Cost-effectiveness analysis of different interventions to reduce PFAS body burden

In order to be able to make a meaningful comparison between the different potential interventions, we need to be able to compare like with like, in terms of how effective the various interventions are at reducing PFAS in the body. It should be noted that several assumptions have been made in these analyses. Where there were a range of half-lives shown in the literature review, the midpoint of that range has been used in all the modelling here. In addition, the modelling of efficacy is solely for the purposes of comparison and does not represent real-world projections of serum levels (ongoing exposure has been excluded from the analysis, for example).

Understanding and exploring relative efficacy of different interventions

Based on the analysis in the literature review, the Panel has calculated the duration of each treatment needed for the individual moieties of PFAS in the body to reduce by half. These overall half-lives are summarised in **Error! Reference source not found.**~~Figure 17~~ **Error! Reference source not found.**~~below~~.

Figure 1~~17~~ - Overall effective half-lives of different PFAS moieties by intervention (months)

	PFHxS	PFOS	PFOA
No Intervention	54.0	36.0	30.0
Phlebotomy	29.8	23.0	20.3
Plasma Removal	18.2	15.2	13.9
Probenecid (no effect)	54.0	36.0	30.0
Bile Acid Sequestrants	9.8	2.0	6.8
High-Fibre Diet	54.0	33.0	28.3
Haemodialysis	15.9	2.6	7.9

Looking at the data, it is clear that there is a very wide range of durations, from 2 months to halve PFOS levels with bile acid sequestrants, up to 54 months for PFHxS to halve in the absence of any intervention. Because Probenecid is not effective, it is not included in the analysis below.

Given that, in every scenario above, PFHxS has the longest half life, and it is generally the moiety with the highest serum level in Jersey residents, we will use those half lives as the unit of comparison. It should be noted that we are not suggesting that one half life of PFHxS should be the duration of treatment, it is just the common unit that we are using to triangulate the costs

Before moving into the actual cost effectiveness analysis, we just wanted to contextualise the meaning, in terms of PFAS levels, of a one PFHxS half life duration of treatment, in terms of its impact on levels of PFAS at the end of that period. **This is a thought experiment, assuming no ongoing exposure through the environment and should not be seen as real world projections but merely a comparative exercise looking at the relative efficacy of the different intervention approaches.**

We have already discussed that the median levels of the different PFAS in the serum of the people from the plume area, tested under the Public Health testing programme in 2022. They were **13ng/mL for PFHxS, 11ng/mL for PFOS and 3ng/mL for PFOA**. If we assume that those are the starting levels for each intervention, we can look at the levels of each of the PFAS moieties after one PFHxS half life of each treatment and how long it will take to get there. These are summarised in **Error! Reference source not found.**~~Figure 18~~, **Error! Reference source not found.**~~below~~.

Figure 2~~18~~ - Levels, in ng/mL of serum, of different PFAS moieties after one effective PFHxS half-life of each intervention

	Duration of intervention (to reduce PFHxS by one half life)	PFHxS[1]	PFOS[1]	PFOA[1]	Total[1]
No Intervention	54 months	6.5	3.9	0.9	**11.3**
Phlebotomy	29.8 months	6.5	4.5	1.1	**12.1**
Plasma Removal	18.2 months	6.5	4.8	1.2	**12.5**
Bile Acid Sequestrants	9.8 months	6.5	0.4	1.1	**8.0**
High-Fibre Diet	54 months	6.5	3.5	0.8	**10.8**
Haemodialysis	15.9 months	6.5	0.2	0.7	**7.4**

1 Assuming zero ongoing exposure

As you will see, even with a greater than five fold variation in the duration of intervention, the total of the three PFAS moieties is fairly similar, other than for bile acid sequestrants and haemodialysis. Just for reference, the starting totals across those three PFAS moieties was 27ng/mL of serum.

On the other hand, if we compare on the basis of twelve months of each of the interventions, there is much more variation. **Once again, just a reminder that there are not real world projections as they ignore any ongoing exposure they are there solely for comparison of different intervention approaches:**

Figure ~~3~~19 - levels of PFAS in ng/mL of serum after twelve months of each intervention scenario based on testing programme baseline levels

	Duration	PFHxS[1]	PFOS[1]	PFOA[1]	Total[1]
No Intervention	12 months	11.1	8.7	2.3	**22.2**
Phlebotomy	12 months	9.8	7.7	2.0	**19.5**
Plasma Removal	12 months	8.2	6.4	1.7	**16.2**
Bile Acid Sequestrants	12 months	5.6	0.2	0.9	**6.6**
High-Fibre Diet	12 months	11.1	8.6	2.2	**21.9**
Haemodialysis	12 months	7.7	0.5	1.1	**9.2**

1 Assuming zero ongoing exposure

As **Error! Reference source not found.**~~Figure 19~~ demonstrates, there are marked differences in the overall benefit of the different intervention strategies over a twelve-month treatment period. While plasma removal, and, to a lesser extent, phlebotomy show incremental improvement over no intervention in this time frame, Bile acid sequestrants and, to a lesser extent, haemodialysis show dramatic reductions in serum PFAS.

Projected costs of different interventions

Looking at the costs of the different intervention approaches is an important step in assessing the proportionality and affordability of a given intervention for Jersey. These costs are divided into two types: capital costs and revenue costs. Capital costs include the purchase and installation of any specialised equipment that might be needed to deliver that service. In this analysis, we have assumed that there does not need to be significant building or rebuilding of facilities where the service could be housed. Revenue costs, on the other hand, are the costs of running the service once it has been established. These include staffing costs, the costs of drugs and consumables, maintenance, calibration and standardisation costs and suchlike. Capital costs are incurred at the purchase and installation of any equipment and can also recur when equipment reaches the end of its lifecycle. In the following analyses, we have assumed that no capital equipment would need to be replaced during an intervention programme. Revenue costs are incurred throughout the time the programme is in progress. Some revenue costs, such as drugs and consumables will vary depending on the throughput of the service, while others, such as staffing and maintenance, will be fixed costs regardless of how much use the service is getting. For the purpose of this analysis (and the later cost-effectiveness analyses), we have made the assumption that fibre supplements, like Psyllium husk, would have the same effect as a high fibre diet and that the government were picking up the cost, rather than Islanders self-funding. As has been noted above, there evidence for fibre supplements is weak such that it would be hard to recommend them as an effective treatment, they have been included here for cost-effectiveness comparison purposes only.

The table below summarises the capital costs for each intervention and the revenue cost per annum of delivering the service to fifty persons

Figure 420 - Capital and revenue costs to deliver a service for fifty persons

	Capital costs	Revenue costs per annum
No Intervention[2]		
Phlebotomy	Nil	£125,000
Plasma Removal	£100,000	£175,000
Bile Acid Sequestrants	Nil	£ 41,510 [1]
Fibre Supplements	Nil	£26,206
Haemodialysis	£100,000	£1,380,000

1 using the most expensive bile acid sequestrant, Colesevelam and a full twelve months of the drug

2 There are no direct costs of doing nothing

Just looking at delivery costs, without considering efficacy, the table shows a greater than thirty fold differential in the cost of delivering a service to fifty persons, with haemodialysis costing close to £1.5 million and bile acid sequestrants (the most expensive such agent, Colesevelam) costing under £50,000.

While fibre supplements appear to be reasonably low cost, it is important to note that the assumption that they are as clinically effective as a high fibre diet is a large leap and unlikely to be actually the case in real life. Furthermore, the fact that they do not reduce PFHxS at all beyond no intervention, mean that they are not a suitable intervention where PFHxS is the most elevated of the PFAS moieties. For these reasons, they have been omitted from the final analysis.

Cost effectiveness analysis

This section brings together the evidence on efficacy with the modelled costs to assess the relative value for money of each treatment approach. This analysis will not look at all the interventions previously considered, but will focus on those where there is evidence of some efficacy over and above no intervention and where costs of regulator approved, licensed drugs, equipment and services are used. Three intervention approaches have been excluded, therefore; not to intervene at all, Probenecid (because it has not outperformed no intervention in studies) and probiotic supplements, because no licensed product is currently available.

The table below models the total cost to treat fifty people until such time as they halve their PFHxS levels. The Panel is not suggesting that that would be the endpoint of any intervention, it has simply been chosen in order to compare the costs of the different treatments on a like for like basis, predicated on outcomes. The costing incorporates capital costs (where relevant) and the revenue costs from the duration of treatment that would be necessary.

As there is no evidence of fibre supplements having effect on PFHxS, they are not part of this analysis.

Figure 5~~21~~ - Cost to treat until PFHxS level is halved

	Capital costs	Revenue costs per annum	Months to halve PFHxS	Cost to halve PFHxS
Phlebotomy	Nil	£125,000	29.8	£310,417
Plasma Removal	£100,000	£175,000	18.2	£365,417
Bile Acid Sequestrants[1]	Nil	£ 41,510	9.8	£33,900
Haemodialysis	£100,000	£1,380,000	15.9	£1,928,500

1 using Colesevelam, the most expensive bile acid sequestrant

As can be seen in the table, even the most expensive bile acid sequestrant therapy is between nine and fifty times more cost-effective than any other potential intervention option. On the face of it, other bile acid sequestrant agents may be even more cost-effective, but they are far more likely to have adherence problems due to adverse effects being more common, and that is likely to significantly reduce and potential cost-effectiveness advantage in the real world. It should be noted, however, that the direct evidence in the literature is for cholestyramine, not colesevelam, and, while it is highly likely that PFAS reduction is a class effect, any programme using colesevelam would require detailed evaluation.

Figure 6~~22~~ - Relative cost effectiveness of different PFAS lowering interventions in lowering PFHxS

	Cost to halve PFHxS	Relative cost-effectiveness
Bile Acid Sequestrants	£33,900	100.0%
Phlebotomy	£310,417	10.9%
Plasma Removal	£365,417	9.3%
Haemodialysis	£1,928,500	1.8%

It should be noted that the figures above represent the likely real-world costs of treating until PFHxS is halved

Those analyses can be repeated, looking at total of the three major PFAS in Jersey, PFHxS, PFOS and PFOA. A key assumption is that the three PFAS moieties are in the same proportions, relative to each other, as they are in the median values from the 2022 PFAS testing programme in the plume area of St Oeun. This is presented in the table below:

Figure 723 - Cost to treat until total PFAS (of 3 moieties) is halved

	Capital costs	Revenue costs per annum	Months to halve PFAS total	Cost to halve PFAS total
Phlebotomy	Nil	£125,000	21.6	£224,615
Plasma Removal	£100,000	£175,000	15.1	£319,652
Bile Acid Sequestrants[1]	Nil	£ 41,510	7.9	£27,494
Haemodialysis	£100,000	£1,380,000	9.1	£1,146,640

This represents the real-world costs of treating until the total of the three PFAS moieties is halved.

A similar analysis can be done to calculate the relative cost-effectiveness of each of the treatment interventions at lowering the total of the three PFAS moieties by half shows similar results:

Figure 824 - Relative cost effectiveness of different interventions at lowering total PFAS

	Cost to halve PFHxS	Relative cost-effectiveness
Bile Acid Sequestrants	£27,494	100.0%
Phlebotomy	£224,615	12.2%
Plasma Removal	£319,652	8.6%
Haemodialysis	£1,146,640	2.4%

This represents the relative cost-effectiveness in practice.

Additional analyses

The analyses above, while useful, do not represent the true cost-effectiveness, because all of the scenarios include periods of natural decay in PFAS levels, and these periods are of varying length. As a result, those treatments that take longer appear to be more cost effective than they should, relative to those treatments that are quicker.

The previous tables represent the real-world changes in PFAS over time in the different intervention scenarios. In order to have a more precise understanding of the cost effectiveness of different interventions, we need to remove any reduction in PFAS that is not attributable to the treatment. To do that, we need to take away any reduction in PFAS that would happen anyway due to the natural half-life of the compounds in the human body. **The tables below are for analytical purposes only and do not represent real world performance (because in the real world there is additional reduction from the natural half life)**. Furthermore, these analyses also ignore any ongoing exposure to PFAS, as the earlier tables did.

Looking at how the interventions would perform if there were no natural reduction of PFAS and no background exposure, we can calculate notional attributable half-lives for each PFAS moiety for each intervention. For completeness, we can also synthesise a half-life for the sum of the three moieties. While this is a synthetic estimate, it may be useful in the future for projecting overall treatment response.

The table below looks at how long it would take for the intervention to reduce PFAS to half its initial level if there were no ongoing exposure and no natural reduction over time (or if those two balance each other out):

Figure 925 – Notional time for PFAS moieties to halve under different interventions. Net of background exposure and natural decay

	Attributable half-life PFHxS	Attributable half-life PFOS	Attributable half-life PFOA	Attributable half-life total PFAS
Phlebotomy	59.5	61.7	63.8	60.9
Plasma Removal	26.8	27.9	28.8	27.4
Bile Acid Sequestrants	14.0	7.7	12.9	10.4
High-Fibre Diet		363.7	479.3	739.6
Haemodialysis	22.7	8.0	14.7	12.5

As stated above, these do not represent the real world and will be used only to compare cost effectiveness. Cells that are greyed out represent where there is no attributable reduction in the PFAS moiety from the intervention.

If we rerun the analysis using notional attributable half-lives and assess the cost for the actual treatment to halve PFHxS levels, rather than relying on time to do part of the job we get a different picture. This is summarised in the table below:

Figure 1026- Notional attributable cost effectiveness of different interventions for reducing PFHxS to half initial value

	Capital costs	Revenue costs per annum	Months to halve PFHxS	Cost to halve PFHxS
Phlebotomy	Nil	£125,000	59.5	£620,073
Plasma Removal	£100,000	£175,000	26.8	£490,492
Bile Acid Sequestrants[1]	Nil	£ 41,510 [1]	14.0	£48,428
Haemodialysis	£100,000	£1,380,000	22.7	£2,710,500

The cost effectiveness of the different treatments for PFHxS reduction relative to bile acid sequestrants is summarised in the table below:

Figure 1127 - Cost-effectiveness for PFHxS reduction of different intervention options, relative to bile acid sequestrants

Treatment	Cost to Halve PFHxS	Relative Cost-Effectiveness
Bile Acid Sequestrants	£44,772	100%
Plasma Removal	£490,492	9.9%
Phlebotomy	£620,073	7.8%
Haemodialysis	£2,710,500	1.8%

The table above illustrates the extent to which bile acid sequestrants outperform other interventions with regard to cost-effectiveness.

A similar analysis can be carried out looking at total PFAS levels of the three moieties prevalent in Jersey. This analysis assumes that the relative proportions of each equate to the relative proportions found In the median values from the plume area population testing programme. Again, this does not represent a real world scenario, and is looking at attributable reductions for the purpose of cost effectiveness estimate synthesis. Because there is an association between fibre consumption and lower PFOS and PFOA, fibre supplements are included in this analysis. The caveats discussed above about extrapolating the effect of dietary fibre to and effect from a fibre supplement still apply. This is summarised in the table below:

Figure 1228 – Notional attributable cost effectiveness of different interventions for reducing total across three PFAS moieties to half initial value

	Capital costs	Revenue costs per annum	Months to halve PFAS	Cost to halve PFAS
Phlebotomy	0	£125,000	60.9	£634,089
Plasma Removal	£100,000	£175,000	27.4	£500,146
Bile Acid Sequestrants	0	£41,510	10.4	£36,083
Fibre Supplements	0	£26,206	739.6	£1,615,259
Haemodialysis	£100,000	£1,380,000	12.5	£1,538,802

The table shows that bile acid sequestrants are again considerably more cost effective that other interventions.

The table below compares the relative cost effectiveness to the most cost effective treatment in this scenario:

Figure 1329 - Cost-effectiveness for total PFAS reduction of different intervention options, relative to bile acid sequestrants

Treatment	Cost to Halve PFAS	Relative Cost-Effectiveness
Bile Acid Sequestrants	£20,215	100%
Plasma Removal	£500,146	7.2%
Phlebotomy	£634,089	5.7%
Haemodialysis	£1,538,802	2.3%
Fibre Supplements	£1,615,259	2.2%

Once again, the table shows the extent to which bile acid sequestrants dominate other interventions, in terms of cost effectiveness. Looking at PFOS or PFOA individually gives a very similar picture, with bile acid sequestrants outperforming other interventions more than tenfold.

As can be seen from the analyses in this section, once natural decay from the duration of treatment is corrected for, the superiority in cost effectiveness of bile acid sequestrants over other interventions is even greater.

In summary

Bile acid sequestrants outperform other interventions in terms of efficacy significantly; they are thirty percent more effective than the next most effective intervention in the real world and have more than double the efficacy of any viable intervention.

Bile acid sequestrants are marginally cheaper than any other form of intervention but are markedly more cost-effective than any other option, more than an order of magnitude better than the next best, in terms of cost effectiveness. These findings persist with each of the three PFAS moieties and with the total of these PFAS.

Capital and revenue requirements for establishing and running a phlebotomy service

Necessary Equipment

- **Sterile Disposable Kits:** Needles, tubing, collection bags, and anticoagulant solutions. Single-use kits prevent cross-contamination and ensure sterility.
- **Medical Examination Equipment:** Blood pressure monitors, haemoglobin testing devices, scales, and temperature gauges. These are used to assess participant eligibility and monitor vital signs pre- and post-donation.
- **Emergency Equipment:** Automated External Defibrillators (AEDs), oxygen tanks, and first aid kits. To address any adverse reactions or medical emergencies promptly.

Required Personnel

- **Lead clinician:** Probably a medical consultant with expertise in transfusion medicine or haematology. Role includes oversight of medical procedures, participant eligibility criteria, and compliance with medical standards (JPAC 2024).
- **Specialist nurses:** To perform vein punctures and monitor participants during the procedure. They need to be certified in phlebotomy.
- **Maintenance and Cleaning Personnel: To e**nsure cleanliness of the facility and proper functioning of equipment. This is critical for infection control and meeting health standards.

Maintenance and Regulatory Compliance

- **Regular Servicing of Equipment**: Defibrillators, monitors and other resuscitation equipment require routine checks and servicing by qualified technicians.

- **Calibration of Equipment**: Medical devices must be calibrated regularly to ensure accuracy [ISO 2022].

- **Facility Cleaning Protocols**: Adherence to strict cleaning schedules for participant areas, equipment, and common spaces.

- **Infection Control**: Implementation of standard precautions to prevent cross-contamination

- **Licensing and Accreditation**: Obtain necessary licenses from health regulatory organisations.

- **Standard Operating Procedures (SOPs)**: Develop and maintain SOPs for all processes, aligning with MHRA, FDA and European Medicines Agency (EMA) guidelines.

- **Staff Training and Certification**: Ongoing education to keep staff updated on best practices and regulatory changes.

- **Audits and Inspections**: Regular internal audits and readiness for external inspections.

Capital cost

The capital costs of a phlebotomy service are limited and can likely be met without additional investment.

Additional Costs to Consider

- **Maintenance and Service Contracts:** Essential for the safe and effective operation of the machine, there will be regular maintenance and calibration, carried out by facility staff. In addition to that there would be a requirement for a service contract with the manufacturer. These can be of the order of £5,000 per annum.
- **Consumables:** Each blood collection procedure requires a single-use kit, costing between £30 and £50 each.
- **Training and Staffing:** In addition, the salary costs of the staff described above, staff must be trained.

In summary

Bringing all of this together, it is a reasonable assumption that the capital outlay for a service would be nil and the revenue costs, assuming 300 phlebotomy activities (6 interventions each for 50 people) in year 1 and half time consultant cover and full time cover from other staff would be between £100,000 and £150,000 per annum.