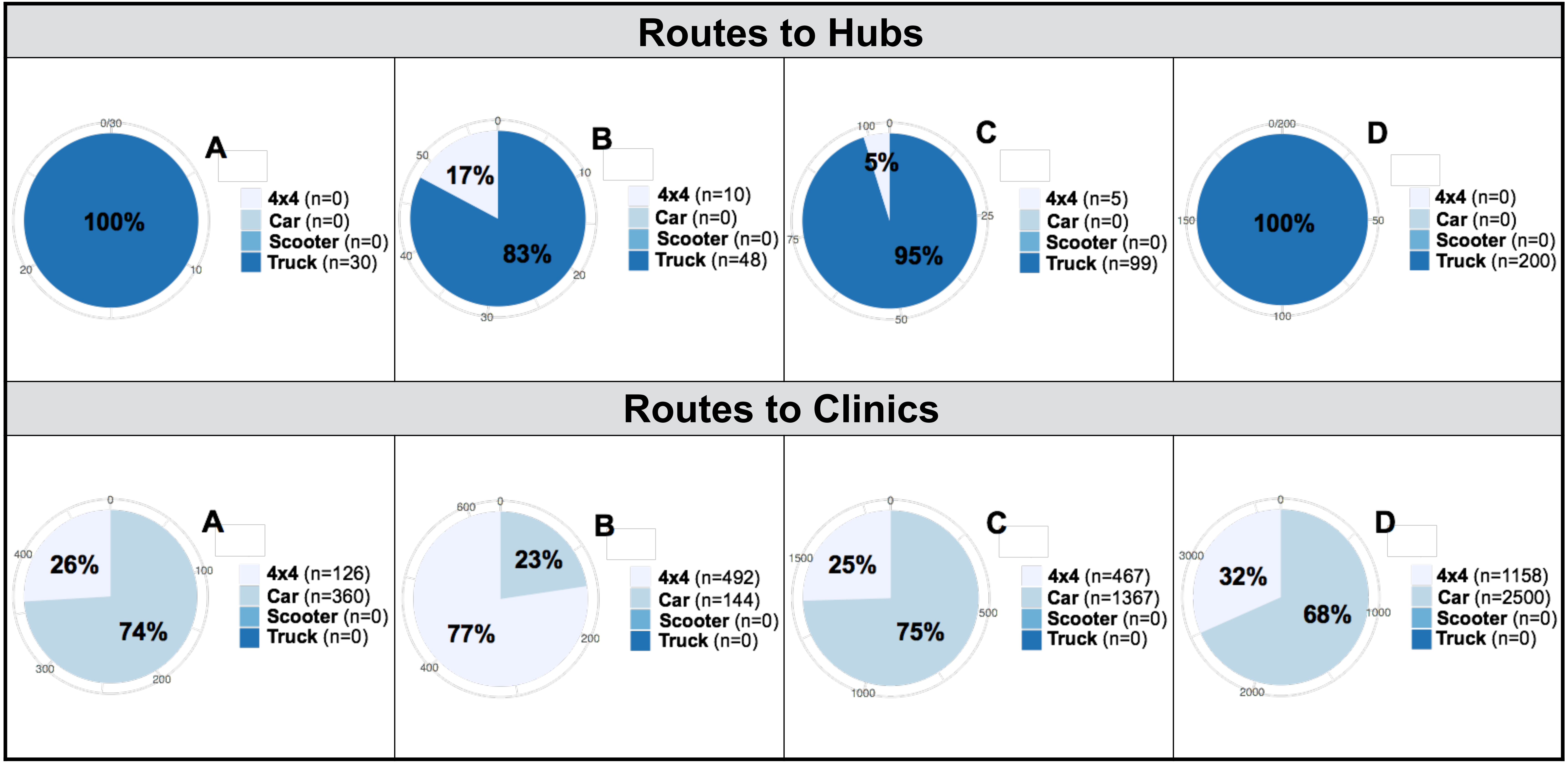
Transportation Cost & Execution Time

Transportation Cost	CPLEX execution time
A=2.06M; **B**=3.14M; **C**=7.26M; **D**=14.73M	**A**=1.72; **B**=3.21; **C**=15.01; **D**=62.87

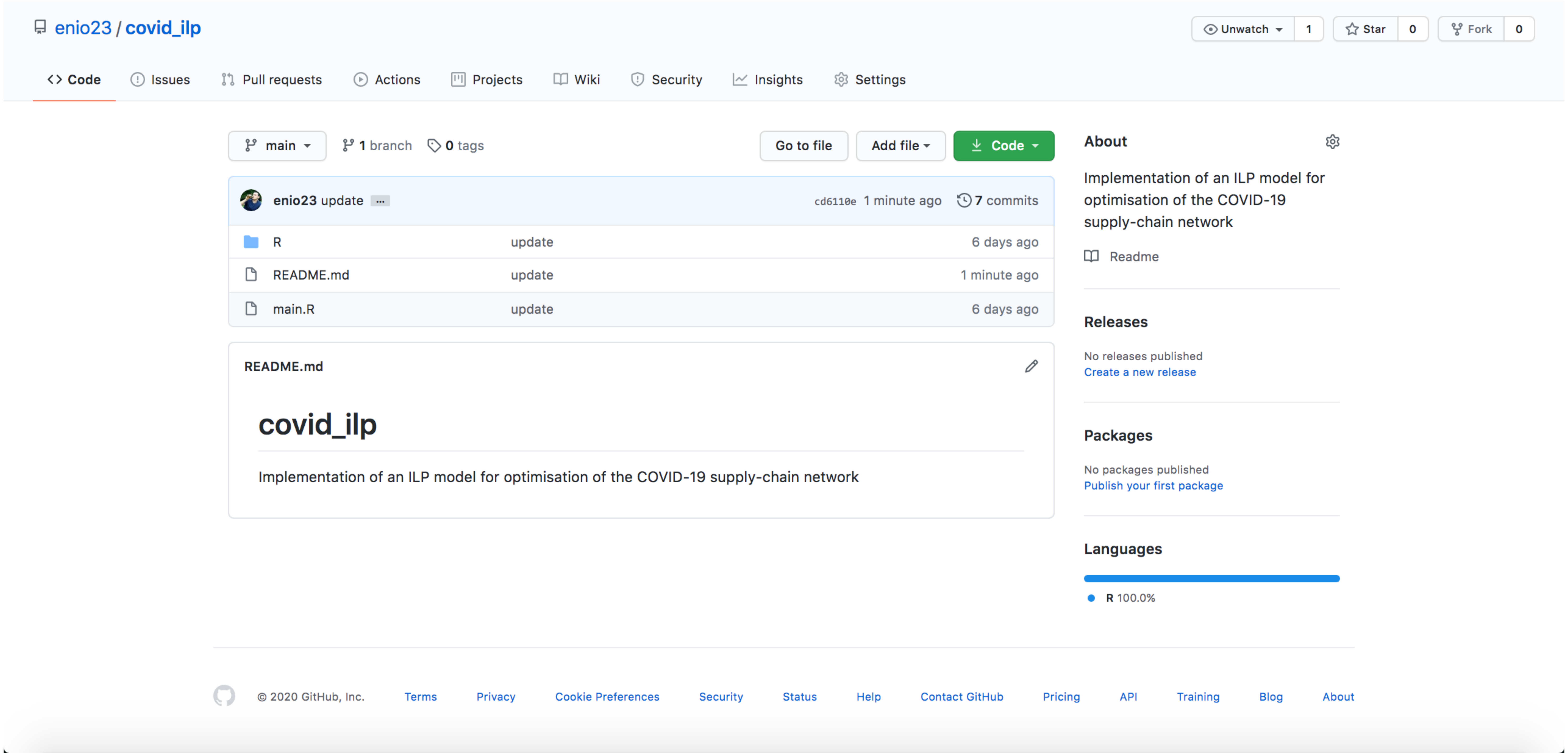




Optimal Solutions



Source Code: https://github.com/enio23/covid_ilp



Final Considerations

- An un-precedent challenge.
- Numerous uncertainties.
- A chance to learn.
- Everyone can help.
- Stay safe! The vaccine is coming!

Thank You!!