Original Article

Peri-operative Replacement of Exogenous Steroids (PREdS): a national audit of current peri-operative prescribing for patients taking therapeutic steroids

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Summary

Introduction

Approximately 1% of the UK population take oral corticosteroids for ≥ 28 days each year for broadly two reasons: deficiency in corticosteroid requiring replacement; or therapeutic corticosteroid for inflammatory conditions. Acute deficiency can occur at times of physiological stress (i.e. surgery), potentially leading to major complications. The Association of Anaesthetists' 2020 consensus guideline provide detailed advice for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency. This national audit aimed to assess compliance with this guideline.

Methods

Data were collected from 59 Trusts over 14 consecutive days for all eligible patients undergoing procedures under the care of an anaesthetist. Patients who were prescribed ≥ 5 mg oral prednisolone equivalents pre-operatively, in whom supplementary corticosteroid would be indicated, were compared with those prescribed < 5 mg oral prednisolone equivalents.

Results

Operations for 21,731 patients were audited: 277 (1.3%) patients were taking therapeutic corticosteroids. Detailed peri-operative data were collected for all patients receiving therapeutic corticosteroids: 201/277 (73%) were ASA physical status ≥ 3; 184/277 (66%) underwent elective procedures; and 252/277 (91%) were prescribed prednisolone pre-operatively of whom 219/277 (79%) were prescribed ≥ 5 mg oral prednisolone equivalents. In the patients who were prescribed ≥ 5 mg oral prednisolone equivalents, 186/219 (85%) received pre-operative glucocorticoid supplementation and 97/219 (42%) received it postoperatively; however, only 67/219 (31%) and 43/219 (20%) respectively received glucocorticoid supplementation according to the guidelines. Overall, peri-operative prescribing was compliant in 19/219 (9%) patients. A similar proportion, 30/219 (14%), received no supplementation. In the patients taking prednisolone < 5 mg oral prednisolone equivalents pre-operatively, 28/58 (48%) received inappropriate supplementation.

Conclusions

Despite 125/277 (45%) of anaesthetists reporting Association of Anaesthetists' guidelines use, compliance remained low with adherence in only 27/126 (22%) patients. Further research is required to identify the correct peri-operative strategy for patients taking therapeutic corticosteroids.

Introduction

Corticosteroid therapy is common. Initial scoping work for this project found that around 1% of the UK population receive oral corticosteroids for ≥ 28 days each year, with a total of approximately 8 million prescriptions for oral corticosteroids in 2020 [1]. Although individual prescriptions are inexpensive, community corticosteroid prescriptions in England were the third largest expenditure cumulatively in 2020 [1]. Patients prescribed corticosteroids comprise those who are either: absolutely deficient in corticosteroids and who require replacement (e.g. primary pituitary or adrenal insufficiency); or taking therapeutic (exogenous) corticosteroids for a range of inflammatory conditions (e.g. asthma, autoimmune diseases).

Physiological stressors, such as surgery, induce cortisol release as part of the 'stress response'. There is no question that patients with absolute corticosteroid deficiency due to adrenal or pituitary disease (termed primary and secondary adrenal insufficiency, respectively) must be given additional supplementary corticosteroids during the peri-operative period. Inadequate supplementation risks complications such as hypoglycaemia, metabolic derangements or even fatal circulatory failure.

Adrenal insufficiency is a recognised consequence of administering long-term therapeutic corticosteroids (termed tertiary adrenal insufficiency). However, the dose and duration at which clinically significant adrenal suppression occurs (such that patients are at high peri-operatively risk) is not known. Although there is growing evidence that the hypothalamic-pituitary-adrenal axis may be downregulated at doses as low as 2.5 mg of daily oral prednisolone, the response to different doses, durations and routes of administration are highly heterogenous [2,3]. In addition, a number of clinical effectiveness trials have failed to show a benefit in giving prophylactic supplementary corticosteroids in this cohort [4]. Biochemical identification of reduced hypothalamic-pituitary-adrenal activity is relatively straightforward, but this is not done routinely as part of pre-operative assessment in the UK. Guidance is therefore very broad to ensure all patients at risk are treated, but with the potential to overtreat those who are not. We have previously shown that supplementation can result in 10 times the normal daily production of cortisol on the day of major surgery [5]. This may be undesirable considering the potential risks of excess corticosteroid, such as poor wound healing; infection; and hyperglycaemia.

This audit was focused on those patients taking therapeutic corticosteroids, who form by far the largest group. These patients may present more frequently than the general population for surgery with

indications related to their diagnosis (e.g. bowel resection for inflammatory bowel disease, joint replacement for inflammatory arthritis), or the consequences of corticosteroid use (e.g. bone fracture due to demineralisation, accelerated coronary artery disease etc.). There are currently no data quantifying any increased risk of surgery in this group.

In 2012, the Association of Anaesthetists, Society for Endocrinology UK, Royal College of Anaesthetists (RCoA) and Royal College of Physicians received a *Report to Prevent Future Deaths* from HM Coroner expressing concern about care standards for patients with potential treatment-induced adrenal insufficiency undergoing surgery. This led to the first national consensus guideline generated by the joint Royal Colleges [6]. Literature reviews to inform this guideline highlighted a paucity of evidence for patients taking therapeutic corticosteroids, specifically about the dose and duration of treatment that increases the risk of adrenal suppression sufficiently to warrant supplementation around the time of surgery (given that supplementation has other risks). Evidence is also lacking for what supplementary regimen is appropriate. This challenge has been echoed in the USA and by the Cochrane Collaboration [7,8]. Published studies have been mechanistic and not powered for robust, clinical endpoints [9,10].

To gain further information about potential supplementation regimens and to audit compliance with the consensus guideline, we performed an RCoA-sponsored survey of > 1200 UK anaesthetists shortly after publication of the guideline, which showed no consensus among clinicians about which patients should be supplemented and at what doses, frequencies and durations [11].

The Association of Anaesthetists' consensus guideline states that adults taking therapeutic oral prednisolone equivalents ≥ 5mg for ≥ 28 days, in the period immediately preceding surgery should receive glucocorticoid supplementation [6] (Table 1). The goal of this audit was to assess the number of patients treated in compliance with the guideline.

Methods

This prospective, multi-centre audit was conducted across the UK with the assistance of anaesthesia Trainee Research Networks.

All patients in the care of an anaesthetist (including procedures performed under general anaesthesia, regional anaesthesia, and/or sedation with monitoring), aged ≥ 18 y and presenting for elective, urgent

or emergency procedures performed by any medical or surgical specialty were included in the audit. Detailed peri-operative data relevant to the audit were collected only in those patients prescribed ongoing corticosteroid treatment pre-operatively. Data fields included: dose and drug formulation; diagnosis; planned procedure; and details around peri-operative corticosteroid prescribing. Operative severity was cross-referenced with the National Institute for Health and Care Excellence guideline to assess appropriateness of the supplementation regimen [12]. Patients who were not receiving pre-operative oral corticosteroids were logged to calculate an overall denominator, indicating whether the population was consistent with the Clinical Practice Research Datalink prescribing data. To avoid clinician bias, only the first procedure per patient entered into the database was analysed, with subsequent duplicates removed.

The audit was co-ordinated by anaesthetic trainees who are members of the Severn Trainee Anaesthetic Research Collaborative. Trainee Research Networks were recruited via email, and information disseminated as a written audit protocol with an additional series of webinars. In participating Trusts, data were collected daily over a 14-day consecutive period. The specific window for data collection was selected by local investigators to enable them to maximise data completion, avoiding public holidays or periods of maximal bed pressures that may impact on elective scheduling. Patients were identified by the local team at each site, using local systems for operating theatre list scheduling.

The NHS Health Research Authority tool confirmed this audit was not defined as research, and therefore did not require ethics committee approval. Approval from the Caldicott Guardian approval at the lead site, University Hospitals Bristol and Weston and audit registration with the clinical audit department of each participating hospital was required before data collection. Data from NHS Trusts in England were handled in accordance with the NHS England National Data Opt-Out introduced in May 2018. Data were captured contemporaneously by either the clinician delivering care or nominated local investigators using paper case report forms (an example is available in online Supporting Information Appendix S2). Patient identifiers were then checked against the NHS spine for National Data Opt-Out status, and data for eligible patients only were entered into the University Hospitals Bristol and Weston REDCap (Research Electronic Data Capture) digital database [13,14]. The REDCap data capture tools were hosted on a secure server within the Health and Social Care Network at University Hospitals Bristol and Weston and were compliant with the standards for collection of sensitive data. University Hospitals Bristol and

Weston is registered under the Data Protection Act 2018 with the Information Commissioner's Office. An additional data sharing agreement was available where required.

We performed descriptive analyses on the data to describe numbers of patients taking regular corticosteroids presenting for procedures, those receiving oral prednisolone equivalents ≥ 5 mg or < 5 mg and the proportion that received peri-operative steroid prescribing in line with the latest guideline [6]. Descriptive analyses were conducted using R statistical software (version R 4.2.1, R Foundation, Vienna, Austria) and guideline compliance using Microsoft Excel (version 16.77.1, Microsoft Corporation, Redmond, WA, USA).

Results

After application of National Data Opt-Out status at source, data from 21,731 patients from 59 NHS Trusts were submitted. We excluded 480 duplicate patient entries (Fig.1). Twenty-four Trusts submitted data for the total number of patient care episodes during the study window (September 2022 to January 2023); the capture rate was calculated in these Trusts at 9120/14,102 (65%). Of the 21,731 records, 320 were for patients taking any corticosteroid. After exclusions (Fig. 1), 277/21,319 (1%) patients on maintenance therapeutic corticosteroids were included for further analysis, of which 219 (79%) were prescribed ≥ 5 mg oral prednisolone equivalents preoperatively. Table 2 summarises the key features of this cohort. The majority of patients underwent elective procedures (184 (66%)) and 201 (73%) were classified as ASA physical status ≥ 3.

The supervising anaesthetist was aware of a guideline for peri-operative corticosteroid management in 186/277 (67%) cases. Where a guideline was known, 125 (67%) of anaesthetists referenced the Association of Anaesthetists' guideline, 42 (23%) local NHS Trust guidelines and the remainder referenced other sources. A smaller proportion of anaesthetists recorded that they had used the guideline in patients who took ≥ 5 mg oral prednisolone equivalents compared with those taking < 5 mg (94/219 (43%) vs. 31/58 (53%), respectively). Awareness of guidelines and pre-, postoperative and combined peri-operative guideline compliance is shown in Table 3.

In total, 187/219 (85%) patients who were taking ≥ 5 mg oral prednisolone equivalents received additional corticosteroid peri-operatively (any time on the day of surgery before knife to skin). The documented indication for administering corticosteroids was 'replacement or supplementation' in 152

(81%) patients; 40 (26%) of these received a second corticosteroid for an additional indication, predominantly for postoperative nausea and vomiting (PONV) (37/40 (93%)). The remaining 35 (19%) patients were administered corticosteroids for an indication other than supplementation: PONV management (33 (94%)); and the remainder were treatment of neurological malignancy and not recorded respectively. In the 187 patients who received glucocorticoid supplementation, 79 (42%) were administered hydrocortisone; 65 (35%) dexamethasone; and 8 (4%) prednisolone or methylprednisolone. Of the 79 patients administered hydrocortisone, 62 (78%) received the correct bolus dose, but only 8 (10%) received both a correct bolus and follow-up infusion. Dexamethasone at an appropriate dose was administered to 59/65 (91%) patients. For those patients administered corticosteroid for another indication, all 35 received dexamethasone. In total, therefore, only 67/219 (31%) of eligible patients received pre-operative corticosteroid supplementation consistent with the Association of Anaesthetists' guideline. In the 152 patients whose treatment was non-compliant with the Association of Anaesthetists' guideline the main reasons included: lack of intra-operative infusion (60 (39%)); incorrect corticosteroid drug or dose (33 (22%)); administration for an indication other than supplementation (35 (23%)); glucocorticoid omitted entirely (30 (20%)); and multiple errors (8 (5%)).

In the 58 patients taking < 5 mg oral prednisolone equivalents, 35 (60%) were administered additional peri-operative corticosteroid: replacement or supplementation (27 (77%)); PONV management (7 (20%)); and no indication documented (1 (3%)). Corticosteroid selection for replacement was almost equally split between hydrocortisone (13/27) and dexamethasone (14/27), with one patient receiving both, and the final patient administered prednisolone only. In total, therefore, 27/58 (47%) patients taking < 5 mg oral prednisolone equivalents received inappropriate pre-operative supplementary corticosteroids.

Postoperatively, in patients taking ≥ 5 mg prednisolone equivalents, 97/219 (44%) were prescribed supplementary corticosteroids: 37 (38%) received hydrocortisone; 51 (53%) received prednisolone; and 15 (15%) received dexamethasone (some patients received more than one corticosteroid). In total, 43/219 (20%) of the patients were prescribed postoperative corticosteroid supplementation that was in accordance with the Association of Anaesthetists' guideline. In the 176 patients whose postoperative treatment was non-compliant with the Association of Anaesthetists' guideline the main deviations included: absence of supplementation (122 (69%)); incorrect drug and/or dose (30 (17%)); or supplementing for too short a duration (24 (13%)). For those patients taking < 5 mg oral prednisolone

equivalents, 13/58 (22%) were prescribed supplementary postoperative corticosteroid. None of these patients received glucocorticoid supplementation in compliance with the Association of Anaesthetists' guideline.

Compliance was also calculated for those patients who received appropriate prescribing in the peri-operative period as whole. Of those patients taking ≥ 5 mg oral prednisolone equivalents 20/219 (9%) were compliant, while 30/58 (52%) of patients taking < 5 mg oral prednisolone equivalents were compliant. There were 30/219 (14%) of patients taking ≥ 5 mg oral prednisolone equivalents, who should have received peri-operative supplementation but received no corticosteroids from the responsible anaesthetist.

Sub-group analysis for guideline compliance where the responsible anaesthetist was aware of the Association of Anaesthetists' guideline is shown in Table 4. For patients taking ≥ 5 mg oral prednisolone equivalents, 86/94 (92%) were administered supplementary pre-operative corticosteroid, with the indication documented in 80/86 (93%) as replacement or supplementation. Similar proportions received dexamethasone or hydrocortisone as a bolus (36/86 (42%) and 40/86 (47%), respectively). Of the 40 patients administered hydrocortisone, 30 (75%) received the correct bolus dose, but only 7 (18%) received both a correct bolus and follow-up infusion. In total, 40/94 (43%) patients were treated pre-operatively in accordance with the Association of Anaesthetists' guideline where the responsible anaesthetist declared awareness. The main deviations from the guideline in the 54 patients whose treatment was non-compliant included: a lack of intra-operative infusion (26 (48%)); incorrect corticosteroid drug and/or dose (15 (28%)); glucocorticoid administered for an indication other than supplementation (6 (11%)); multiple errors (4 (7%)); or omitted entirely (8 (15%)).

Postoperatively, 56/94 (60%) patients were prescribed additional corticosteroids: in 24 (43%) patients hydrocortisone was administered, but only 5 (9%) were dosed according to the guideline. Prednisolone was prescribed to 33 (59%) patients, but only 23 (41%) of those prescriptions were in accordance with the guideline. Among the cases where anaesthetists declared awareness of the guideline, only 28/94 (30%) administered postoperative corticosteroids at the recommended dose. The main deviations from the guideline in the 66 patients whose postoperative treatment was non-compliant with the guideline were: incorrect corticosteroid drug and/or dose (12 (18%)); supplementing for too short a duration (15 (23%)); or omitted entirely (39 (59%)). Where Association of Anaesthetists' guideline usage was

reported, 8/94 (9%) patients taking ≥ 5 mg oral prednisolone equivalents, who should be supplemented peri-operatively, received no corticosteroids.

For those patients taking < 5 mg oral prednisolone equivalents, 22/31 (71%) were also administered additional pre-operative corticosteroid, with the indication documented in 19/22 (86%) as 'replacement or supplementation'. Corticosteroid selection was almost equally split between hydrocortisone (9/19) and dexamethasone (10/19), with one patient receiving both, and the final patient administered prednisolone only. None of these regimens were compliant with the Association of Anaesthetists' guideline. Postoperatively, 9/32 (28%) patients were prescribed additional corticosteroid. These patients had also received pre-operative corticosteroid and remained non-compliant.

In total, peri-operative prescribing was correct for 16/94 (17%) patients taking ≥ 5 mg oral prednisolone equivalents, and 11/31 (35%) for those taking < 5 mg oral prednisolone equivalents. To examine compliance with recommendations from the USA, we also applied a threshold of oral prednisolone 20 mg equivalents per day. Using this threshold, only 5/36 (14%) of patients were treated appropriately.

The study was designed to capture data on patients taking therapeutic corticosteroids rather than replacement corticosteroids for intrinsic deficiency. Despite this, 28/320 (1%) of observations were for patients with primary or secondary adrenal insufficiency normally taking replacement. Pre-operative supplementation was received by 27/28 patients, and 19/28 received supplementation postoperatively. The attending anaesthetist was aware of a guideline in 18/28 cases and this was the Association of Anaesthetists' guideline in 12/28 cases.

Discussion

The audit showed that around 1% of patients presenting for medical or surgical procedures are taking regular therapeutic corticosteroids. These patients were considered by the attending anaesthetist to be substantially comorbid, with 73% ASA physical status ≥ 3, compared with only 27% in the general UK population from the 7th National Audit Project of the RCoA [16].

Less than 1 in 10 patients taking ≥ 5 mg of oral prednisolone equivalents pre-operatively were administered peri-operative corticosteroid supplementation that complied with the Association of Anaesthetists guideline, and a greater proportion of 1 in 8 received no supplementation at all. Despite

two-thirds of anaesthetists stating awareness of any and half who knew of the most recent consensus guideline, only 1 in 5 of all patients were treated in accordance with this guidance. Concerningly, failure to treat was higher in those who needed supplementation most, with only 1 in 10 patients taking ≥ 5 mg oral prednisolone equivalents treated appropriately, although this improved to 1 in 5 where Association of Anaesthetists' guidance was known. The main failures in compliance were the lack of intra-operative hydrocortisone infusion, failure to correctly increase postoperative dose/duration or the lack of peri-operative adjustments at all.

Previous work from our group had captured UK anaesthetic practice using a survey; this study was designed to capture the 'say-do' gap [11]. The heterogeneity in practice seen in the data from this study agrees with our previous survey work. It remains true that clinicians appear to have a variable threshold for prescribing supplementary corticosteroids and do so at a lower dose and for a shorter duration than the guideline recommend. This remains true even where the attending anaesthetist declared they had knowledge of the Association of Anaesthetists' guideline. It is important that we recognise that in a small number of patients, supplementation was administered in excess of guideline, confirmed by free-text entries suggesting this was appropriate to the clinical situation, for example, in transplant surgery or due to local specialist recommendations.

This audit demonstrated an overall failure to supplement patients in accordance with the Association of Anaesthetists' guideline and significant heterogeneity in practice. There was both a lack of guideline awareness and a failure of clinicians to conform even when they report being informed of guidance. In part, this could be due to the nuances within the current guideline which, rather than a 'one-size-fits-most' approach, gives detailed regimens for many scenarios [6]. This makes the guideline difficult to remember and follow. Further challenges include advocating the use of hydrocortisone infusions (rather than repeat boluses) which increase the postoperative resource burden by potentially altering the location in which patient care is delivered, requiring additional equipment (e.g. syringe drivers) and inhibiting early patient mobilisation. The guideline also had limited implementation or dissemination work, perhaps due to their release during the early part of the COVID-19 pandemic, which may have negatively impacted clinician awareness.

While there is lack of compliance with guideline, the evidence on which they are based is sparse and controversial. This conflicting literature has subsequently created varied advice not only at local

institutions, but also between national bodies in different countries. Although there are many mechanistic and studies of efficacy, there are few (if any) studies of the effectiveness of corticosteroid replacement [17]. There are no formal guidelines for corticosteroid replacement in North America or in the Asia-Pacific region. In 2017, Liu et al. published recommendations for treatment in the USA and acknowledged the lack of grade A or B evidence to support supplementation [7]. The threshold for treatment within this guideline is set at prednisolone ≥ 20 mg per day for > 3 weeks, four times the daily threshold of the comparative UK guideline [7]. In addition, the guideline recommends formal assessment of the hypothalamic-pituitary-adrenal axis with a tetracosactrin test for moderate-risk patients (where time allows). Withholding supplementation in otherwise healthy patients, with a low threshold for rescue therapy in cases of peri-operative refractive hypotension is also endorsed [7]. Liu et al. conclude that this pragmatic approach is recommended until such a time that the evidence base is sufficient to determine an agreed standard of care. Our data suggest that guideline compliance would still be poor if a more liberal threshold of oral prednisolone 20 mg equivalents per day (such as that in the USA) is applied. This may suggest that practitioners do not follow the guidance because they either are unaware of it or think it irrelevant, rather than perceiving that low-dose corticosteroids do not require supplementation.

Literature reviews in Korea, Europe and the USA published since Liu et al. [7] and the UK consensus guidelines [6] have all come to similar conclusions [4,18,19]. Seo (Korea) identifies that the UK consensus guideline has significant differences to those published by Liu et al. [7], with the clinical trials on which they are based comprising low level evidence and inadequate statistical power [18]. Laugesen et al. (Denmark) concluded that current evidence shows significant variation in identifying which patients, and at which dose of corticosteroid, confers risk of adrenal suppression [19]. Chen Cardenas et al. suggest guidance available is inconsistent and current research suggests that continuing pre-operative corticosteroids peri-operatively is probably sufficient, with parenteral administration only for those patients who are unable to continue [4]. They cite 15 further literature reviews dating from 1975 to the present day with similar conclusions; lower doses and a shorter duration of peri-operative corticosteroid treatment are effective in maintaining homeostasis [4]; this is a clear juxtaposition to UK guideline. It is quite feasible that these differences influence UK clinician practice, reinforcing the lack of consensus within the wider medical community [20].

The Cochrane group has also recently published its intention to perform a meta-analysis of existing evidence, acknowledging that previously published and now withdrawn Cochrane reviews have concluded there is no evidence for supplementary corticosteroids in those taking therapeutic corticosteroids [21]. Considering all these publications there is a consistent message; 'further research is required'. This, in practice, means adequately powered, prospective randomised controlled trials designed around clinical outcomes. While these studies may be unattractive to funders (adequately powered studies are likely to be large, costly, and challenging to recruit for), they would answer an important clinical question.

In the absence of this evidence, policymakers should design guidelines that are pragmatic and simple to remember and apply. Corticosteroid supplementation may only be a single component in a multifaceted care episode, but consistency in care delivery is known to be important. Public Health England's Atlas of Variation analyses discrepancies contributing to worse outcomes, hoping that identification can lead to targeted improvements in patient outcomes [22].

Specific strengths of our study are the large number of records captured, prospective nature of data collection, inclusion of elective and emergency surgery and wide geographical capture from 59 NHS Trusts across the UK, allowing a good insight into real-world clinical practice. The proportion of patients presenting for procedures taking therapeutic corticosteroids is in line with previous work from our group using Clinical Practice Research Datalink data, suggesting appropriate data capture. Data on total numbers of patients were available for a subset of these NHS Trusts, giving an estimated capture rate of total patient procedures of 65%, further supporting our study as a representative sample of UK practice. A limitation of this audit is that it was designed to assess capture rate to allow conclusions relating to the proportion of all patients receiving corticosteroids. These data were only available from 24 sites. Participating clinicians reported that these data were often difficult to ascertain, particularly in locations where operating lists are not digitised. It is possible therefore that our 65% capture rate creates a skewed dataset, with 1.3% of patients taking corticosteroids being artificially over- or underreported. We were also unable to collect the identities of individual anaesthetists whose patients are included; this means that we cannot know, for example, whether non-compliance is confined to a minority of anaesthetists who anaesthetised the majority of patients, although this is unlikely considering the scale of our audit. We did not study patients receiving long-term corticosteroids via other routes. The 2020 guideline inclusion criteria included inhaled, intranasal, intra-articular or topical corticosteroids,

alongside oral, that equate to ≥ 5 mg oral prednisolone equivalents. The variability in systemic absorption, compliance with treatment, the difficulties in obtaining an accurate history and anecdotal evidence that they are often overlooked by the attending anaesthetist, all factored in our decision to exclude them. Little information was collected about the attending clinician, which may have strengthened our conclusions; do trends in supplementation exist based on specific clinician's practice, or did valid clinical reasoning exist to explain deviation from guideline?

Additionally, this audit was insufficient in scope to assess postoperative complication rates and limited in its ability to make recommendations for immediate change. The data are suggestive of inherent failure to apply the guidance, with particularly poor postoperative compliance. Both the number of patients treated when not indicated and the number with no treatment when at risk, would suggest a degree of confusion. Our recommendation would be to revise the guideline with the engagement of all stakeholders utilising the principles of co-design, with an increased focus on simplicity and pragmatism.

In conclusion, despite the presence of the UK consensus guideline, our audit shows there is little application of it. The published guideline acknowledges that there is no conclusive evidence in the form of randomised trials on which to base recommendations, and this is repeated by other reviews and guidelines. This, the impact of the COVID-19 pandemic on dissemination and implementation of the guideline and resource constraints in NHS hospitals may all contribute to its sparse use.

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Anonymized data are available upon reasonable request for each patient episode, including demographics, preoperative corticosteroid prescribed, operation, perioperative corticosteroid administration, and guideline usage.

Code Availability

Code for analysis of the dataset using R statistical software are also available upon reasonable request.

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Table 1: Summary of Association of Anaesthetists' recommended supplementation regimen for adult patients receiving potentially adrenosuppressive doses of corticosteroid (≥ 5 mg oral prednisolone equivalents for ≥ 28 days) [7].

	Intra-operative steroid replacement	**Postoperative steroid replacement**
Major surgery	Intravenous hydrocortisone 100 mg at induction, immediately followed by 200mg.24 h^{-1} infusion OR intravenous dexamethasone 6–8 mg	If nil by mouth: intravenous hydrocortisone 200mg.24 h^{-1} OR 50 mg 6 hourly intramuscularly Uncomplicated recovery: resume pre-operative dose Complicated recovery: double oral dose for up to 7 days
Body surface and intermediate surgery	Intravenous hydrocortisone 100 mg at induction, immediately followed by 200mg.24 h^{-1} infusion OR Intravenous dexamethasone 6-8 mg	Uncomplicated recovery: double pre-operative dose for 48 h only
Bowel procedures requiring laxatives/enema	Continue pre-operative dose. Equivalent intravenous dose if prolonged nil by mouth. Treat as per primary adrenal sufficiency if concerned about hypothalamic-pituitary-adrenal axis function, and risk of adrenal insufficiency	
Labour and vaginal delivery	Intravenous hydrocortisone 100 mg at onset of labour, immediately followed by 200 mg.24 h^{-1} infusion OR intramuscular hydrocortisone 100mg, followed by 50 mg 6 hourly	
Caesarean section	See major surgery	

Table 2: Summary of patient characteristics for those receiving pre-operative oral prednisolone equivalent (OPE) [3]. Values are number (proportion).

	≥ 5 mg OPE **n = 219**	**< 5 mg OPE** **n = 58**
Elective	145 (66%)	39 (67%)
ASA physical status		
1	1 (<1%)	0
2	59 (27%)	16 (28%)
3	134 (61%)	35 (60%)
4	25 (11%)	7 (12%)
Operative severity		
Major	128 (59%)	35 (60%)
Intermediate	90 (41%)	23 (40%)
Labour	1 (<1%)	0
Type of corticosteroid treatment		
Prednisolone	199 (92%)	53 (91%)
Hydrocortisone	3 (1%)	2 (3%)
Methylprednisolone	0	0
Dexamethasone	14 (6%)	3 (5%)
Budesonide	3 (1%)	0
Reason for corticosteroid treatment		
Musculoskeletal disorder	69 (32%)	27 (47%)
Solid organ transplant	40 (18%)	2 (3%)
Respiratory Disorders	25 (11%)	4 (7%)
Malignancy	21 (10%)	5 (9%)
Vasculitis	18 (8%)	8 (14%)
Gastrointestinal	16 (7%)	3 (5%)
Neurological	9 (4%)	0
Dermatological	7 (3%)	4 (7%)

Inflammatory eye disease	4 (2%)	1 (2%)
Renal	3 (1%)	0
Haematological	2 (1%)	0
Appetite stimulant	1 (<1%)	0
Unknown	3 (1%)	4 (7%)

Table 3: Summary of awareness of the Association of Anaesthetists' guideline on the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency, and pre-, post- and peri-operative corticosteroid prescribing and compliance with the guideline in patients taking pre-operative oral prednisolone equivalent (OPE) [3]. Values are number (proportion).

	≥ 5 mg OPE n = 219	**< 5 mg OPE n = 58**
Awareness of peri-operative steroid guidelines		
- Any type of guideline	148 (68%)	38 (66%)
- Association of Anaesthetists guideline	94 (43%)	31 (53%)
Peri-operative		
- Corticosteroid administration	187 (85%)	35 (60%
- Compliant with Association of Anaesthetists guideline	67 (31%)	30 (52%)*
Postoperative		
- Corticosteroid administration	97 (44%)	13 (22%)
- Compliant with Association of Anaesthetists guidelines	41 (19%)	45 (78%)
Peri- and postoperative		
- Corticosteroid administration	95 (43%)	13 (22%)
- Compliant with Association of Anaesthetists guideline	20 (9%)	30 (52%)
Indication for peri-operative corticosteroid		
Supplementation	152 (69%)	27 (47%)
Other*	35 (16%)	7 (12%)
Unknown	0	1 (2%)

*Some of those administered corticosteroids were for other indications, e.g. postoperative nausea and vomiting (PONV) prophylaxis; these instances have been classified as guideline compliant.

Table 4: Summary of peri-operative corticosteroid prescribing and compliance with the Association of Anaesthetists' guideline (where the responsible clinician was aware of the guideline) on the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency, in patients receiving pre-operative oral prednisolone equivalent (OPE) [3]. Values are number (proportion).

	≥ 5 mg OPE n = 94	**< 5 mg OPE n = 31**
Peri-operative		
- C**orticosteroid** administration	86 (92%)	22 (71%)
- **Compliant with Association of Anaesthetists guideline**	40 (43%)	9 (29%)*
Postoperative		
- C**orticosteroid administration**	56 (59%)	9 (29%)
- **Compliant with Association of Anaesthetists guideline**	28 (30%)	22 (71%)
Peri- and postoperatively		
- **Corticosteroid administration**	56 (60%)	9 (29%)
- **Compliant with Association of Anaesthetists guideline**	16 (17%)	11 (35%)*
Indication for corticosteroid		
Supplementation	80 (85%)	19 (61%)
Other*	6 (6%)	2 (6%)
Unknown	0	1 (3%)

*Some of those administered corticosteroids were for other indications, e.g. postoperative nausea and vomiting prophylaxis; these instances have been classified as guideline compliant.

Figure 1 Study flow diagram. Non-surgical procedures were identified using the American College of Surgeons definition (cardioversion, n = 3; peripherally inserted central catheter, n = 1) [15]. OPE, oral prednisolone equivalents.

Online Supporting Information

Appendix S1 – Peri-operative Replacement of Exogenous Steroids (PREdS) collaborators.

Appendix S2 – Example of paper case report form.