**Incremental Peritoneal Dialysis**

**Running Title: Incremental Peritoneal Dialysis**

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**Summary Statements:**

1. Incremental Peritoneal Dialysis (PD) is a strategy by which less than standard ‘full dose’ PD is prescribed in people initiating PD so that the combination of residual renal and peritoneal clearance achieved is sufficient to achieve individualized clearance goals; it is done with the intention of increasing the peritoneal prescription if and when residual renal clearance subsequently declines. (Level of Evidence – Not Applicable as this is a proposed Definition)
2. Incremental PD is not the prescription of less than standard full dose PD because of financial constraints or because a person is on a palliative trajectory or because clearance goals or targets are not considered important (Level of Evidence – Not Applicable as this is a proposed Definition).
3. Incremental PD strategies use less PD solution than standard full dose PD prescription and so cost less (This is a Statement and not a Recommendation. Level of Evidence - A).
4. Incremental PD strategies are less workload for people doing PD and for caregivers assisting them and will be associated with less peritoneal glucose exposure (This is a Statement and not a Recommendation. Level of Evidence – B)
5. Incremental PD strategies are supported by a low-to-moderate quality body of evidence suggesting that they achieve outcomes for people doing PD that are at least as good as those with a full dose PD prescription. The evidence base is predominantly observational and relatively weak but shows no signal of any harm resulting from incremental PD. As a strategy it does not obviate the need for measuring clearances (peritoneal and renal) as these remain key pieces of information supporting the setting and attainment of shared treatment goals. (Level of Evidence – 2C; This is a Practice Point)

**Abstract:**

Incremental peritoneal dialysis (PD) has been variably defined. It involves taking advantage of the residual renal function that is usually present at initiation of dialysis to initially prescribe less onerous lower doses of PD while still achieving individualized clearance goals . We propose that incremental PD be defined as a strategy, rather than a particular regime, in which: (1) less than standard ‘full dose’ PD is initially prescribed, recognising the value of residual renal clearance; (2) peritoneal clearance is initially less than the individualized clearance goal while combined peritoneal plus renal clearance achieves or exceeds that goal clearance; (3) There is a clear intention to increase dose of PD as renal clearance declines and/or symptoms appear.

Incremental PD by its nature lessens the workload of dialysis for those doing PD, reduces cost and exposure of the peritoneal membrane to glucose and may lessen mechanical symptoms. Evidence that incremental PD improves clinical outcomes compared to the use of full dose PD is lacking but one randomized controlled trial, multiple observational studies and a systematic review all suggest that outcomes are at least as good. Given that incremental PD costs less and is inherently less onerous , it is reasonable, pending larger randomized trials, to adopt this strategy.

**Defining Incremental PD:**

Incremental peritoneal dialysis (PD) is discussed frequently but means different things to different practitioners and there is a need to clarify the definition and to distinguish it from other types or strategies of PD prescription.

Incremental PD was first described and defined in the late 1990s in the context of clearance targets for PD. It referred to a strategy of starting PD with a less than ‘full dose’ PD prescription that does not on its own meet the clearance target for the person doing PD but which does so when combined with residual renal function (1,2,3,4). It required subsequent increases in PD clearance when residual renal function declined. This is the definition that this paper will endorse. However, instead of targeting a single clearance value as was the case in the past, the definition used here will take into account the new International Society of Peritoneal Dialysis recommendation that each person doing PD receive high quality, goal directed PD and have an individualized clearance target (5). This may be a particular Kt/V value such as 1.7 per week but is best thought of as the amount of clearance required to keep the person concerned well (5). It needs to be emphasized that this definition of incremental PD has 3 requirements –

1. that the initial PD prescription be less than ‘full dose’;
2. that the peritoneal clearance be less than the individualized clearance goal, but that the total peritoneal plus renal clearance combined does achieve that target (6,7,8,9);
3. that there be an intention to increase the peritoneal clearance if required when residual renal clearance declines. The rationale behind this concept is that people newly started on PD almost always have significant residual renal function and that the clearance provided by a ‘full dose’ PD prescription is therefore not immediately required.

It is emphasized that incremental PD is a strategy and not a prescription. An incremental approach has many potential advantages (10) . It allows the person doing PD to have a less onerous prescription initially, which might allow for less anxiety and stress starting PD, more time to build confidence, and perhaps facilitate better adherence. It also may facilitate greater life participation by those on PD, an endpoint that’s importance has recently been emphasized in surveys of what matters most to people doing PD (11). Incremental PD has added benefits – it typically requires less PD solution and so costs less. The person on PD will be exposed to less glucose and so potentially to less of its adverse local and systemic effects. Lower dwell volumes result in lower intraperitoneal pressure and so may lead to less mechanical side effects, such as back pain, abdominal fullness and heartburn. If less daily PD procedures are involved there may theoretically be a lower risk of peritonitis. There has even been speculation that incremental PD may lead to slower loss of residual renal function as this has been noted with incremental hemodialysis (HD) (12). Incremental PD is also a more person centered approach in that it individualizes PD prescription and attempts to minimize workload and therapy related symptoms.

What is the ‘full dose’ PD prescription that this definition is based on? In continuous ambulatory PD (CAPD), the standard adult prescription in most high income countries since the first decription of this modality has been 4 2-liter dwells daily, 7 days a week (13). Therefore, incremental CAPD prescriptions would include those with less than 4 dwells daily, less than 2 L dwell volumes, less than 7 days a week treatment or some combination of these (Table 1). In some countries or centers, 3 2-liter dwells daily is the standard initial CAPD prescription and so some authors have defined incremental CAPD as 2 or less dwells daily (12,14,15) . However, 3 CAPD dwells daily would not usually achieve typical clearance goals without residual renal function and so this is itself often a form of incremental PD and not a ‘full dose’ prescription. In smaller people where CAPD with 3 dwells daily does achieve typical clearance goals independent of renal function, the prescription is not incremental PD under the above definition. In other words the definition requires both a PD prescription that is less than full dose and a peritoneal clearance that is less than the goal. In such situations 2 dwells, or even one, daily would likely meet the incremental CAPD definition. Other popular incremental CAPD rescriptions include icodextrin dwells, typically of 8 to 12 hours duration, done once or twice daily (15,16).

For automated PD (APD) the ‘full dose’ adult prescription in most high income countries has been at least 8 liters delivered daily by cycler and at least one 2 liter long dwell, all for 7 days a week (17) Incremental APD prescriptions would comprise either APD without a long dwell, less than 8 liters daily delivered by cycler and day dwells, treatment for less than 7 days a week or some combination of these (Table 1). Again some have suggested that incremental APD be defined as cycling 5 or less days weekly (12,14), but this would omit prescriptions such as ‘day dry’ APD which usually do not achieve traditional clearance goals without residual renal function and which therefore can be and often are part of an incremental strategy (10). The particular APD prescription chosen for an incremental APD strategy can be decided though a shared decision making process involving the person on PD and the PD team (18).

Again, the minority of people on PD who achieve typical clearance goals with ‘day dry’ APD alone, independent of renal function, could not be called incremental because they do not meet all requirements of the definition. Such people could drop their prescription to 4 or 5 nights a week ‘day dry’ cycling to meet the incremental PD definition.

In all this discussion of typical incremental PD prescriptions, it should be remembered that, as emphasized already, incremental PD is a strategy and not a prescription. It should again be emphasized that the clearance targets alluded to throughout this paper are individualized clearance goals as proposed in these ISPD Recommendations rather than the previous uniform tragets of Kt/V 1.7 weekly and/or a creatinine clearance of 50 liters weekly, which had a weak evidence base (5).

**Approaches to Incremental Increase of PD Dose:**

The approach to management once residual renal function starts to decline is another area where the practice of incremental PD varies. The original theory, recommended in the 1996 DOQI guidelines on PD, is that residual renal clearance is closely monitored and measured to ensure that the sum of peritoneal and renal clearance meets a clearance target which in PD up to recently has been typically a Kt/V of 1.7 weekly and/or a creatinine clearance of 50 liters weekly (1,6-9). This approach which has been widely used requires regular measurement of both peritoneal and renal clearance with 24 hour dialysate and urine collections, typically starting about 6 weeks after initiation and then every 4 to 6 months, and with upward adjustment of the PD prescription if the target is not being achieved. In time therefore many of the people doing incremental PD gradually switch to standard prescriptions and in some cases to even more intense prescriptions (10,19). Under the now recommended approach of individualized clearance goals for each person on PD, a similar titration approach can be used to achieve the goal clearance (5).

An alternative incremental PD approach is to simply monitor clinical well-being and only move to a standard or more aggressive prescription if there is a clinical indication (20). This approach does not require routine measurement of peritoneal and residual renal clearance, and the rationale is that clinical assessment can detect any important inadequacy of dialysis. A safer approach would include measurement of urine volume which can be done in the clinic or at home by the person on PD. Knowledge of urine volume is helpful not only to assess renal clearance but also to assess potential to control volume status (21). Other approaches include monitoring of blood levels of creatinine, urea and phosphate or even serum beta-2-microglobulin level. All these methods should include routine questions about frequency and volume of urination, and about potential uremic symptoms as an indication to re-measure urinary clearance and/or augment peritoneal clearance.

The authors recommend that the PD prescription in a person following an incremental PD strategy be reviewed in detail by the PD team at least every 3 months and more frequently if the person has new or unexplained symptoms. The review should include a careful assessment of clinical symptoms and signs, with particular attention to urine output, volume status and features suggestive of uremia. It should also include laboratory investigations looking especially for changes in blood levels of urea, creatinine and phosphate that might suggest loss of residual renal function. Ideally it should also include 24 hour urine and dialysate colleactions to allow calculation of Kt/V and/or creatinine clearance and of urine volume and peritoneal ultrafiltration, but it is recognized that these can be onerous for some people doing PD and could be deferred if the person is very stable and clearly well. If there is loss of residual renal function, the PD prescription should be altered in consultation with the person doing PD in order to achieve the individualized clearance goal (18).

The well described Hong Kong approach to PD prescription is a variant of incremental PD (22). Typically, people on PD in Hong Kong initiate dialysis with a 3 x 2 liter CAPD prescription and stay on this unless they develop symptoms suggestive of inadequate clearance, at which stage the prescription is increased. This approach is widely used internationally and can be defined as incremental PD provided there is an intention to increase the prescription if and when residual renal function declines and provided the initial peritoneal clearance delivered by 3 dwells daily does not on its own exceed the clearance goal or target.

Substantial residual renal function may last many years in people on PD (23,24). Often the patient receives a kidney transplant or dies or switches to hemodialysis for a non-clearance related reason before renal function is lost and so a transition from the incremental to the full prescription is never required (10,12,14) . When applied in practice as many as 50% of people being treated in a PD program at any point in time may have sufficient residual clearance to be maintained on an incremental PD prescription so the cumulative impact of terms of relief of workload for these people, glucose exposure and cost may be substantial (10). Of course, PD prescriptions may need to be changed for reasons other than small solute clearance goals. Alterations may be required for volume management or for serum phosphate control and this may modify how incremental PD is practiced.

Recently attention has been given in the literature to incremental hemodialysis (HD) and this is likely to accentuate interest in incremental PD (14, 25). The increasing focus on person centered individualized dialysis prescription is also likely to focus attention on incremental approaches to PD as they give more weight to people’s symptoms and less to treating everyone the same way (26). It is important to inform people doing PD and their families or caregivers in advance about the option and implications of incremental PD (18). They need to hear that their PD prescription will be less onerous initially but they also need to hear that their prescription and residual renal function will need to be monitored regularly and that at some stage they may need to share in a decision to have the PD prescription augmented (18). They need to know that this can sometimes be a challenge in that it may be associated with more procedures or mechanical side effects.

**Other PD Prescription Strategies:**

1. **Low Clearance Non-Incremental PD:**

Some other patterns or types of PD prescription need to be defined and distinguished from incremental PD (Table 2) . An approach in which less than full PD prescriptions are used from initiation of PD with no intention to increase them later, regardless of renal function or uremic symptoms, is quite common, mainly in low and middle income countries or regions (27,28). It is by its nature not an incremental form of PD because there is no intention or capacity to subsequently be ‘incremental’. It is best defined as ‘low clearance PD’. It is most common in settings where those doing PD have to bear some or all of the cost of PD solutions and where it may be used in association with low protein diets (27). However, it may also be used by choice in countries where PD is fully funded and where the purpose is to lessen the load of PD for the person concerned and where the prescriber is unconvinced by the evidence supporting clearance goals or targets. Distinguishing this approach from incremental PD is very important. Indiscriminate use of low clearance PD is often a form of rationing dialysis to reduce costs and, while it may be essential in some lower income settings, it has been associated with adverse outcomes (28).

1. **Palliative PD:**

Another scenario is where standard or augmented prescriptions have being used to achieve clearance goals or targets but where the person on PD is struggling to manage the associated workload or side effects of the therapy and is requesting a less aggressive approach. Such people are frequently elderly or frail or both and may have multiple comorbidities. They are candidates for discussions about discontinuing dialysis but they or their families may decide they are not ready to make that choice. A decision is then made to pay less attention to clearance levels and relatively more to symptom management and quality of life. The PD prescription is therefore reduced to make it less onerous. In CAPD, dwells may be decreased in number or in volume. In APD, day dwells may be reduced in number or volume or discontinued. In both types of PD, days off therapy may be proposed.

This process is of course the opposite of incremental PD, which does still focus on clearance goals, and so can be termed ‘decremental’ PD. It is more often referred to as ‘palliative PD’ (29) . In a sense it is a form of goal-directed PD with no overt clearance target other than avoidance of severe symptom burden. For some prescribers, palliative PD may raise ethical concerns about systematic under-dialysis but the people on PD in these situations are typically approaching the end of their lives and palliative care principles apply. Others, in countries such as the United States, may be concerned about funding penalties from regulatory agencies for not achieving clearance targets but typically these policies allow for a percentage of those on dialysis not to achieve targets before such penalties are applied. This approach has not so far been reported widely in the PD literature (29) .

1. **Early Initiation of Peritoneal Dialysis:**

It should be noted that the original descriptions of incremental PD occurred at a time when early initiation of dialysis was being advocated (1-4). The relevance of incremental prescriptions is greatest when people with a lot of residual renal function initiate dialysis, because in such situations very low dose PD prescriptions, when added to residual renal clearance, can meet clearance goals . The practice of early dialysis start was largely discredited by the publication of the IDEAL randomized trial in 2010 and so incremental dialysis is no longer seen as a strategy to facilitate early dialysis initiation (30) . However there is still lots of room to use incremental dialysis with contemporary conventional timing of dialysis start (10) .

1. **Person Centered Peritoneal Dialysis:**

Incremental PD can be considered as an example of person centered care principles applied to PD prescription. The approach by its nature promotes individualization of PD prescription and a move away from a ‘one size fits all’ approach. This topic is reviewed elsewhere in these ‘Guidelines’ (18).

1. **Urgent Start Peritoneal Dialysis:**

A lot of attention has recently been given to urgent start or early start PD. These terms are used to describe the practice of starting PD within 14 days and sometimes within as few as 3 days of catheter insertion because of symptoms or fluid overload or refractory biochemical findings (31). In these situations the risk of peritoneal leaks is higher than normal and so an initial prescription with lower and exclusively supine dwell volumes is attractive. People initiating PD in this context , by their nature, tend to have less residual function than elective PD starts. Initially clearance goals are not a priority and the combined peritoneal plus renal clearance often does not achieve a typical target. Urgent start PD is therefore by definition not incremental PD . However, once the abdominal wall has had time to heal after catheter insertion a person doing urgent start PD may of course follow an incremental PD strategy.

**What is the Evidence?**

There is one randomized trial comparing an incremental CAPD strategy with conventional CAPD. It was done at a single center in China and randomized 139 people intiating CAPD to 3 versus 4 dwells daily and followed them for 2 years (32). This study did not describe the strategy used in the 3 dwell daily group as incremental. However, it was incremental in that the intial prescription was not ‘full dose’ and in that there was an intention to increase the PD dose if total Kt/V dropped below 1.7 weekly and there were uremic symptoms. Indeed 12 of the 70 people concerned had a fourth dwell added during the 2 year follow up. The 4 dwell daily group was not incremental in that it received full dose CAPD rom the start. The study showed no difference in residual renal function, which declined at the same rate in both groups. Other outcomes such as mortality and technique survival did not differ but the study was underpowered to evaluate these. It did show a borderline significantly longer time to first peritonitis in the incremental group. Ultrafiltration volume was significantly greater in the conventional group but there was no difference in net fluid removal as defined by urine volume plus ultrafiltration combined.

There are observational studies that attempt to compare outcomes with incremental PD versus those with conventional PD but they are small and, without randomization, they are susceptible to confounding by indication. One study compares outcomes in 29 people treated with incremental CAPD versus 76 in the same Italian center who received conventional PD (12). Residual renal function was retained to a significantly greater degree after 6 months in the incremental CAPD group and so was the likelihood of staying hospitalization free. Incremental CAPD was associated with a lower peritonitis rate and a lower mortality rate but neither observation was statistically significant (12). A Canadian study compared mortality in one PD program, which used incremental APD routinely, with mortality in all PD programs across the country and found no difference (10). Multiple other uncontrolled studies, including descriptions of outcomes in Hong Kong with routine 3 2-liter dwells daily report good outcomes with incremental PD (15,16, 33-36). In all this literature the nature of incremental PD varies with most using incremental CAPD, but others using incremental APD.

Garofalo et al have recently published a systematic review of all studies comparing incremental and conventional dialysis – both HD and PD (14). Only 7 of the 22 eligible studies involved people on PD and all were small and most looked at very few outcomes. The review overall found that incremental dialysis was associated with significantly slower decline in residual renal function compared to conventional dialysis. On average the incremental strategy delayed full dose dialysis start by 12 months. Both these findings were driven by the incremental HD studies predominantly. Overall, the systematic review showed no evidence of any harmful effect of incremental HD or PD (14).

Despite the paucity of randomized trials, there is therefore a modest body of evidence to support incremental PD. Observational data, the systematic review and one randomized controlled trial show no evidence of any adverse effect of incremental PD (10,12,14,15,16,33-36 ). Some PD studies, but not the randomized trial, suggest a benefit in delaying loss of residual kidney function (12). There is, however, no reported evidence of an improvement in mortality or technique survival.

It should be emphasized that the incremental approach described in these studies achieves total clearances that are by definition consistent with previous national and international guidelines (6-9). The same incremental strategy can be used to achieve the now recommended strategy of individualized clearance goals (5). It should also be noted that neither previous clearance targets nor full dose PD prescription are well validated by high level clinical evidence. Observational data and one well powered, high quality, randomized controlled trial show no association between peritoneal clearance and mortality within the therapeutic range (37,38) . The literature clearly shows a consistent association between better residual function and survival in people on PD , but there is no evidence that those with residual renal function achieve better survival with the prescription of larger versus smaller amounts of peritoneal clearance (37,38). Furthermore, the conventional ‘full dose’ approach to PD prescription is more onerous for people on PD and more costly. The case for incremental PD is also somewhat supported by the HD literature which suggests, but does not prove, better outcomes with incremental compared to conventional HD (14).

All this suggests that incremental PD is a good strategy but it must be stated that it cannot be completely excluded that full dose PD could lead to superior outcomes compared to lower PD doses in people with substantial residual renal function. It would therefore be ideal if large randomized trials comparing incremental and full dose PD strategies and powered to detect differences in survival were carried out. In the meantime, and in the absence of definitive evidence as to whether incremental or full dose dialysis prescription is best, it seems reasonable to advocate an incremental approach.

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**Table One**

Typical Incremental PD Prescriptions

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| --- | --- |
| **CAPD** | **APD** |
| 3 x 2 L daily | APD with no day dwell |
| 2 x 2L daily (1 or both Icodextrin) | APD 5 nights a week |
| 1 x 2L Icodextrin long dwell daily | APD 3 nights a week |
| 4 x 1.5 L daily | APD with 1.5 L dwell volumes |
| CAPD 4 to 6 days a week | APD for 6hours each night |