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RESEARCH ARTICLE

Colonoscopic polyp detection rate is stable throughout the workday including evening colonoscopy sessions [version 1; peer review: 2 approved]

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Abstract

Objective: Polyp detection rate (PDR) is an accepted measure of colonoscopy quality. Several factors may influence PDR including time of procedure and order of colonoscopy within a session. Our unit provides evening colonoscopy lists (6-9 pm). We examined whether colonoscopy performance declines in the evening.

Design: Data for all National Health Service (NHS) outpatient colonoscopies performed at Norfolk and Norwich University Hospital in 2011 were examined. Timing, demographics, indication and colonoscopy findings were recorded. Statistical analysis was performed using multivariate regression.

Results: Data from 2576 colonoscopies were included: 1163 (45.1%) in the morning, 1123 (43.6%) in the afternoon and 290 (11.3%) in the evening. Overall PDR was 40.80%. Males, increasing age and successful caecal intubation were all significantly associated with higher polyp detection. The indications 'faecal occult blood screening' (p<0.001) and 'polyp surveillance' (p<0.001) were strongly positively associated and 'anaemia' (p=0.01) was negatively associated with PDR. Following adjustment for covariates, there was no significant difference in PDR between sessions. With the morning as the reference value, the odds ratio for polyp detection in the afternoon and evening were 0.93 (95% CI = 0.72-1.18) and 1.15 (95%CI = 0.82-1.61) respectively. PDR was not affected by rank of colonoscopy within a list, sedation dose or trainee-involvement. **Conclusions:** Time of day did not affect polyp detection rate in clinical practice. Evening colonoscopy had equivalent efficacy and is an effective tool in meeting increasing demands for endoscopy. Standardisation was shown to have a considerable effect as demographics, indication and endoscopist varied substantially between sessions. Evening sessions were popular with a younger population

Keywords

Adenomas, cancer, endoscopy

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	Invited Reviewers		
	1	2	
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Open Peer Review

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Any reports and responses or comments on the article can be found at the end of the article.

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Competing interests: ILPB is Chair of the Trainee's Section of the Joint Advisory Group (JAG) Quality Assurance Working Group, on Endoscopy Training and Co-director of the Norwich Endoscopy Training Centre and is interested in the adoption of safe and effective endoscopy training and performance, and the application of formal validated assessment tools to assess competence and performance in endoscopy.

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Introduction

Colonoscopy is an important screening and surveillance tool. Much attention has focussed on optimising its effectiveness at diagnosing pre-malignant lesions. Polyp detection rate (PDR) or adenoma detection rate (ADR) can be used as markers for colonoscopy quality. The implication is that careful and optimal mucosal visualisation enhances polyp detection and is a reliable marker of a colonoscopist performing appropriately and effectively^{1,2}. Recent data have demonstrated the importance of adenoma detection rate as not only a metric of colonosocopy performance but as an independent predictor of protection against subsequent colorectal cancer³. PDR is defined as the detection of one or more polyps at colonoscopy. Several factors may influence PDR, obviously including patient selection and case mix, but recently it has been suggested that the time the procedure is performed and the order of colonoscopy within a session also influence colonoscopy performance.

Inconsistent results examining the PDR of colonoscopies throughout the workday have been reported. A number of studies have reported that PDRs decrease as the day^{4,5} or endoscopy list⁶ progress, and that PDRs in morning lists are higher than afternoon lists⁷. However this effect does not appear to be universal across endoscopy units with other studies reporting no such reduction in polyp detection overall⁸ or when colonoscopies are performed in half day blocks⁹ or 3-hour shifts¹⁰.

This effect, where shown, has been generally attributed to endoscopist fatigue^{4,11} although this was not independently assessed in those studies. This effect appears logical and correlates with increasing errors in other repetitive or tiring vocations such as errors by house officers related to time in hospital¹², inadvertent errors at simulated laparoscopy as mental and physical workload increases¹³ and impairment in perceptual and motor ability in nurses toward the end of nightshifts¹⁴. Queue position has been suggested as a novel surrogate measure for operator fatigue⁶. There has also been a suggestion that endoscopists may rush procedures later in the list¹⁵. Another possible hypothesis is that bowel preparation may be a factor, the inference being that bowel preparation is often prescribed appropriately for morning endoscopies but the regimen is not appropriately altered for optimum bowel preparation in the afternoon.

This apparent effect of reduced PDR throughout the work day has been superimposed on top of the difference in performance between endoscopists, which has been reported on multiple occasions; even within a group of fully competent endoscopists there appears to be spectrum of polyp detection rates^{3,16,17}. This endoscopist effect has not been consistently accounted for in the published data examining the effect of timing on PDR⁷.

The optimisation of colonoscopy will impact upon its safety and cost-effectiveness. Increasing numbers of endoscopies are being performed both in the UK¹⁸ and USA¹⁹, partly as a result of successful screening programmes¹⁸. This has led to higher patient flow though endoscopy units. To accommodate this increase in demand, units have had to expand their provision of colonoscopies by number of endoscopy rooms, length of lists or extra lists.

To accommodate this extra-workload, our unit has run regular evening lists (6–9pm) for over two years to meet this increasing demand and improve patient convenience and we are aware of other endoscopy units developing similar strategies. However it is not known whether evening colonoscopy is as effective as traditional day-time colonoscopy. As evening colonoscopy makes up a significant and increasing amount of our overall workload, it is important to establish that the service in terms of performance metrics is appropriate. It is also unknown whether colonoscopy performance declines in the evening; this specific effect, as opposed to morning or afternoon colonoscopy has not been examined in the previous studies. This study aims to review polyp detection rates in our routine clinical practice, with particular reference to this evening session. We aimed to test the hypothesis that polyp detection would be reduced in the evening sessions. The majority of evening colonoscopists will have already worked a full working day. Although not specifically assessed, they may be assumed to be more fatigued than those working in the morning or afternoon lists. We also aim to review PDRs in relation to other factors in routine clinical practice.

Methods

Endoscopy session data was collected retrospectively from the Hospital's booking system for all NHS outpatient colonoscopies booked for weekdays in the Norfolk and Norwich University Hospital in 2011. Endoscopy sessions were classified as: 'Morning' 08.00 to 12.00, 'Afternoon' 13.00 to 17.00 and evening 17.30 to 21.00 with colonoscopies usually afforded 30–45 minutes per slot. The times of colonoscopies were recorded; each colonoscopy was grouped by session (morning, afternoon, evening) and ranked by order within their session. Lists sometimes included other endoscopic procedures which were each assigned a value of 1 in the ranking. For example a colonoscopy performed after two oesophago-gastroduodenoscopies would be ranked number 3 in its session although it was the 1st colonoscopy. Private patients were excluded.

The Gastroenterology Endoscopy Unit at the Norfolk and Norwich University Hospital provides a full diagnostic and therapeutic endoscopy service to the local population and tertiary referral services in advanced colonoscopic polypectomy, small bowel enteroscopy, endoscopic ultrasound and upper GI endoscopic mucosal resection. The unit is multidisciplinary with colonoscopy performed by medical gastroenterologists, colorectal surgeons and independent nurse endoscopists, with patients booked to most procedures from a common waiting list, although the specific bowel cancer screening lists are only performed by 6 of the endoscopists. The majority of colonoscopy procedures are performed on colonoscopy-only lists, a smaller number are on mixed lists. It is usual practice for our endoscopists to only perform one colonoscopy session (morning, afternoon or evening) per day; in the relatively rare occurrence of an endoscopist providing two sessions within the same day, our usual policy is to have one as a predominantly gastroscopy session.

The unit is the regional endoscopic training centre and an accredited bowel cancer screening centre. The study was approved by and registered with the Audit and Clinical Governance Department at Norfolk and Norwich University Hospital, (project code 34810) the project was regarded as service evaluation and approval from a Research Ethics Committee was not required.

Computerised records were retrieved individually for each colonoscopy from the endoscopy reporting system, Scribes[®] (iSoft Health, Banbury UK). Patient demographics, indication, endoscopist, trainee-involvement and sedation information were recorded retrospectively along with information specific to the procedure itself, namely bowel prep quality, diagnosis and polyps detected.

Colonoscopy patients received 2 sachets of Picolax[®] (Sodium picosulfate with magnesium citrate, Ferring Pharmaceuticals Ltd, West Drayton UK) bowel preparation, 1 sachet at 6pm the day prior to procedure and 1 sachet at 6am on the day of procedure, for morning and afternoon endoscopies and at 6am and 2pm on the day of the procedure for evening colonoscopies. Quality of bowel prep was subjectively recorded as poor, satisfactory or good by the endoscopist at the time of the procedure. Throughout the study period Olympus-240 and -260 series video-endoscopes were used. Endoscopists recorded their findings themselves immediately after each procedure with polyps qualitatively described and site recorded as accurately as possible.

The indication for colonoscopy was recorded and later simplified into 6 categories for numerical analysis, such that each category contained had at least 10 colonoscopies in each of morning, afternoon and evening sessions and at least 50 procedures overall. Categories with fewer than this were grouped under 'other'. Thirty different endoscopists performed colonoscopies throughout the year. Those performing over 30 colonoscopies were treated as independent variables and those with fewer than 30 to their name were grouped under 'other' for analysis.

Sample size calculations were not formally performed as the intention was to review one year's colonoscopy practice; the final number of procedures included exceeds those calculated to be required by other similar studies⁸.

PDR was defined as the detection of one or more polyps at colonoscopy. Unadjusted PDRs were calculated and demographic information, indication and endoscopists assessed for each colonoscopy session. Due to the considerable variability in these factors between these sessions multivariate regression analysis was performed to adjust for differences. Stata[®] 12 (StataCorp LP, Texas USA) was used to perform multivariate regression analysis with the variables outlined in the results section below Results are expresses as adjusted odds ratio (OR) for polyp detection with 95% confidence intervals. Differences between groups were considered statistically significant if the "p" value was < 0.05.

Results

Data from 2576 colonoscopies were included: 1163 (45.1%) were performed in the morning, 1123 (43.6%) in the afternoon and 290 (11.3%) in the evening.

Mean age was lower in the evening sessions (58.2) compared to morning (64.7) and afternoon (62.3). Table 1 demonstrates the breakdown of demographic and endoscopic information between the three sessions. Trainee-involvement was higher in the evening (17.9%) and afternoon (14.6%) compared to the morning sessions (5.5%). Caecal intubation rates (uncorrected for bowel preparation and impassable strictures) were above 94% in each of the three sessions without any significant difference between sessions. Full data on all procedures included are included in the associated data files.

Unadjusted PDR in the morning, afternoon and evening session were 46.4%, 35.9% and 37.2% respectively.

Factors associated with polyp detection were assessed by multivariate logistic regression (Table 2). Male gender (odds ratio (OR) = 1.76, 95% confidence intervals (CI) 1.48 - 2.11, p<0.001), increasing age (OR = 1.04, 95%CI = 1.03 - 1.06, p<0.001) and successful caecal intubation (OR = 2.48, 95%CI = 1.53 - 4.01, p<0.001) were all significantly independently associated with higher polyp detection. The indications 'faecal occult blood (FOB) screening' (those subjects in the UK national bowel cancer screening programme) (p<0.001) and 'polyp surveillance' (p<0.001) were strongly positively associated and 'anaemia' (p=0.01) negatively associated with PDR. Subjectively 'Good' bowel preparation was significantly associated with a higher PDR as compared to 'Poor' bowel prep. As Table 1 demonstrates, a considerable proportion of the morning endoscopies were performed for FOB screening. Indeed 54.90% of all FOB screening colonoscopies at our unit were performed in the morning sessions. This correlates with the increased mean age in the morning session and high unadjusted PDR in the morning.

Following standardisation of covariates, there was no significant difference in PDR between sessions. With the morning as the reference value, the odds ratio for polyp detection in the afternoon and evening were 0.93 (95%CI = 0.72 - 1.18) and 1.15 (95%CI = 0.82 - 1.61) respectively. PDR was not shown to be affected by rank order of colonoscopy within a list (p=0.904), sedation type or trainee-involvement.

Dataset showing all procedures included in analysis of polyp detection study

2 Data Files

http://dx.doi.org/10.6084/m9.figshare.1016982

Discussion

Our data correlate with much larger cohorts that have purely analysed colonoscopic diagnoses without any reference to time of procedure in demonstrating a higher PDR in males than females and with increasing age^{20} . Overall, the PDR and caecal intubation rates are comparable to, and in fact slightly better, than those reported in the recent UK-wide audit of colonoscopy practice (which reported an uncorrected caecal intubation rate of 92.3% and polyp detection rate of $32.1\%)^{21}$. In our study PDR was significantly higher with complete caecal intubation demonstrating the validity of this as a performance metric of colonoscopy quality. When more of the colon is visualised, more polyps will be detected and it is also likely that the most skilled and careful colonoscopists are both more likely to complete a colonoscopy to the caecum and visualise the mucosal completely.

Our data do not support our original hypothesis that evening PDR might be lower than other sessions in the day. Our data suggest there is no significant difference in detection of polyps in either the evening compared to the morning, or based on an endoscopy's rank

Factor	Morning	Afternoon	Evening
	n = 1163 (45.1%)	n = 1123 (43.6%)	n = 290 (11.3%)
Age, mean (SD)	64.68 (10.05)	62.29 (12.68)	58.15 (14.02)
Female (%)	513 (44.1%)	515 (45.9%)	147 (50.7%)
Trainee-involvement (%)	64 (5.5%)	164 (14.6%)	52 (17.9%)
Indication			
Other	221 (19.0%)	310 (27.6%)	105 (36.2%)
Anaemia	82 (7.1%)	81 (7.2%)	74 (25.5%)
Family history	48 (4.1%)	71 (6.3%)	14 (4.8%)
FOB screening	627 (53.9%)	456 (40.6%)	59 (20.3%)
Surveillance	163 (14.0%)	158 (14.1%)	16 (5.5%)
Haematochezia	22 (1.9%)	47 (4.2%)	22 (7.6%)
Bowel prep			
Not recorded	2 (0.2%)	3 (0.3%)	0 (0.0%)
Poor	120 (10.3%)	64 (5.7%)	23 (7.9%)
Satisfactory	355 (30.5%)	131 (11.7%)	63 (1.7%)
Good	686 (59.0%)	925 (82.4%)	204 (70.3%)
Caecal intubation	1110 (95.4%)	1060 (94.4%)	275 (94.8%)
Any polyps detected (%)	540 (46.4%)	403 (35.9%)	108 (37.2%)

Table 1. Demographic, indication and endoscopic findings by colonoscopy session.

order within a session. This is contrary to some previous reports in the literature⁴⁻⁶. The reasons for this are unclear. Our unit aims to minimise pressures on endoscopists by allowing 30 minutes per colonoscopy (45 minutes for bowel cancer screening colonoscopy) and by strictly avoiding more than 5 colonoscopy procedures per endoscopy list. Also, as demonstrated by our large number of endoscopists (30 in this study), we believe our staff are less likely to fatigue. Endoscopy remains part of a varied working life for both physicians and surgeons within our hospital, rather than operators performing solely endoscopy. Equally apart from the bowel cancer screening specific lists, the majority of colonoscopy lists include a variety of patients with different indications. During the course of this study evening colonoscopy was performed by some consultant staff either working the evening as a planned session within their job plan or by other consultant staff or nurse endoscopists working and remunerated for extra sessions above their full job plan. Arguably the latter group may be more fatigued, but again our data show no deterioration of colonoscopy performance when this group was analysed separately.

We would therefore recommend evening colonoscopy sessions as a potential solution to safely and effectively meet increasing endoscopy demand. We feel it is important that any unit instigating evening colonoscopy carefully audits performance-metrics to ensure that colonoscopy performance is satisfactory in these later sessions. It may be that factors related to individual endoscopy units are important in explaining the differences in polyp detection reported in relation to endoscopy timings. The setting was an endoscopy training centre with an internal high priority on quality of endoscopy and well-established practices of governance, peerreview and teaching and it is possible these are drivers that help maintain PDR. Anecdotal evidence within our patient group suggests these sessions are popular with patients also. The evening sessions were popular with a considerably younger demographic (mean age 58.2) which may be assumed to represent more convenience for working individuals.

Our data suggest evening lists allowed a higher degree of traineeinvolvement. This may be due to ward or clinic commitments of trainees in the morning, indeed some registrars chose to stay later for evening colonoscopy lists, when they have no other distractions, in order to gain further experience and enhance their portfolio of procedures.

It is interesting to note that type of sedation made no difference to PDR, however, patient comfort or length of procedure was not measured (although ongoing audits separate to this study show low and appropriate pain scores and high patient satisfaction). A large Italian prospective study showed caecal intubation rates of only 81.6% of unsedated patients²², although data from the UK bowel cancer screening programme suggests that, as in the current study, colonoscopy without intravenous analgesia and/or sedation is not associated with impaired caecal intubation or adenoma detection²³. In our study it is also unknown whether a procedure was attempted without sedation and sedation later given (although in practice the later addition of sedation seems unusual).

One of the flaws in this dataset is the reliance on accurate documentation by endoscopists on each endoscopy report. Parts of their report, such as bowel preparation, are easily open to subjectivity. Equally, we used PDR as our performance metric: at present the information technology available is not suitable for readily determining the ADR, but we believe that the PDR is a useful surrogate Table 2. Multivariate regression outputs showing the odds ratio and 95% confidence intervals for the detection of 'any polyp' for each independent variable. Results expresses as adjusted odds ratio for detection of any polyp. CI, confidence interval: NS, not significant

Group	Variable	Odds Ratio	Lower 95%Cl	Upper 95%Cl	Р
Age	Age (per year)	1.04	1.03	1.06	< 0.01
Gender	Female	1.00			
	Male	1.76	1.48	2.11	< 0.01
Trainee-involvement	No trainee	1.00			
	Trainee involved	1.10	0.74	1.64	NS
Indication	Other	1.00			
	Anaemia	0.59	0.40	0.88	0.01
	Family history	0.86	0.52	1.42	NS
	Screening	2.19	1.58	3.03	< 0.01
	Polyp surveillance	2.15	1.58	2.94	< 0.01
	Haematochezia	1.87	1.14	3.07	0.01
Bowel prep quality	Poor	1.00			
	Satisfactory	1.41	0.97	2.06	NS
	Good	1.46	1.03	2.07	NS
Sedation	Nil	1.00			
	Pethidine & Midazolam	1.12	0.85	1.48	NS
	Entonox only	1.10	0.70	1.73	NS
	Pethidine & Midazolam & Entonox	1.28	0.55	2.94	NS
	Other	2.78	0.91	8.48	NS
Caecal Intubation	No	1.00			
	Yes	2.47	1.53	4.00	< 0.01
Session	AM	1.00			
	PM	0.93	0.72	1.19	NS
	Evening	1.15	0.82	1.61	NS
Endoscopist with regular evening session in job plan	AM	1.00			
	PM	0.92	0.69	1.45	NS
	Evening	1.19	0.77	1.69	NS
Endoscopist performing evening lists above job plan	AM	1.00			
	PM	0.96	0.73	1.34	NS
	Evening	1.11	0.80	1.70	NS

marker of the care taken during colonoscopy and has the advantage that this can be readily compared to other large datasets such as the UK colonoscopy audit²¹. That the PDR was higher when bowel preparation was recorded as 'good' compared to 'poor' (OR=1.46, 95%CI = 1.03-2.07) may indeed reflect this subjectivity when endoscopists blame the quality of images for the inability to visualise any polyps.

Although it was not a primary outcome measure, we noted that the proportion of colonoscopies recorded as having 'good' bowel preparation was much higher in the afternoon (82.4%) compared to the morning (59.0%) sessions. We had not assessed patients' adherence to laxative dosing protocols but if adherence were equivalent this may suggest the protocols we use require adjustment. Previous recommendations have proposed split-dose bowel preparation as the standard of care²⁴, which we adhered to.

A validated bowel preparation scale used prospectively may improve the reliability of these data and it is recommended that this be included in future evaluations.

Other limitations of this study are inherent within its design. It was retrospective, without any randomisation to different sessions. The external generalizability of the data may also be questioned although we believe we have a balanced workforce of medical, surgical and specialist-nurse endoscopists that is fairly representative of a modern UK NHS unit. We did not record data on withdrawal time on the non-bowel cancer screening colonoscopies. This would have been useful in comparing these data to other datasets which provide this information.

In conclusion, this study shows that the detection of polyps at colonoscopy is independent of the time of day that the procedure is performed. Specifically, evening colonoscopy is no less effective at detecting polyps than morning colonoscopy. We attribute this consistency to appropriate colonoscopy scheduling and an interested, engaged workforce with varied working patterns, both of which could be directly tested in prospective studies. Evening colonoscopy is a suitable initiative to increase procedure numbers but we recommend continued governance of performance metrics to ensure that timing of procedures does not adversely influence outcomes.

Data availability

figshare: Dataset showing all procedures included in analysis of polyp detection study, http://dx.doi.org/10.6084/m9.figshare.1016982²⁵

Author contributions

DT and ILPB jointly conceived the study. DT, MP, JT, IM, CS collectively designed the study, performed the data collection and jointly analysed the data. DT wrote the original draft of the manuscript and ILPB revised and wrote the final draft and is the guarantor of the paper. All authors agree with the final draft.

Competing interests

ILPB is Chair of the Trainee's Section of the Joint Advisory Group (JAG) Quality Assurance Working Group, on Endoscopy Training and Co-director of the Norwich Endoscopy Training Centre and is interested in the adoption of safe and effective endoscopy training and performance, and the application of formal validated assessment tools to assess competence and performance in endoscopy.

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The authors describe the practice of performing colonoscopy during an evening session. With increasing demand on endoscopic services in the UK the move towards 7 day & 3 lists per day working will become more commonplace. Given the concerns about deterioration in performance it is important to know that the quality of the procedure is not affected by when the procedure is performed.

The authors describe the polyp detection rate, a marker of quality of colonoscopy, in a retrospective dataset gathered from their hospital records. The data are used to construct a model which predicts changes in PDR.

The data suggests that the quality of colonoscopy is maintained in evening sessions. This provides evidence supporting this evolving change of practice that will provide units with the assurances that this change in work pattern is a viable option. The paper is therefore useful and timely.

One possible confounder that the authors do not describe is the number of colonoscopists that perform evening endoscopies - if it is just a few enthusiasts then they may be more vigilant, compared with the daytime regular endoscopists. It would be useful to know that the proportion of procedures performed by each endoscopist was the same throughout the 3 sessions as any differences may be due to the technical skills of these endoscopists.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response (*F1000Research Advisory Board Member*) 07 Aug 2014 Ian Beales, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK

We thank the reviewer for his very pertinent comments. We entirely agree that colonoscopist enthusiasm and interest are important variables that could influence polyp detection rates in evening sessions. All the relevant data are contained in the data file, but in total 26 different colonoscopists did at least one evening colonoscopy but in fact only 10 colonoscopists performed more than 10 evening procedures in the study period. So it is possible that this is a self-selecting group of more vigilant colonoscopists and indeed our data may not be more generalisable if fixed evening endoscopy becomes a routine part of most endoscopists' job plans and on the volunteer basis that we currently utilise.

We agree that the ideal analysis would be to examine the variability of polyp-detection for each endoscopist individually through all 3 sessions of the day. At present, it is not possible to draw any reliable conclusions from these data as the numbers in each subgroup are small. As might be expected from working practices in the United Kingdom NHS, where endoscopy (including gastroscopy, colonoscopy and often ERCP) generally fits into a working pattern with inpatient and outpatient work, very few of our endoscopists performed an even distribution of colonoscopy throughout all 3 sessions. In fact only two of the colonoscopists performed more than 40 procedures in each of the 3 sessions: their crude polyp detection rates, uncorrected for case mix, were 28%, 23%, 38% and 59%, 44% 59% in morning, afternoon and evening respectively.

We are continuing to collect data on this important area and hope that a larger cohort (or combination of data, possibly using the data accessibility inherent with *F1000Research* publications) will enable analyses with sufficient power to examine this further.

We agree with the reviewer that the individual technical skill and interest of the colonoscopist is possibly the most important variable, but do not feel this alters our overall conclusion that evening colonoscopy is both feasible and effective. We feel it is important to stress that ongoing quality assurance for performance metrics (including polyp detection) is essential and that time of day should be assessed in such assessments.

Competing Interests: No competeing interests.

Reviewer Report 19 June 2014

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Adam Haycock

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This paper is timely and addresses a problem that will be of increasing importance as units struggle to meet waiting time targets. This is the first paper as far as I am aware to look at the quality of colonoscopy done on evening lists, although there is literature supporting evidence of fatigue for colonoscopy elsewhere.

The paper is well written, with clear title, methodology, statistics, results and discussion, including limitations. I have no additions or amendments to suggest.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response (*F1000Research Advisory Board Member*) 07 Aug 2014 Ian Beales, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK

Thank you for the reviewer's comments.

Competing Interests: No competeing interests.

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