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Has the Two Week Rule improved cancer detection rates for gastrointestinal cancers? A systematic literature review

Dr Kymberley Thorne*¹, Dr Hayley A. Hutchings¹ and Prof Glyn Elwyn²

1 Centre for Health Information, Research & Evaluation, College of Medicine, Swansea University, Swansea, UK

2 Department of Primary Care and Public Health, Cardiff University, Cardiff, UK

*Corresponding author: Biobank Suite, Room 251, Grove Building, College of Medicine, Swansea University, Swansea, SA2 8PP, UK; E-mail: k.thorne@swansea.ac.uk; Tel: +44 (0)1792 606372

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Abstract:

Introduction: The UK government introduced the two-week rule (TWR) to improve the diagnosis and treatment of gastrointestinal (GI) cancers. This updated review systematically identifies new articles since 2009 and presents an overview of the previous and new findings combined for both upper GI cancer (UGCs) and colorectal cancers (CRCs).

Methods: We analysed all peer-reviewed articles and conference abstracts with GI cancer detection rates following TWR referral and/or the proportion of TWR-referred GI cancers from the total number diagnosed during the study period. We reported average cancer detection rates and split the data according to four time periods to determine whether TWR effectiveness improved over time.

Results: The average cancer detection rate by the TWR for all studies was 11.6% for CRC and 8.3% for UGC. We found a decrease in cancer detection rates over time for CRC from 14.4% in 2000-2002 to 7.2% in 2009-2012. However, UGC detection rates increased over time from 8.5% in 2000-2002 to 11.4% in 2005-2008. We found that on average, 30.8% of CRCs and 28.8% of UGCs were detected following referrals using the TWR system and that these proportions had increased over time from 30.6% to 38.4% for CRC and from 26.8% to 52% for UGC.

Conclusion: The TWR is not still sufficiently effective in diagnosing GI cancers in patients, suggesting that the referral guidelines need to be improved. Our findings do suggest that the TWR is being used more frequently than alternative routes.

BACKGROUND

The Two-Week Rule (TWR) referral (1) was implemented by the UK's New Labour government in 2000 to reduce the number of cancer-related deaths by 20% in people under the age of 75 years by 2010, thereby saving approximately 130,000 lives (2). The TWR was designed to decrease the time taken from General Practitioner (GP) appointment to the diagnosis of a potential cancer to a maximum of two weeks. In the case of gastrointestinal (GI) cancers, guidelines (3, 4) were issued to advise GPs on the key symptoms required to make a patient eligible for the TWR so as not to overload the system with unnecessary referrals but to ensure an increase in early cancer detection rates. The TWR referral from the GP would result in the fast tracking of a patient for an upper or lower GI endoscopy to diagnose any cancers in the GI tract as quickly as possible, significantly improving the health outcome of patients with a subsequently confirmed cancer.

We have previously reviewed the literature up to 2009 (5, 6), although these reviews did not cover a sufficiently long period to determine the true impact of the TWR. The aim of this review was to update the data available to determine whether the TWR has improved cancer detection rates in the last decade for upper GI cancers (UGCs) and colorectal cancers (CRCs).

METHODS

A literature search was performed using Pubmed and the Cochrane Library employing a text search for peer-reviewed research articles. The search terms used were "colorectal", "CRC", "upper gastroint*", "upper GI", "gastrointestinal", "oesophageal" and "gastric" in combination with "urgent referral*", "two week*", "2-week*", "fourteen day*" and "fast track". In addition to this, peer-reviewed abstracts presented at the British Society of Gastroenterology conferences and Association of Coloproctology of Great Britain and Ireland Annual Meetings since 2000 were hand-searched to locate suitable abstracts for inclusion. Finally, a secondary literature search of all bibliographies was done.

Only peer-reviewed studies commenting on the effectiveness of the TWR in diagnosing GI cancers were selected. Studies performed in non-NHS organisations were excluded. Data describing the TWR GI cancer detection rate and the proportion of GI cancer patients diagnosed using the TWR identified were extracted and split according to cancer type (UGC or CRC).

Data were extracted into the following four outcomes for analysis: Number of TWR referrals received; number of cancers diagnosed from those TWR referrals; TWR cancer detection rate; and the proportion of all cancers diagnosed that were referred by the TWR.

Data were also allocated into one of four sets of three-year time periods according to the study start and end dates to determine whether cancer detection rates had improved over time: Jan 2000 and Dec 2002 (Group 1); Jan 2003 and Dec 2005 (Group 2); Jan 2006 to Dec 2008 (Group 3) and Jan

2009 to Dec 2012 (Group 4). Those studies with no start and end dates reported were allocated into a time period which was a minimum of 12 months prior to their publication date.

RESULTS

After critically appraising all articles and abstracts found in the literature search, there were 57 research articles and peer-reviewed abstracts with comparable data on CRCs (see Table 1) and 26 with comparable data on UGCs (see Table 2).

Colorectal Cancers

When combining the data from all articles we found that of the 28,858 patients with a suspected CRC referred by their GP using the TWR, only 2,940 (10.2%) were subsequently diagnosed with CRC. The lowest rate was 4.4% (7) and the highest rate was 43% (8). The average cancer detection rate for 49 studies reporting these data was 11.6%.

When we split the data according to when the studies were conducted, we found that the average cancer detection rate for each time frame was: 14.4% for 25 Group 1 studies; 9.4% for 12 Group 2 studies; 9.1% for 6 Group 3 studies; and 7.2% for the 6 Group 4 studies.

We found that on average, 30.8% of CRCs were detected following referral using the TWR as opposed to alternative methods such as routine referrals and emergency referrals. When we split the data according to when the studies were conducted, we found that the average proportion of CRCs detected using the TWR for each time frame was: 30.6% for 19 Group 1 studies; 29.1% for 14 Group 2 studies; 43% for the single Group 3 study; and 38.4% for the 2 Group 4 studies.

Upper GI Cancers

When combining the data from all articles we found that of the 10,001 patients with a suspected UGC referred by their GP using the TWR, only 692 (6.9%) were subsequently diagnosed with UGC. The lowest rate was 2.1% (9) and the highest rate was 24.8% (10). The average cancer detection rate for the 26 studies reporting these data was 8.3%.

When we split the data according to when the studies were conducted, we found that the average cancer detection rate for each time frame was: 8.5% for 17 Group 1 studies; 6.2% for 6 Group 2 studies; and 11.4% for 3 Group 3 studies. No Group 4 studies were retrieved.

We found that on average, 28.8% of UGCs detected following referral using the TWR as opposed to alternative methods such as routine referrals and emergency referrals. When we split the data according to when the studies were conducted, we found that the average proportion of UGCs

detected using the TWR for each time frame was: 26.8% for 10 Group 1 studies; 24.4% for 6 Group 2 studies; and 52% for 2 Group 3 studies. No Group 4 studies were retrieved.

DISCUSSION

For each type of GI cancer, the average cancer detection rate by the TWR was still extremely low (11.6% for CRC and 8.3% for UGC). We found a decrease in cancer detection rates over time for CRC from 14.4% in studies starting between 2000-2002 to 7.2% in studies starting between 2009-2012. However, UGC detection rates increased over time from 8.5% in studies starting between 2000-2002 to 11.4% for studies starting between 2005-2008. We found that on average, 30.8% of CRCs and 28.8% of UGCs were detected following referrals using the TWR system and that these proportions had increased over time for both cancer types.

This paper reviewed all relevant peer-reviewed evidence from studies reporting on the impact of the TWR on NHS services. All datasets have been included from all eligible studies for analysis, making this review as comprehensive as possible. However, there were a limited amount of peer reviewed research articles in this field, so we opted to include peer-reviewed abstracts presented at major conferences since 2000. In doing so we identified a total of 84 peer-reviewed publications meeting our inclusion criteria and containing comparable, eligible datasets, some for multiple time periods or for both GI cancers.

There were far fewer sources of information on TWR effectiveness for latter study periods compared with the years following implementation of the TWR in 2000. For this reason, data for Groups 3 and 4 were limited and any averages were likely to be representative of a small sample size.

The low cancer detection rates for CRCs and UGCs following a TWR referral at all intervals suggests that the guidelines were not effective at implementation and are still not effective in recent years, although the low sample size in latter time periods offer a less reliable picture of TWR effectiveness. A recent study called for an evidence-based approach to the referral criteria for suspected CRC (11) as existing guidelines are not sensitive or specific enough to identify suspected GI cancers without flooding the TWR pathway. For example, there is evidence that the age threshold should be lowered (12). It is also possible that GPs are still inappropriately referring patients using the TWR, although most hospitals have implemented a triaging system as part of the TWR pathway to screen patients prior to an endoscopy. Referral proformas have also been proven to improve guideline compliance, resulting in higher cancer detection rates (13).

This review reports an increase in the proportion of cancers being detected following a TWR referral as opposed to other routes such as emergency and routine referrals indicating that of those referred, more are being done so correctly via the TWR. It is possible that patients are presenting to their GP with the key symptoms requiring a TWR referral rather than having later stage symptoms which end

up being emergency referrals. This could be attributed to more prominent health campaigns and increased patient awareness of GI cancer.

The TWR has placed a significant burden on the resources of most gastroenterology services in the NHS with little gain in identifying malignancies (14). Most hospitals have a dedicated TWR referral list to ensure their Trust meets the strict two-week target. This should, in theory, have a negative impact on all other aspects of the service, although little evidence of this has been found to date. Three studies reported a decline in the routine endoscopy waiting lists following the introduction of the TWR (7, 15, 16), possibly due to an increased awareness of the guidelines for patient referrals, the more efficient organisation of services or the introduction of nurse endoscopists to cope with increased demand.

What little evidence exists on the short and long term effect of the TWR suggests no significant benefits in survival for CRC (17-21). This is most likely because those identified via the TWR present to their GP with classic symptoms of GI cancers which, whilst making them eligible for fast tracking and a reduced time to diagnosis and treatment, also mean that they are likely to be in the later, less treatable stages of the disease.

To summarise, we have strong evidence of consistently low GI cancer detection rates and even though more cancer patients are being referred via the TWR, many studies are reporting no difference in survival compared with those diagnosed using alternative routes. The findings suggest that there is a need to consider revising or replacing the TWR as in its current state, as there appears to be limited health benefits to be gained by patients

CONCLUSION

The findings of this review suggest that after more than 10 years, the TWR still has low cancer detection rates for both CRCs and UGCs. An update to the guidelines for GPs may be necessary to better screen patients and increase cancer detection rates, whilst patients should be continuously encouraged to visit their GP with any worrying symptoms so that cancers can be detected and treated earlier.

Table 1. Studies retrieved with TWR data for CRC, ordered alphabetically.

Author (ref)	Time period	No. TWR referrals	No. CRCs detected	CRC detection rate (%)	% CRCs diagnosed via TWR	Start period assigned
Adeosun (22)	Not stated	319	29	9.1	20.5	1
Aljarabah (23)	Apr-Sept 06	217	22	10.1	-	3
Allgar (24)	Jan-01 to Dec-02	632	51	8.1	21.3	1
Anderson (25)	Jan-02 to Dec-05	978	78	8.0	-	2
Aryal (26)	Not stated	-	-	-	35	1
Ballal (27)	Not stated	508	57	11	-	1
Barrett (8)	Jan-Dec 02	-	-	43	27.9	1
Barwick (28)	Jan-Aug 01	144	14	9.7	-	1
Baughan (29)	Jan-Jul 2008	3370	452	13.4	-	3
Bennis (30)	Aug-02 to Jul-03	388	164	42.3	-	1
Bevis (31)	Oct-02 to Sept-04	-	97	-	50.2	2
Bhangu (32)	Jan-06 to Jul-09	1725	108	6.3	-	3
Boulton-Jones (33)	Not stated	394	46	11.7	37.4	1
Chandran (34)	Jan to Dec 01	275	48	17.4	29.9	1
	Jan to Dec 02	-	-	-	29.9	1
	Jan to Dec 03	-	-	-	33.9	2
	Jan to Dec 04	470	62	13.1	32.6	2
Chaudhri (35)	Not stated	243	115	6.2	-	1
Chohan (36)	Jul-00 to Dec-01	462	64	13.9	32.8	1
Currie (21)	Jan-00 to Dec-05	-	-	-	41	1
Davies (37)	Nov-99 to Oct-02	2294	257	11.2	40.5	1
Debnath (38)	Aug-00 to Jul-01	237	21	8.9	21.9	1
Eccersley (39)	Jun-00 to May-01	173	26	15	17.9	1
El-Himadie (40)	Jan-Dec 05	482	49	10.2	-	2
	Jan-Dec 10	915	66	7.2	-	4
Flashman (41)	Jul-00 to Jun-01	758	65	8.6	26.1	1
Foster (42)	Oct-00 to Sept-01	147	10	6.8	9.5	1
Foster (43)	Not stated	-	-	-	8	1
Gandy (44)	Jun-00 to Nov-01	543	73	13.4	-	1
Glancy (45)	Aug-00 to Nov 01	326	32	9.8	-	1
John (46)	Apr-04 to Mar-05	534	60	11.2	34.3	2
John (47)	Not stated	-	-	-	43	3
Leung (48)	Not stated	1100	81	7.3	37	4
Linn (49)	Jan-Jun 06	381	27	7.1	-	3
MacDonald (50)	Not stated	50	6	12	-	1
Maruthachalam (51)	Jan-Dec 03	188	19	10.1	-	2
Marsden (52)	May-03 to Oct-04	-	-	-	12	2
Maruthachalam (53)	Mar-04 to Jun-05	96	9	9.4	-	2
Moreea (54)	Not stated	25	4	16	-	1
Padwick (11)	Jan-Dec 10	940	50	5.3	39.7	4
Peacock (55)	Feb-Apr 2012	544	32	6	-	4
Rai (56)	Not stated	1000	100	10	25	2

	Not stated	222	14	6	15.9	2
Rao (7)	Jun-Dec 03	319	14	4.4	25.9	2
Schneider (20)	Oct-02 to Sept-04	-	-	-	51	2
Scott (57)	Not stated	-	-	-	10.6	2
Shabbir* (12)	Jan-01 to Dec-05	-	9	-	24	2
Shaw (58)	Sept-05 to Sept-06	204	12	5.9	-	3
Shenderey (59)	Jan-Dec 03	-	-	-	28.9	2
Sidhu (60)	Jan-Jun 03	122	13	10.7	26.5	2
Smith (61)	Jan-02 to Dec-04	2748	174	6.3	36.4	2
Spencer (62)	Jul-Dec 2000	243	36	14.8	-	1
Stoker (63)	Not stated	151	18	11.9	-	1
Stone (10)	Jan-Sept 00	264	37	14	-	1
Taylor (64)	Jan-Dec 01	-	-	17.4	-	1
	Jan-Aug 04	-	-	12.9	-	2
Trickett (65)	Nov-00 to Oct-01	-	30	-	20.4	1
Vaughan-Shaw (66) *	Jul-07 to Jul-11	2735	214	7.8	-	4
Vaughan-Shaw (67)	Dec-11 to Jun-12	397	37	9.3	-	4
Vieten (68)	Mar-00 to Dec-01	420	51	12.1	37	1
Vijayan (69)	Not stated	102	12	12	-	3
Walsh (16)	Aug-Oct 00	73	11	15.1	47.8	1
Zafar (17)	Jan-Dec 02	-	-	-	77	1

NOTES:

Start period was coded (1=2000-2; 2=2003-5; 3=2006-8; 4=2009-12). Where no date was available, the authors checked the submission date for the article and selected the code which was ~12 months prior to that date.

* Patients aged <50y only

**Includes repeat referrals

Table 2. Studies retrieved with UGC detection rates via TWR, ordered alphabetically.

Author (ref)	Time period	No. TWR referrals	No. UGCs detected	UGC detection rate (%)	% UGCs diagnosed via TWR	Start period assigned
Aung (70)	Sept-00 to Dec-01	307	29	9.4	27.6	1
Barbour (71)	Oct-01 to Mar-02	172	17	9.9	48.6	1
Baughan (29)	Jan-Jul 08	1844	207	11.2	-	3
Boulton-Jones (33)	Not stated	280	27	9.6	35.5	1
Cairns (72)	Jan-02 to Mar-04	-	-	-	55	1
Carty (9)	Jan-01 to Dec-01	191	4	2.1	25	1
Dewar (73)	Jan-04 to Dec-04	321	12	3.7	16	2
Gera (74)	Jan-02 to Dec-02	157	6	3.8	10.5	2
	Jan-04 to Aug-04	175	16	9.1	51.6	2
	Jan-05 to Dec-05	261	24	9.2	38.7	2
Irving (75)	Apr-0- to Apr-08	295	34	11.5	64.2	3
Kapoor (76)	Jul-00 to Feb-02	1852	70	3.8	-	1
	Mar-02 to Feb-03	1785	52	2.9	-	1
Lassman (77)	Not stated	79	12	15.2	-	1
Loehry (78)	Apr-01 to Sept-01	79	3	3.8	-	1
Mahmood (79)	Not stated	45	2	4.4	-	1
Mohammed (80)	Nov-99 to Dec-01	-	16	-	11.1	1
Moran (81)	Jan-03 to Dec-03	356	18	5.1	14.5	2
Ng (82)	Oct-03 to Mar-04	125	8	6.4	15.1	2
Patel (83)	Apr-06 to Oct-07	345	36	11.4		3
Radbourne (84)	Jul-00 to Dec-01	153	16	10.5	14.7	1
Reilly (85)	Aug-00 to Jul-01	79	8	10.1	26.7	1
Sharpe (19)	Jan-06 to Dec-07	-	135	-	39.7	3
Spahos (15)	Sept-00 to Aug-02	623	38	6.1	15.4	1
Spencer (62)	Jul-Dec 00	222	28	12.6	-	1
Stoker (63)	Not stated	112	7	6.3	-	1
Stone (10)	Jan-Sept 00	105	26	24.8	-	1
Subramanian (86)	Jul-00 to Aug-01	199	11	5.5	-	1
Warner (87)	Not stated	146	10	6.8	8.7	1

NOTES:

Start period was coded (1=2000-2; 2=2003-5; 3=2006-8; 4=2009-12). Where no date was available, the authors checked the submission date for the article and selected the code which was ~12 months prior to that date.

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