

Supplementary File 4 Quality assessment of included full-text publications

Author	Country	Study design, as described in the article	Retrospective or prospective, as described in the article	In case of a case-control study, were groups similar at outset of the study by prognostic factors?	Was the intervention used appropriately?	Were the outcome measures reliable?	Were the outcome measures valid?	Was statistical analysis conducted appropriately?	Was quality of reporting appropriate?	Can the study results be generalized to routine practice?	Comments (based on the authors viewpoint in the individual articles)
Kesavadev et al. 2015 [52]	India	cohort	prospective	NA	yes	yes	yes	yes	yes	yes	- Single center study - Open label, non-comparative design are the limitations - Variety of co-prescriptions given to patients
Thomsen et al. 2015 [45]	Denmark	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	HbA1c measurements within the right timeframe were available only for two-thirds of eligible patients
Mezquita-Raya et al. 2015 [57]	Spain	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	Large and representative sample size compared to other retrospective observational studies
Buysschaert et al. 2015 [29]	Belgium	cohort	prospective	yes	yes	yes	yes	yes	yes	yes	Large sample size of study sample compared to other retrospective observational studies
Nyeland et al. 2015 [58]	UK	cohort	retrospective	yes	yes	yes	yes	yes	yes	yes	- Patients included may not be fully representative of all patients, as not all the patients attending the National Health Service are included. - Inability to track actual medication fills, as the prescription information highlights those prescriptions written by the participating physician. - Depending on the standards of the physician practice, tests and assessments (e.g. HbA1c, weight, BMI, etc.) or interventions may not be conducted routinely and/or be

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											conducted but not recorded.
Cotugno et al. 2015 [31]	Italy	cohort	retrospective	yes	yes	yes	yes	yes	yes	yes	Limited sample size, and only a single-center experience – thus limited generalizability
Russo et al. 2015 [44]	Italy	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	- Low sample size - Applicable to outpatient setting - Lack of information on changes in diet or physical activity
Kondo et al. 2015 [55]	Italy	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	- Small sample size - Short-term follow-up
Zavattaro et al. 2015 [47]	Italy	cohort	prospective	NA	yes	yes	yes	yes	yes	not clear	- Patients with renal impairment - Limited generalizability to the background T2DM population - Small sample size
Bashier et al. 2015 [48]	UAE	cohort	prospective	NA	yes	yes	yes	yes	yes	not clear	- High statistical power (95%) - Generalizability to other geographical areas may be affected if there are lifestyle peculiarities in the Arab population
Jinnouchi et al. 2015 [66]	Japan	cohort	prospective	NA	yes	yes	yes	yes	yes	not clear	- Small number of patients - Short-term intervention - Selection bias may be present
Lapolla et al. 2015 [39]	Italy	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	- Large number of patients - Good generalizability to real-world practice
Chiefari et al. 2015 [30]	Italy	cohort	retrospective	yes	yes	yes	yes	yes	yes	yes	- Large population size - Study groups were balanced with respect to the baseline variables that were measured - Patients were similarly assessed during the follow-up period, to minimize

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											potential interfering factors
Buysman et al. 2015 [28]	USA	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	- Based on claims data - Can be generalized to patients on therapies in stable managed care settings receiving frequent care from their providers - No information on baseline characteristics
Ghuman et al. 2015 [37]	UAE	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	- Small sample size of subgroups - Specific to Emirates patients
Rigato et al. 2015 [43]	Italy	cohort	retrospective	yes	yes	yes	yes	yes	yes	no	- Selection bias - Limited sample size - Subjective eligibility criteria
Gomez-Peralta et al. 2015 [65]	Spain	cohort	retrospective	yes	yes	yes	yes	yes	yes	no	- Study done in obese patients with T2DM to assess excessive daytime sleepiness - Good generalizability - No interventions or new procedures other than physician daily routine was conducted
Gautier et al. 2015 [78]	France	cohort	prospective	NA	yes	yes	yes	yes	yes	yes	- To minimize the limitations associated with the design of an observational study, physicians were chosen at random from a large sample and the number of patients recruited by each physician was limited to prevent a cluster effect. - All contact between the sites and the sponsor went through the research organization to avoid bias in the delivery of routine care.

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											- Quality control applied to each step of handling data, specifically safety. - Good generalizability
Díaz-Soto et al. 2014 [64]	Spain	cohort	prospective	NA	yes	yes	yes	yes	yes	no	- Small sample size - Short term follow-up
Li et al. 2014 [56]	USA	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	- Based on administrative claims data - Specific criteria for inclusion compared to real-world settings
DeKoven et al. 2014 [50]	USA	cohort	retrospective	yes	yes	yes	yes	yes	yes	yes	- Patients that had evidence of insulin use in either the pre- or post-index periods and cohorts were limited to consist of patients being persistent on their index therapy for a 6-month post-index period - Good generalizability
Toyoda et al. 2014 [61]	Japan	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	- Moderate sample size - Generalizability to Japanese patients due to approved dosage in Japan which is different from that in the US and EU
Heymann et al. 2014 [51]	Israel	cohort	retrospective	NA	not clear	yes	yes	yes	yes	yes	- Treatment was assessed by evaluating drug purchases obtained from pharmacies; authors could not assess the dose that patients were actually taking - Large sample size - Limited exclusion criteria increase the robustness of the findings and potentially improve generalizability of liraglutide effect to the broader population - Well-established electronic medical

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											record, automatic data capture and use of one central laboratory increase the confidence in this database.
Inoue et al. 2014 [38]	Japan	cohort	prospective	NA	yes	yes	yes	yes	no	no	• Small sample size • Generalizability to Japanese patients due to approved dosage in Japan which is different from that in the US and EU
Chitnis et al. 2014 [49]	USA	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	• Laboratory and clinical measures at 6-month follow-up were unavailable for many patients • Analyses did not adjust for potential confounding by measured and unmeasured factors • Statistical power: 40–50%; except weight (90%)
Kaur et al. 2014 [67]	India	cohort	prospective	NA	yes	yes	yes	yes	yes	no	• Narrow eligibility criteria • Short follow-up period
Evans et al. 2014 [33]	UK	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	• Treatments initiated according to NICE recommendations • Good level of generalizability to routine clinical practice
Vitagliano et al. 2014 [46]	Italy	cohort	retrospective	NA	NA	yes	yes	yes	yes	yes	• Small sample size
Rizzo et al. 2014 [59]	Italy	cohort	prospective	cohort	NA	yes	yes	yes	yes	no	• No control for important covariates such as HbA1c, BMI, and duration of diabetes due to lack of available data
Thong et al. 2014 [60]	UK	cohort	prospective	no	yes	yes	yes	yes	yes	no	• Small sample size • Generalizability limited to outpatient setting in the UK

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Usui et al. 2013 [70]	Japan	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	• Small sample size • Single center experience • Generalizability limited to Japanese patients due to approved dosage in Japan which is different from that in the US and EU
Mulligan et al. 2013 (34)	UK	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	• Absence of a fixed timeline for the first visit; single-center • Varied usage of concomitant medications which changed during the course of the study
Kondo et al. 2013 [54]	Italy	cohort	retrospective	NA	yes	yes	yes	yes	not clear	No	• Limited generalizability due to low sample size • Patients with low BMI compared to Western countries
Evans et al. 2013 [32]	UK	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	• Treatments initiated according to NICE recommendations • Good level of generalizability to UK routine clinical practice
Funch et al. 2013 [35]	USA	cohort	prospective	NA	no	yes	yes	yes	yes	no	• Intervention: Patient attributes may impact the choice of specific therapy. For example, latent pancreatic cancer may affect glycemic control and result in the initiation of newer antidiabetic therapies, including liraglutide. • Confounding variables not addressed between intervention and comparator group • Follow-up duration was short to assess the risk of pancreatitis associated with liraglutide

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											Generalizability limited as the findings are from an interim analysis
Ahern et al. 2013 [63]	UK	cohort	prospective	NA	yes	yes	yes	yes	yes	no	Sample size too small
Ponzani et al. 2013 [42]	Italy	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	Limited sample size, thus limited generalizability to clinical practice
Perušičová et al. 2013 [41]	Czech Republic	cohort	retrospective	NA	yes	yes	yes	yes	yes	yes	- Missing data at follow-up - Good generalizability to clinical practice
Fadini et al. 2013 [34]	Italy	cohort	prospective	NA	yes	yes	yes	yes	yes	no	- Good generalizability but restricted to outpatient setting - Residual biases or unmeasured variables artificially affect the results - Sample size was relatively small and subgrouping of patients might lead to a critical reduction in statistical power to detect significant differences
Ohki et al. 2012 [40]	Japan	cohort	retrospective	yes	yes	yes	yes	yes	yes	yes	Median dosing period of MET was not uniform within the three study groups
Kesavadev et al. 2012 [53]	India	cohort	prospective	yes	yes	yes	yes	yes	yes	no	- Single-center study - Very small sample size - Open label, and non-comparative design
Varanasi et al. 2012 [62]	India	cohort	retrospective	NA	yes	yes	yes	yes	yes	no	- Small sample size - Generalizability limited to the Indian population
Mori et al. 2011 [68]	Japan	cohort	prospective	NA	yes	yes	yes	yes	yes	no	- Pilot study - Small sample size

NA=not available; MET=metformin; HbA1c=glycated hemoglobin; BMI=body mass index; NICE= The National Institute for Health and Care Excellence