

Multiproduct Supply Chain Network Design with Applications to Healthcare

Anna Nagurney¹ Min Yu¹ Qiang Qiang²

¹Department of Finance and Operations Management
Isenberg School of Management
University of Massachusetts
Amherst, Massachusetts 01003

²Management Division
Pennsylvania State University
Great Valley School of Graduate Professional Studies
Malvern, Pennsylvania 19355

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- Background and Motivation
- An Overview of the Relevant Literature
- The Multiproduct Supply Chain Network Design Model
- Potential Applications to Pharmaceutical Firms
- The Algorithm
- Numerical Examples
- Summary and Conclusions

Background and Motivation

With the advent of increasing globalization, viruses are spreading more quickly and creating new challenges for medical and health professionals, researchers, and government officials.

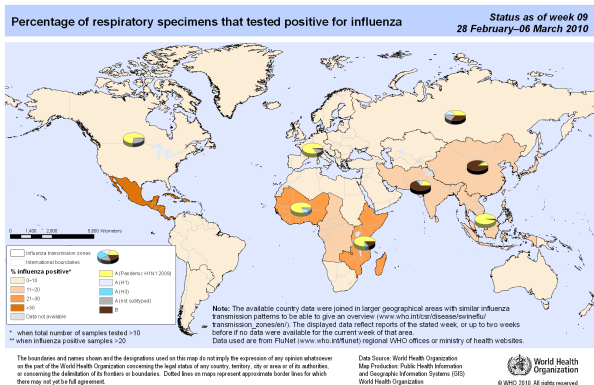


Figure: Map of Influenza Activity and Virus Subtypes (WHO (2010))

Background and Motivation

The vaccine supply chain often relies on only one or two manufacturers for critical products (see Mowery and Mitchell (1995), and Treanor (2004)). The number of licensed vaccine manufacturers in the United States decreased from 26 in 1967 to only 6 in 2006 (Klein and Myers (2006)).

Between 2000 and 2004 there were nationwide shortages in the United States of six recommended childhood vaccines.

New illnesses, in turn, pose further stresses for vaccine (and medicine) development, production, and distribution.

H1N1 (Swine) Flu

The epidemic of the H1N1 virus (also known as the swine flu) in 2009 took more than **18,449** lives with over **214** countries reporting confirmed cases (WHO (2010)).

Parts of the globe experienced serious flu vaccine shortages, both seasonal and H1N1 (swine) ones, in late 2009.



Background and Motivation

With the urgent demand for H1N1 vaccine, all the flu vaccine manufacturers switched from the production of seasonal flu vaccine to the production of the H1N1 vaccine, causing **increased shortages** of the former and **delayed deliveries** of the latter (see McNeil Jr. (2009)), which resulted in severe shortfalls in the vaccine supply chains.

Cytarabine

In the past year, the US experienced shortages of the critical drug, cytarabine, due to manufacturer production problems.



Due to the severity of this medical crisis for leukemia patients, Food and Drug Administration is exploring the possibility of importing this medical product (Larkin (2011)).

Hospira re-entered the market in March 2011 and has made the manufacture of cytarabine a priority ahead of other products.

Background and Motivation

When it comes to healthcare supply chains, appropriate supply chain designs may positively affect the health and wellbeing of citizens, with broader impacts on the economy and even national security (Raja and Heinen (2009))

However, there have been few studies that integrate systems and network approaches to assist in the understanding of healthcare processes (Keen, Moore, and West (2006)).

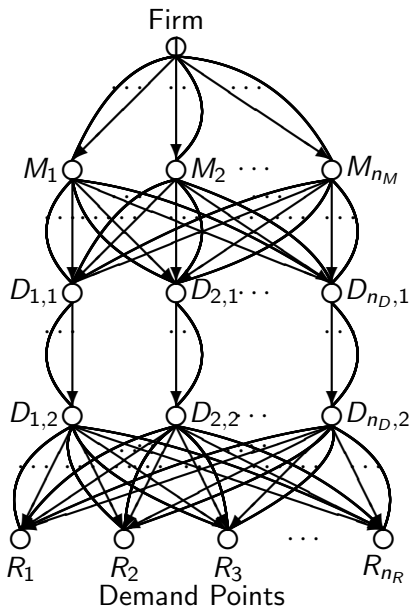
An Overview of the Relevant Literature

- L. G. Papageorgiou, G. E. Rotstein, and N. Shah, 2001. Strategic supply chain optimization for the pharmaceutical industries, *Industrial and Engineering Chemistry Research* 40, 275-286.
- J. A. Pacheco and S. Casado, 2005. Solving two location models with few facilities by using a hybrid heuristic: a real health resources case, *Computers and Operations Research* 32, 3075-3091.
- K. H. Tsang, N. J. Samsatli, and N. Shah, 2006. Modeling and planning optimization of a complex flu vaccine facility, *Food and Bioproducts Processing* 84, 123-134.
- According to the recent review by Melo, Nickel, and Saldanha da Gama (2009), there are only a limited number of research publications that combine both capacity expansion with locational decisions.

An Overview of the Relevant Literature

- A. Nagurney, 2010a. Optimal supply chain network design and redesign at minimal total cost and with demand satisfaction, *International Journal of Production Economics* 128, 200-208.
- A. Nagurney, 2010b. Supply chain network design under profit maximization and oligopolistic competition, *Transportation Research E* 46, 281-294.
- A. Nagurney, T. Woolley, and Q. Qiang, 2010. Multiproduct supply chain horizontal network integration: Models, theory, and computational results, *International Transactions in Operational Research*, 17, 333-349.
- A. Nagurney, M. Yu, Q. Qiang, 2011. Supply chain network design for critical needs with outsourcing, *Papers in Regional Science* 90, 123-142.

Supply Chain Network Topology



The Multiproduct Supply Chain Network Design Model

The firm seeks to determine the optimal levels of capacity investments in its supply chain network activities coupled with the optimal levels of each product processed on each supply chain network link subject to the minimization of the total cost where the total cost includes the total cost of operating the various links for each of the products and the total cost of capacity investments.

Demands, Path Flows, and Link Flows

Let d_k^j denote the demand for product j ; $j = 1, \dots, J$, at demand point R_k . Let x_p^j denote the nonnegative flow of product j on path p . Let f_a^j denote the flow of product j on link a .

The following conservation of flow equations

$$\sum_{p \in P_{R_k}} x_p^j = d_k^j, \quad j = 1, \dots, J; \quad k = 1, \dots, n_R. \quad (1)$$

$$f_a^j = \sum_{p \in P} x_p^j \delta_{ap}, \quad j = 1, \dots, J; \quad \forall a \in L. \quad (2)$$

The Operation Costs, and Investment Costs

The total cost of a link associated with a product is assumed to be a function of the flow of all the products on the link.

$$\hat{c}_a^j = \hat{c}_a^j(f_a^1, \dots, f_a^J), \quad j = 1, \dots, J; \quad \forall a \in L. \quad (3)$$

The nonnegative existing capacity on a link a is denoted by \bar{u}_a , $\forall a \in L$. We assume that the firm is considering the addition of capacity to link a , $\forall a \in L$.

$$\hat{\pi}_a = \hat{\pi}_a(u_a), \quad \forall a \in L. \quad (4)$$

The total cost associated with each product and each link is assumed to be a *generalized cost*, which can capture not only the capital cost, but also the time consumption, risk, etc, associated with the various supply chain activities.

The total cost functions are assumed to be convex and continuously differentiable.

The Multiproduct Supply Chain Network Design Model

$$\text{Minimize } \sum_{j=1}^J \sum_{a \in L} \hat{c}_a^j(f_a^1, \dots, f_a^J) + \sum_{a \in L} \hat{\pi}_a(u_a) \quad (5)$$

subject to: Constraints (1), (2), and

$$\sum_{j=1}^J \alpha_j f_a^j \leq \bar{u}_a + u_a, \quad \forall a \in L, \quad (5)$$

$$u_a \geq 0, \quad \forall a \in L, \quad (6)$$

$$x_p^j \geq 0, \quad j = 1, \dots, J; \quad \forall p \in P. \quad (7)$$

Variational Inequality Formulation

The optimization problem is equivalent to the variational inequality problem: determine the vector of link flows, link enhancement capacities, and Lagrange multipliers $(f^*, u^*, \lambda^*) \in \mathcal{K}$, such that:

$$\begin{aligned} & \sum_{j=1}^J \sum_{l=1}^J \sum_{a \in L} \left[\frac{\partial \hat{c}_a^l(f_a^{1*}, \dots, f_a^{J*})}{\partial f_a^j} + \alpha_j \lambda_a^* \right] \times [f_a^j - f_a^{j*}] \\ & + \sum_{a \in L} \left[\frac{\partial \hat{\pi}_a(u_a^*)}{\partial u_a} - \lambda_a^* \right] \times [u_a - u_a^*] \\ & + \sum_{a \in L} [\bar{u}_a + u_a^* - \sum_{j=1}^J \alpha_j f_a^{j*}] \times [\lambda_a - \lambda_a^*] \geq 0, \quad \forall (f, u, \lambda) \in \mathcal{K}, \quad (8) \end{aligned}$$

where $\mathcal{K} \equiv$

$\{(f, u, \lambda) | \exists x, \text{ such that (1), (2), (6), and (7) hold, and } \lambda \geq 0\}$.

In the case of a single product, the variational inequality formulation (8) collapses to: determine $(f^, u^*, \lambda^*) \in \mathcal{K}$, such that*

$$\sum_{a \in L} \left[\frac{\partial \hat{c}_a(f_a^*)}{\partial f_a} + \alpha \lambda_a^* \right] \times [f_a - f_a^*] + \sum_{a \in L} \left[\frac{\partial \hat{\pi}_a(u_a^*)}{\partial u_a} - \lambda_a^* \right] \times [u_a - u_a^*] \\ + \sum_{a \in L} [\bar{u}_a + u_a^* - \alpha f_a^*] \times [\lambda_a - \lambda_a^*] \geq 0, \quad \forall (f, u, \lambda) \in \mathcal{K}. \quad (9)$$

Potential Applications

The model developed here can be utilized by a pharmaceutical firm to evaluate how much it will cost to manufacture, store, and have distributed its portfolio of products, which can include vaccines and medicines, at minimal total cost, given the demands for its various products.

By realizing what the minimal total costs are, the firm can then plan accordingly and also contract wisely with the cognizant governments or other authorities, including humanitarian organizations.

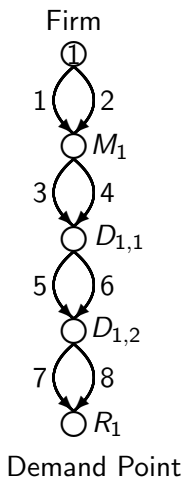
In addition, we explicitly allow for alternative technologies associated with manufacturing, different storage technologies, and different modes of transportation/shipment.

The Algorithm

We adopted the modified projection method (see Korpelevich (1977) and Nagurney (2006)) for all the numerical examples . We embedded it with the general equilibration algorithm of Dafermos and Sparrow (1969) to solve the fixed demand network optimization problems at each step for the product flows.

The resolution of the modified projection method for the multiproduct supply chain network design yields closed form expressions for the capacity investments and the Lagrange multipliers at each iterative step.

Numerical Examples with a Single Product



Example 1: Supply Chain Network Design

There were no initial capacities on the links. The demand at the demand point was $d_{R_1} = 1,000$, and α was assumed to be 1.

Table: Total Cost Functions and Solution

| Link a | $\hat{c}_a(f_a)$ | $\hat{\pi}_a(u_a)$ | f_a^* | u_a^* | λ_a^* |
|----------|-------------------|--------------------|---------|---------|---------------|
| 1 | $f_1^2 + 2f_1$ | $.5u_1^2 + u_1$ | 571.15 | 571.15 | 572.15 |
| 2 | $.5f_2^2 + f_2$ | $1.5u_2^2 + 3u_2$ | 428.85 | 428.85 | 1,286.59 |
| 3 | $.5f_3^2 + f_3$ | $2.5u_3^2 + u_3$ | 454.91 | 454.91 | 2,275.54 |
| 4 | $f_4^2 + f_4$ | $1.5u_4^2 + 5u_4$ | 545.09 | 545.09 | 1,640.27 |
| 5 | $.5f_5^2 + f_5$ | $u_5^2 + 2u_5$ | 188.92 | 188.92 | 379.84 |
| 6 | $.25f_6^2 + f_6$ | $.1u_6^2 + u_6$ | 811.08 | 811.09 | 163.22 |
| 7 | $1.5f_7^2 + 2f_7$ | $u_7^2 + u_7$ | 56.32 | 56.32 | 113.64 |
| 8 | $.1f_8^2 + .5f_8$ | $.05u_8^2 + u_8$ | 943.68 | 943.68 | 95.37 |

Increasing Demand Examples

The demand of 1,000 was increased to 2,000, to 3,000, to 4,000, and, finally, to 5,000.

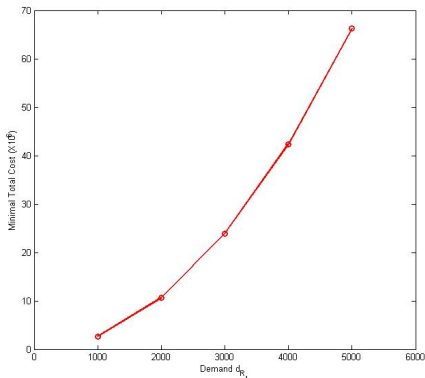


Figure: Minimal Total Cost Obtained for Example 1 Supply Chain Network Design as Demand Increases

Example 2: Supply Chain Network Redesign

Suppose that the firm has been operating according to the optimal design for the particular production period but now $d_{R_1} = 2,000$.

Table: Total Cost Functions, Initial Capacities, and Solution

| Link a | $\hat{c}_a(f_a)$ | $\hat{\pi}_a(u_a)$ | \bar{u}_a | f_a^* | u_a^* | λ_a^* |
|----------|-------------------|--------------------|-------------|----------|---------|---------------|
| 1 | $f_1^2 + 2f_1$ | $.5u_1^2 + u_1$ | 571.15 | 1,040.80 | 469.65 | 470.65 |
| 2 | $.5f_2^2 + f_2$ | $1.5u_2^2 + 3u_2$ | 428.85 | 959.20 | 530.35 | 1,594.05 |
| 3 | $.5f_3^2 + f_3$ | $2.5u_3^2 + u_3$ | 454.91 | 967.57 | 512.66 | 2,564.30 |
| 4 | $f_4^2 + f_4$ | $1.5u_4^2 + 5u_4$ | 545.09 | 1,032.43 | 487.34 | 1,467.01 |
| 5 | $.5f_5^2 + f_5$ | $u_5^2 + 2u_5$ | 188.92 | 436.38 | 247.46 | 496.93 |
| 6 | $.25f_6^2 + f_6$ | $.1u_6^2 + u_6$ | 811.08 | 1,563.61 | 752.53 | 151.51 |
| 7 | $1.5f_7^2 + 2f_7$ | $u_7^2 + u_7$ | 56.32 | 116.37 | 60.05 | 121.10 |
| 8 | $.1f_8^2 + .5f_8$ | $.05u_8^2 + u_8$ | 943.68 | 1,883.63 | 939.95 | 95.00 |

Iterated Redesign with Increasing Demands

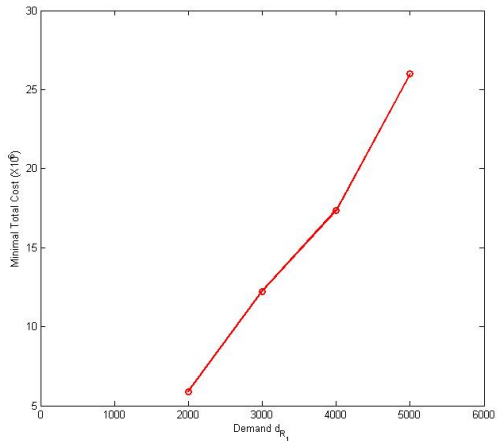
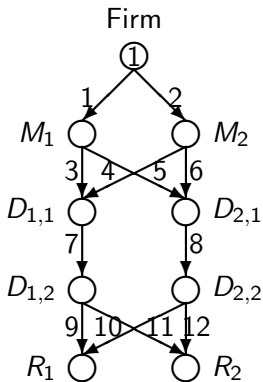


Figure: Minimal Total Cost Obtained for Example 2 Iterated Supply Chain Network Redesigns as Demand Increases

Multiproduct Supply Chain Network Design Case Study

A firm is assumed to be involved in the production of two vaccines, which correspond to two products, such as, for example, a seasonal flu vaccine and the H1N1 vaccine, referred to as vaccine 1 and 2, respectively.



Example 3: Design Problem

In the design problem, the initial link capacities are all zero, that is, $\bar{u}_a = 0$ for all links $a = 1, \dots, 12$. Also, since the two vaccines are assumed to be similar products in size, for transparency and simplicity, that $\alpha_1 = \alpha_2 = 1$. The demands for the two vaccines at the demand points were:

$$d_{R_1}^1 = 100, \quad d_{R_2}^1 = 200, \quad d_{R_1}^2 = 300, \quad d_{R_2}^2 = 400.$$

Table: Total Cost Functions

| Link a | $\hat{c}_a^1(f_a^1, f_a^2)$ | $\hat{c}_a^2(f_a^1, f_a^2)$ |
|----------|---|---|
| 1 | $1(f_1^1)^2 + .2f_1^2 f_1^1 + 11f_1^1$ | $3(f_1^2)^2 + .2f_1^2 f_1^1 + 7f_1^2$ |
| 2 | $2(f_2^1)^2 + .4f_2^2 f_2^1 + 8f_2^1$ | $4(f_2^2)^2 + .4f_2^2 f_2^1 + 4f_2^2$ |
| 3 | $3(f_3^1)^2 + .25f_3^2 f_3^1 + 7f_3^1$ | $4(f_3^2)^2 + .25f_3^2 f_3^1 + 6f_3^2$ |
| 4 | $4(f_4^1)^2 + .3f_4^2 f_4^1 + 3f_4^1$ | $4(f_4^2)^2 + .3f_4^2 f_4^1 + 6f_4^2$ |
| 5 | $1(f_5^1)^2 + .2f_5^2 f_5^1 + 6f_5^1$ | $1(f_5^2)^2 + .2f_5^2 f_5^1 + 4f_5^2$ |
| 6 | $3(f_6^1)^2 + .3f_6^2 f_6^1 + 4f_6^1$ | $4(f_6^2)^2 + .3f_6^2 f_6^1 + 9f_6^2$ |
| 7 | $4(f_7^1)^2 + .2f_7^2 f_7^1 + 7f_7^1$ | $4(f_7^2)^2 + .2f_7^2 f_7^1 + 7f_7^2$ |
| 8 | $4(f_8^1)^2 + .3f_8^2 f_8^1 + 5f_8^1$ | $2(f_8^2)^2 + .3f_8^2 f_8^1 + 5f_8^2$ |
| 9 | $1(f_9^1)^2 + .3f_9^2 f_9^1 + 4f_9^1$ | $4(f_9^2)^2 + .3f_9^4 f_9^1 + 3f_9^2$ |
| 10 | $2(f_{10}^1)^2 + .6f_{10}^2 f_{10}^1 + 3.5f_{10}^1$ | $3(f_{10}^2)^2 + .6f_{10}^2 f_{10}^1 + 4f_{10}^2$ |
| 11 | $1(f_{11}^1)^2 + .5f_{11}^2 f_{11}^1 + 4f_{11}^1$ | $4(f_{11}^2)^2 + .5f_{11}^2 f_{11}^1 + 6f_{11}^2$ |
| 12 | $4(f_{12}^1)^2 + .6f_{12}^2 f_{12}^1 + 6f_{12}^1$ | $3(f_{12}^2)^2 + .6f_{12}^2 f_{12}^1 + 4f_{12}^2$ |

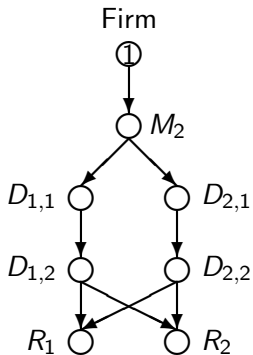
Table: Link Capacity Investment Cost Functions

| Link a | $\hat{\pi}_a(u_a)$ |
|----------|-------------------------|
| 1 | $5u_1^2 + 100u_1$ |
| 2 | $4u_2^2 + 80u_2$ |
| 3 | $u_3^2 + 20u_3$ |
| 4 | $u_4^2 + 10u_4$ |
| 5 | $1.5u_5^2 + 10u_5$ |
| 6 | $u_6^2 + 15u_6$ |
| 7 | $4u_7^2 + 110u_7$ |
| 8 | $4.5u_8^2 + 120u_8$ |
| 9 | $u_9^2 + 10u_9$ |
| 10 | $.5u_{10}^2 + 15u_{10}$ |
| 11 | $u_{11}^2 + 20u_{11}$ |
| 12 | $.5u_{12}^2 + 10u_{12}$ |

Table: Optimal Multiproduct Flows, Link Capacities, and Lagrange Multipliers

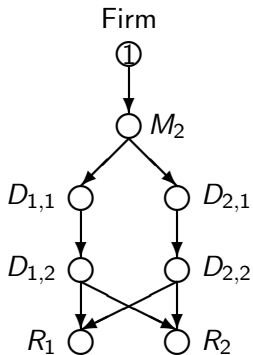
| Link a | f_a^{1*} | f_a^{2*} | u_a^* | λ_a^* |
|----------|------------|------------|---------|---------------|
| 1 | 97.84 | 392.69 | 490.51 | 5005.05 |
| 2 | 202.16 | 307.31 | 509.44 | 4155.55 |
| 3 | 53.65 | 197.92 | 251.58 | 523.15 |
| 4 | 44.19 | 194.77 | 238.96 | 487.91 |
| 5 | 118.06 | 145.71 | 263.77 | 801.23 |
| 6 | 84.10 | 161.60 | 245.70 | 506.40 |
| 7 | 171.10 | 343.64 | 515.32 | 4232.54 |
| 8 | 128.29 | 356.36 | 484.63 | 4481.70 |
| 9 | 30.23 | 188.32 | 218.56 | 447.11 |
| 10 | 141.47 | 155.31 | 296.78 | 311.78 |
| 11 | 69.77 | 111.68 | 181.44 | 382.89 |
| 12 | 58.53 | 244.69 | 303.22 | 313.21 |

Sensitivity Analysis



When the fixed cost associated with the investment capacity on link 1 was equal to 20,000 (or greater), the first manufacturing plant would not be constructed and the manufacturing of both vaccines would take place exclusively at manufacturing plant 2.

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Example 4: Redesign Problem

Table: Link Capacities (Original) for Redesign Problem Example 4

| Link a | \bar{u}_a |
|----------|-------------|
| 1 | 400.00 |
| 2 | 500.00 |
| 3 | 200.00 |
| 4 | 200.00 |
| 5 | 300.00 |
| 6 | 300.00 |
| 7 | 500.00 |
| 8 | 400.00 |
| 9 | 200.00 |
| 10 | 200.00 |
| 11 | 100.00 |
| 12 | 300.00 |

Table: Optimal Multiproduct Flows, Enhanced Link Capacities, and Lagrange Multipliers

| Link a | f_a^{1*} | f_a^{2*} | u_a^* | λ_a^* |
|----------|------------|------------|---------|---------------|
| 1 | 89.38 | 391.00 | 80.37 | 903.70 |
| 2 | 210.62 | 309.00 | 19.63 | 237.00 |
| 3 | 43.30 | 190.40 | 33.70 | 87.39 |
| 4 | 46.08 | 200.60 | 46.68 | 103.36 |
| 5 | 141.16 | 159.61 | 0.76 | 12.29 |
| 6 | 69.47 | 149.39 | 0.00 | 0.00 |
| 7 | 184.45 | 350.01 | 34.46 | 385.65 |
| 8 | 115.55 | 349.99 | 65.54 | 709.84 |
| 9 | 49.48 | 196.62 | 46.10 | 102.21 |
| 10 | 134.97 | 153.39 | 88.35 | 103.35 |
| 11 | 50.52 | 103.38 | 53.90 | 127.79 |
| 12 | 65.03 | 246.61 | 11.65 | 21.65 |

Summary and Conclusions

- We developed a multiproduct supply chain network design model with applications to healthcare, which can handle both link capacities and product flows as decision variables, along with nonlinear cost functions to capture congestion, as well as risk.
- We demonstrated that the optimization problem underlying this multiproduct supply chain network design problem can be formulated and solved as a variational inequality problem, with nice features for computational purposes.
- A firm involved in the production and distribution of healthcare products can utilize this model to identify the total cost associated with the provision of its products.
- The framework can handle both the design and the redesign problem with the latter being especially relevant for healthcare.

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Thank You!