Technoleg Iechyd Cymru
Health Technology Wales

Convalescent plasma: A costing review

Economic evaluation

The deployment of convalescent plasma as a treatment option for COVID-19 may be achieved through the collection of whole blood, however, the perceived high demand suggests that a more scalable approach would be optimal. The use of plasmapheresis machines allows for patients to donate plasma whilst retaining the other components of whole blood, this allows for a higher frequency of donations when compared to whole blood collection. Plasmapheresis allows for a donor to donate plasma once every two weeks compared to whole blood donation frequency of once every three months. In addition to the increased safe frequency, the collection process permits the collection of multiple plasma units (250ml), typically two units are collected from each donation.

This economic analysis takes the limited perspective of the plasma collection and therapeutic delivery cost. Due to the time horizon discounting is not included. Costs are reported in 2019/20 GBP (£).The collection analysis takes the form of a micro costing approach. The procedural structure aims to reflect planned deployment of plasmapheresis machines in Wales.

The analysis looks at the procurement of 60 plasmapheresis machines for the use of delivering convalescent plasma to patients with COVID-19. The patient specification delineates into three defined groups. Group one consists of the intensive care unit (ICU) patients. Group two are hospitalised patients (not in ICU). Group three is high risk staff.

Economic structure

The model aims to capture each distinct aspect of collection, this can be broadly characterised into four steps presented in Figure 1 and described in more detail below.

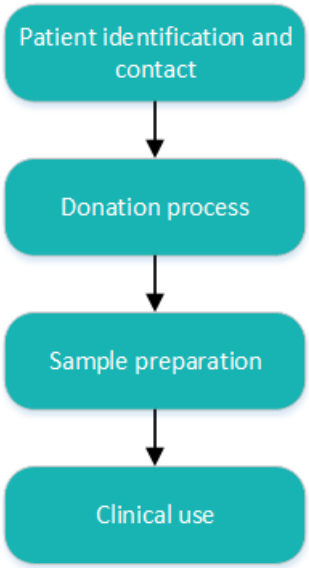

Figure 1

Patient identification and contact

Patient identification and contact is the process of selecting the appropriate donors and subsequently inviting them to donate plasma. Currently the criteria limits to Males aged between 17 and 66 that are 30 days following the cessation of symptoms of COVID-19. Donors are excluded if they've previously received a blood transfusion.

The cost of patient identification is relatively dependant on scale, currently the level of effort being undertaken to identify patients and apply criteria is above that which is expected to be seen once economies of scale are enjoyed. To reflect a cost which is aligned with the scale of the proposed deployment of convalescent plasma a general cost is used. It is thought that smaller scale patient recruitment may incur higher unit costs. An estimate from a US micro-costing study by Prioli (2016) offers a figure of $5.85 which equates to £4.07 after exchange rate and inflation adjustments.

Donation process costs

The cost associated with plasma collection vary according to the structure of the donor process. Variables such as staff levels and number of machines per location can have an impact on cost per unit collected. For this analysis, the unitary components are presented and applied to the collection process proposed for NHS Wales. Plasmapheresis machines take between 60 and 90 minutes to collect the donation, this can vary based on volume collected and flow rate. Suitability to donate is assessed through a clinic appointment. Taking into account set up process and donation duration, each machine is assumed to have a capacity of four collections daily. A satellite approach to collection centres is adopted with an aim to minimise the travel distances for donors. Table 1 shows the staffing levels required.

Table 1: Plasmapheresis deployment structure

Resource	Number per centre
Plasmapheresis machine	6
Plasma collection nurse (grade 5 or 6)	3
Plasma collection Assistant (grade 2 or 3)	2

The cost of each collection centre is developed, where possible, using a fixed cost allocation for capital items, a time duration cost for staffing and a unitary variable cost approach for consumables. The cost per plasmapheresis machine is reported to be £20,000. The machinery is assumed to have a working life of 10 years. However, in this special assessment case the duration used is 16 weeks. A 16 week horizon is chosen in line with the increased crucial care bed occupation levels reported by Ferguson et al. (2020). Alternative durations are assessed in the sensitivity analysis. A residual value of 50% is applied following the initial use duration to reflect the lower repurposing utility of the plasmapheresis machines following their primary use, this assumption is varied in the sensitivity analysis. The micro costing approach takes a weekly cycle as its base unit and offers a 'per plasma unit' and per treatment cost shown in Table 2.

Table 2. Costs per collection centre week.

Resource	Unit cost	Calculation	Total cost per week
Plasmapheresis machine (n=6)	£20,000	6*[(20,000*50%)/16]	£3,750
Medical freezer (n=1)	£1,050	1*[(£1,050*50%)/16]	£33
Staffing cost (per collection centre week)			
Band 6 nurse	3	£1,725 (per Nurse)	£5,175
Band 2 support staff	2	£932 (per staff member)	£1,863
		Total cost	£10,821

The weekly costs per collection centre not associated with volume is estimated at £10,821. Each donation requires a single use harness which is estimated to cost £72.66 (WBS figures). The capacity of each plasmapheresis machine is estimated at 20 donations per week; four donations daily with a working week of five days. A capacity of seven days a week capacity is modelled in the sensitivity analysis. The capacity of each collection centre is 120 collection per week. Table 3 shows the variable costs per week associated with a collection site, note that this includes the patient identification costs as these vary with volume.

Table 3. Variable costs

Resource	Units	Unit cost	Total cost
Patient identification and contact	120	£4.07	£488
Plasmapheresis harness	120	£72.66	£8,719
		Total cost	£9,208

The patient identification and donation process cost per collection site each week is estimated at £20,029. Plasmapheresis machines are able to collect two units of plasma per donation, this results in an estimated 240 units per collection centre per week at a 'per unit' cost of £83. Higher and lower yields are assessed in the sensitivity analysis.

Sample preparation

Convalescent plasma differs from more standard uses of plasma due to the additional testing required to assess the viability of the plasma for therapeutic use. Welsh Blood Service estimates the laboratory testing associated with SARS-CoV 2 testing to cost approximately £40. Testing is implemented to assess the antibody potential of the plasma, expert opinion suggested that 30% of collected plasma would be deemed to have a sufficiently high titer (sufficient levels of antibody within the plasma) as to be usable. Table 4 below summarises costs to the point of antibody testing.

Table 4. Cost of convalescent plasma per collection centre week

Resource	Units	Unit cost	Total cost per week
Machine and staff		£20,029	£20,029
Antibody testing	240	£40	£9,600
		Total cost	£29,629
Therapeutic units (30% of total number)		72	
		Cost per therapeutic unit	£412

The cost per therapeutic plasma unit can be calculated according to the 30% yield on 240 units (72 units). The total cost of the collection site of £29,629 is divided by therapeutic plasma units (72) to offer a 'per unit' cost of £412.

Clinical use

Stokes et al. (2018) report delivery costs associated with the use of plasma in UK NHS. The delivery cost of plasma includes laboratory cost, nursing inputs and wastage. Delivering the initial unit of plasma cost £58.30 whilst subsequent units incurred less nursing input and were estimated at a cost of £35.67. There is an assumption that each patient received two units of plasma, which is in line with the REMAP-CAP protocol. The total cost of delivering convalescent plasma per patient is approximately **£917** ((412*2) + 58.30 + 35.67). This approach applies no value to plasma which doesn't meet the antibody testing threshold, it is noted that France are looking to implement an antibody testing approach with an expected 65% therapeutic yield.

Sensitivity analysis

A range of one way sensitivity analyses have been undertaken to help characterise the impact of the uncertainly surrounding selected model components. The variables chosen for inclusion in the sensitivity analysis are those where there is a higher level of uncertainty or those which have a significant impact on the overall costs. The one way sensitivity analysis adjusts the component in question in order to better understand the impact that component has on the overall cost. Each variable is adjusted in the model with all other factors remaining constant. The cost per unit of therapeutic plasma and the cost per treatment are reported for each variable input. Extending the working week to seven days reduces the cost per therapeutic unit to £396 and cost per treatment to £887.

Duration of use

Duration of use is varied within an eight week to 52 week time horizon. Table 5 reports the range of costs.

Table 5. Duration of use

Duration of use	Cost per unit of plasma	Cost per treatment
8 weeks	£464	£1,022
12 weeks	£429	£952
16 weeks	£412	£917
20 weeks	£401	£896
26 weeks	£391	£877
52 weeks	£375	£844

Residual capital value

The current procurement situation is based on the use of the plasmapheresis machines in the collection of convalescent plasma. The duration of the current pandemic is unknown and the subsequent use of the plasmapheresis machines is not fully defined. The base model assumes a 50% residual value to reflect the prospect of a sub-optimal repurposing. Residual values are reported, in table 6, ranging from 0% to full value, in this case a 10 year horizon with straight line depreciation for the 16 weeks already used (97%). The residual value of the additional freezers are subjected to the same residual value.

Table 6. Residual value

Residual value percentage (%)	Cost per unit of plasma	Cost per treatment
0%	£464	£1,022
25%	£438	£970
50%	£412	£917
75%	£385	£864
97%	£362	£818

Collection levels per donation

Whilst the process of plasmapheresis is associated with an increase in overall plasma capacity given the same number of donors, the amount collected from each donor on each visit may vary. The base model assumption that two units of plasma are collected from each donor is varied within the range of 0.5 to 3 at 0.5 increments. Table 7 reported the one way sensitivity analysis of units per session.

Table 7. Plasmapheresis donation yield

Average plasma units per session	Cost per unit of plasma	Cost per treatment
0.5	£1,246	£2,586
1	£690	£1,473
1.5	£504	£1,102
2	£412	£917
2.5	£356	£806
3	£319	£732

Within this analysis the conservative collection rate of four sessions per day is used, this is partially motivated by desire to offer an appropriate representation of an achievable production level given the appreciation that a scheduled appointment is not always going to lead to the collection of plasma. The range of average plasma units can be seen as a representation of plasma yield per appointment scheduled, this may be reduced by missed appointments or individuals being unable to donate.

Antibody threshold

The base case model assumes that only 30% of collected plasma will include a sufficiently high titer as to be deemed clinically useful convalescent plasma. The titer threshold is aligned with the inclusion criteria for the trial REMAP-CAP which uses the EUROIMMUN assay and a score of 9.1. The clinical efficacy of convalescent plasma is not well define, nor is the relationship between titer level and effectiveness. To reflect the uncertainty surrounding the useful percentage of collected plasma, a range from 10% to 100% is included in this sensitivity analysis. Results from the antibody testing variation sensitivity analysis is reported in table 8.

Table 8. Titer yield

Percentage of plasma deemed of therapeutic level	Cost per unit of plasma	Cost per treatment
10%	£1,235	£2,563
20%	£617	£1,328
30%	£504	£1,102
50%	£247	£588
75%	£165	£423
100%	£123	£341

Budget impact modelling

The budget impact modelling take two forms, capital costs and total cost of delivery. The capital cost approach looks at the initial cost associated with capital items (plasmapheresis machines and freezers). The figure of 60 machines is used and 10 freezers. The total initial budget impact is (60*£20,000) + (10* £1,050) = £1,210,500.

Total cost of delivery over 16 week horizon

The total cost of deploying 60 machines in the 10 pod structure over a 16 week working horizon is approximately £5.9m. The variable cost per pod per week is £29,229. The total variable costs for the 10 pods over 16 weeks is approximately £4,676,590. The capital costs are £1,210,500.

References

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Stokes EA, Wordsworth S, Staves J, Mundy N, Skelly J, Radford K, Stanworth SJ. Accurate costs of blood transfusion: a microcosting of administering blood products in the United Kingdom National Health Service. Transfusion. 2018 Apr;58(4):846-53.

Appendix

1. Unit cost table

Item	Cost	Reference
Donor recruitment contact	£4	Prioli (2016)
Nurse (Band 6)	£1,725	PSSRU 2019/20
Nurse (Band 5)	£1,388	PSSRU 2019/20
Collection support (Band 3)	£1,020	PSSRU 2019/20
Collection support (Band2)	£932	PSSRU 2019/20
Plasmapheresis machine	£20,000	Welsh Blood reported costs
Plasmapheresis harness	£73	Welsh Blood reported costs
Medical Freezer	£1,050	LEC clinical freezer cost
SARS-COV 2 testing	£40	Welsh Blood reported costs
Plasma delivery to patient (1^{st})	£58	Stokes et al. (2018)
Plasma delivery to patient (2^{nd}+)	£36	Stokes et al. (2018)